“Lost in Trauma: Post-Traumatic Stress Disorder, spatial processing and the Brain- Derived Neurotrophic Factor gene.”

Jessica Katherine Miller

A thesis submitted in partial fulfilment of the requirements of Bournemouth University for the degree of Doctor of Philosophy

June 2016

COPYRIGHT STATEMENT

This copy of the thesis has been supplied on condition that anyone who consults it is understood to recognise that its copyright rests with its author and due acknowledgement must always be made of the use of any material contained in, or derived from, this thesis.

ABSTRACT

This study enquired into a puzzling feature of Post-Traumatic Stress Disorder (PTSD); a loss of wayfinding ability (Osofsky et al., 2010; Ehringa et al., 2006; Lubit et al., 2003; Kowitz, 2011; Adler et al., 2009; Handley et al., 2009; Butler et al., 1999). Previous research by Smith et al. (2015) demonstrated that in cases of PTSD allocentric processing was impaired. This thesis pursued this line of enquiry and assessed the impact of PTSD and of *any trauma exposure* on navigation performance using a static perspective taking task and a more 'active' navigation paradigm. The study also introduced navigation questionnaires to these assessments, to see how accurate individuals with different experiences of trauma (including combat) were in their perceptions of their own navigation competence (or indeed impairment). Finally, the thesis approached the issue of genetics and explored the influence of the Brain-Derived Neurotrophic Factor (BDNF) gene on experiences of PTSD and on navigation behaviour.

In summary, the study's findings confirmed those of Smith et al. (2015) that PTSD impaired allocentric processing. What is more, this thesis revealed that PTSD also impaired egocentric navigation and that allocentric navigation performance was also impaired in *healthy trauma exposed* individuals who reported no ill-effects from their trauma. The thesis demonstrated for the first time that PTSD brought with it an associative bias which was transferable to navigation behaviour. This was interpreted as being the consequence of a competition for hippocampal resources between trauma processing and navigation in otherwise healthy individuals (Vasterling & Brewin, 2005). When it came to perceptions of navigation competence, healthy trauma exposed participants were accurate in their self-reported competence, but those with PTSD-related navigation impairment (including those who had been military trained) were not. Notably, the correlation between self-reported and actual navigation competence was limited to allocentric (not egocentric) navigation competence. This was explained using models of neural processing which present hippocampal dependent memory systems as being more declarative than associative memory systems (e.g. Morris in Andersen et al., 2007). In the final chapter, the explorative analysis of the BDNF gene produced some noteworthy findings. Zhang et al. (2014) speculated that the relationship between BDNF and PTSD is likely confounded by environmental conditions (i.e. the diversity and extent of trauma exposure and opportunities individuals have to process it). BDNF did not influence the PTSD prevalence or severity in this study which did not control for such conditions. In terms of navigation, there were no distinct performance disadvantages from carrying the met allele and this is in line with many similar studies (e.g. Sanchez et al., 2011, etc.). Nonetheless, BDNF met carriers showed different patterns of egocentric performance to valval homozygotes. What is more, met carriers showed an inability to accurately describe their competence at allocentric navigation and observations were made of data that indicated a delay in their uptake of allocentric strategy during navigation (similar to significant findings of Banner et al., 2011). The observations were consistent with Lövdén et al.'s (2011) suggestion that met carriers may require more 'obvious' cues to apply allocentric processing to a given task than valval homozygotes do. The implications of these genetic differences in approach to allocentric processing are considered in terms of both trauma processing and navigation training interventions.

PREFACE

This study began unfunded and the researcher owes much to the generosity of charities, sponsors and academic institutions which together enabled the study to develop exploratory analysis of genetics in its second year.

The project raised £28 000 match funding through the military charity Army of Angels (registered charity number 1143612), Santander, the Bournemouth University (BU) Post Graduate Research (PGR) fund and BU's Vice Chancellor award scheme.

The project also helped release £150 000 of National Institute of Health Research (NIHR) funding in 2014 for clinical research for the Dorset HealthCare University Foundation Trust (DHCUFT) enabling the DHCUFT to meet its annual performance indicator for clinical research participation.

ACKNOWLEDGEMENT

This study exists principally because of the open-mindedness and fortitude of Assoc. Prof. Jan Wiener and the inspiration of Prof. Chris Brewin. Thanks also goes to the dedicated and gentle expertise of Prof. Sine Mc Dougall and Dr Sarah Thomas during its write-up.

Prof. Sue Clarke and Prof. Bob Remmington bestowed a certain professional grace on its development and the generosity of time and desk space offered by Dr Sophie Rushbrook and all the staff at the Branksome Clinic (Poole) is much appreciated.

The acceptance of this potentially contentious study by Prof. Sir Simon Wessely and Dr Walter Busuttil at Combat Stress was hugely encouraging as was the professional review of the initial publication in *Frontiers in Human Neuroscience* by Prof. Nicola Fear at the King's Centre for Military Health Research.

The author would like to thank Cambridgeshire and Dorset Police (in particular, Detective Cheryl Pinner, Chief Superintendent Simon Megicks and Inspector Les Fry) and all the officers across both forces who gave their time and energy during a difficult time of budget and staffing cuts.

My greatest respect goes to the twenty five veterans at Combat Stress whose insight, patience and determination taught me much: spending my birthday at Tyrwhitt House (Surrey) in 2014 will be not be forgotten. Thank you for your humour, interest and tenacity.

Finally, I would like to thank Ian Denness, my partner and my friend who listened to my first idea when I didn't think I had anything to say, and who has put up with me every day since.

This is for you, Den.

AUTHOR'S DECLARATION

This thesis includes an article that has previously been published. The contribution of the author to this paper is addressed below:
Miller, J. K., & Wiener, J. M. (2014). PTSD recovery, spatial processing, and the val66met polymorphism. *Frontiers in Human Neuroscience*, *8*, 100. DOI: 10.3389/fnhum.2014.00100
The author was primarily responsible for constructing the theory for the Opinion Paper above.

Prof. Chris Brewin and Kirsten Smith (Royal Holloway and University College London) kindly collected and shared data from thirteen participants from a previous cohort from a study in 2012 which was later to be published as:
Smith, K., Burgess, N., Brewin, C.R. and King, J.A. (2015). Impaired allocentric spatial processing in posttraumatic stress disorder. *Neurobiology of Learning and Memory,* 119, 69–76.

Contents

List of Tables

List of figures

SUMMARY

Without the brain's trauma response, the human race would not survive. Without a sense of danger, of horror or of helplessness, we would not know how to stay safe, how to appreciate times of peace, or how to protect ourselves. However, an established literature about the negative effects of traumatic stress on the brain makes it clear that for many, the impact of trauma can be profound. Post-Traumatic Stress Disorder (PTSD) is becoming an increasingly familiar term in contemporary society and has frequently been used to describe the experience of police officers, other emergency responders and some UK military personnel returning from Afghanistan and Iraq.

An emerging body of research is beginning to look at some neuropsychological effects of PTSD. These effects are surprisingly far-reaching and recent research now suggests that PTSD impairs allocentric processing, a form of spatial processing which is crucial for individuals to be able to navigate effectively (Smith et al., 2015). Ironically, effective navigation is a critical skill amongst military and civil emergency service personnel, the very professional groups who are likely to experience major trauma. While there are references to PTSD affecting travel behaviour and willingness to explore the environment in trauma literature (e.g. Osofsky et al., 2010; Ehring et al., 2006; Lubit et al., 2003; Kowitz, 2011; Ehlers et al., 1998; Adler et al., 2009; Handley et al., 2009; Butler et al., 1999) there are no specific studies which investigate the direct relationship between trauma and navigation. This thesis develops this line of enquiry and examines the impact of PTSD and trauma exposure on active navigation and also assesses individuals' perceptions of their own navigation competence. The study then explores the potential influence of a gene (the Brain-Derived Neurotrophic Factor, or 'BDNF' gene) on an area of the brain known to be involved in both processing of trauma and in navigation, the hippocampus (Miller & Wiener, 2014).

This study recruited 150 participants to a series of experiments and assessments. Each chapter deals with different aspects of the study. Participants were grouped according to whether they had experienced trauma or not, and if they had experienced trauma, whether they had developed PTSD from that trauma or not. This equated to three experimental groups: *Trauma Unexposed, Trauma Exposed No PTSD,* and *PTSD.*

The first experiment (Chapter 3) uses a static topographical (allocentric) memory test, the Four Mountains task, (Hartley et al., 2007) to measure the impact of PTSD on spatial processing performance. The task is used to compare the impact of PTSD with the impact of trauma exposure on healthy individuals (i.e. those who have not developed PTSD). Results were consistent with those of a contemporary study by Smith et al. (2015) and suggested that PTSD impaired performance on the task. Importantly, the trauma exposed participants who did not develop PTSD did not perform significantly worse than those who had not been exposed to any trauma.

Chapter 4 extended the investigation by introducing a more complex wayfinding paradigm, the Alternative Route (AR, Wiener et al., 2013), which assessed two forms of spatial processing

used in navigation: allocentric processing and egocentric processing. Allocentric spatial processing is viewpoint *in*dependent and involves the encoding of information about the location of one object relative to another object (as opposed to egocentric processing which is viewpoint *dependent* and involves the encoding of information about an object in relation to the location to the self). Findings showed that PTSD impaired both egocentric and allocentric processing. The AR paradigm was also sensitive to the impact of trauma exposure (as well as to the impact of PTSD) and, for the first time, the study demonstrated that trauma exposure in healthy individuals can impair allocentric processing.

The focus of Chapter 5 was to explore whether those in the sample without PTSD (to whom one refers as 'healthy participants' in this study) had accurate perceptions of their own abilities to navigate using egocentric and allocentric strategies. Three validated self-reported navigation questionnaires were used: the Santa Barbara Sense of Direction (SBSOD; Hegarty et al., 2002); the Questionnaire of Spatial Representation (QSR; Pazzaglia & De Beni, 2001); and the Fragebogen Räumliche Strategien" (FRS, i.e., the 'questionnaire on spatial strategies'; Münzer & Hölscher, 2011). Self-reported confidence in egocentric and allocentric navigation were correlated with actual egocentric and allocentric performance on the AR paradigm. Results showed that only allocentric navigation performance positively and significantly correlated with self-reported allocentric confidence. This finding supports general theories of spatial learning which depicts allocentric processing as being more declarative and verbally accessible than more egocentric neural processes (e.g. Vermetten et al., 2003; Brewin & Burgess, 2014; Morris in Andersen et al., 2007; Buckley et al., 2015).

Chapter 6 repeated the analysis of Chapter 5 but with participants with PTSD. The focus of this chapter was to examine if having had military navigation training made any difference to how accurate individuals with PTSD were about their own navigation competence. Participants who had military experience (i.e. those with Combat-Related PTSD, CR-PTSD) were compared with those without that military experience (i.e. those with non-combat related PTSD). In all cases of PTSD, self-reported confidence did not correlate with either allocentric or egocentric navigation performance. While those with military experience self-reported higher levels of confidence in allocentric navigation than those without, there were no group differences in navigation performance.

Chapter 7 presents an exploratory investigation into the influence of the Brain-Derived Neurotrophic Factor (BDNF) gene on the relationship between trauma and navigation behaviour. The BDNF gene is known to influence the integrity of the hippocampus which is an area of the brain which is crucial for trauma processing and allocentric spatial processing (Notaras et al., 2015; Hariri et al., 2003; Chaieb et al., 2014; Miller & Wiener, 2014; Smith et al., 2015). There are three variants of this BDNF gene (valval, valmet, and metmet). Those who are carriers of the 'met' allele (i.e. valmet and metmet genotypes, representing 30% of the Caucasian population) have been shown to exhibit reduced hippocampal plasticity than valval homozygotes (representing the other 70% of the Caucasian population). This is as a result of met carriers secreting less hippocampal BDNF protein when it is required than valval homozygotes secrete (Pretryshen et al., 2010; Notaras et al., 2015; Lövdén et al., 2011).

Carrying the ‘met’ allele of the BDNF gene has long been researched in association with the development of PTSD (e.g. Suliman et al., 2013; Valente et al., 2011, etc.), typically by virtue of its role in the regulation of the stress response; but this association has only been confirmed in one recent study (Zhang et al., 2014). The findings by Zhang et al. (2014) were not replicated in this study, and a likely explanation for this was the lack of control for environmental conditions (such as trauma exposure and trauma processing opportunities). Previous research into BDNF has also shown some disadvantages of carrying the met allele for hippocampal related activity (e.g. Chen et al., 2006; Sanchez et al., 2011; Erickson et al., 2010) but not for spatial processing or navigation performance (e.g. Raz et al., 2009; Sakata et al., 2013; Dennis et al., 2011). The navigation data in this study demonstrated no disadvantage in carrying the met allele of the BDNF gene for gross allocentric navigation performance. Surprisingly, BDNF met carriers demonstrated higher overall self-reported navigation confidence than valval homozygotes and a different pattern of egocentric strategy use in a navigation task to valval homozygotes. The lack of gross performance differences between BDNF genotypes, but observations of differences in strategy use was consistent with recent findings (Banner et al., 2011). Lövdén et al. (2011) suggested that differences in navigation between BDNF genotypes may be less to do with absolute performance disadvantage *per se* and more to do with the possibility that met carriers may need more ‘obvious cues’ to apply allocentric to a given task than the dominant valval homozygote would do. The speculation in this thesis is that BDNF genotype may influence *how individuals approach spatial processing*, and how they apply spatial processing to navigation tasks or to the processing of traumatic experiences. Differences in how individuals apply spatial processing techniques may account for BDNF group differences in hippocampal dependent function found by previous research (e.g. Egan et al., 2003; Hashimoto et al., 2008; Sanchez et al., 2011). Differences in how individuals apply spatial processing techniques to trauma processing may also account for the BDNF group differences in PTSD severity and prevalence found in populations who share similar experiences of trauma exposure (see Zhang et al., 2014).

THESIS OUTLINE

This thesis investigates the relationship between trauma (including combat trauma), navigation and the BDNF gene and it does so over several stages. The first stage sought to establish if there was an impact of trauma exposure and PTSD on spatial processing and navigation behaviour (Chapters 3 and 4).

The second stage (Chapter 5) used navigation questionnaires and related participants' responses to their navigation behaviour to assess if healthy individuals were accurate in their perception of their own navigation competence. In Chapter 6 the same approach as that in Chapter 5 was used to investigate whether participants with combat-related PTSD (i.e. military navigation training experience) were any more accurate in their perception of their navigation competence than those with PTSD who had not had the same access to navigation training.

Finally, in the third stage (Chapter 7), the role of BDNF was tentatively explored. The analysis undertaken in Chapters 3 and 4 was repeated in Chapter 7 but between groups based on BDNF genotype (rather than trauma status). Analysis explored the potential influence of BDNF genotype over navigation behaviour, and how this may or may not be related to trauma exposure.

1 GENERAL INTRODUCTION

1.1 POST-TRAUMATIC STRESS DISORDER (PTSD)

Post-Traumatic Stress Disorder (PTSD) is defined by the DSM-V (American Psychiatric Association, APA, 2013) as comprising:

> "a history of exposure to a traumatic event ...that meets specific stipulations and symptoms from each of four symptom clusters: intrusion, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity" (APA, 2013).

In the United Kingdom, the National Health Service (NHS) summarise PTSD symptoms as involving:

(i) Re-experiencing: flashbacks, nightmares or repetitive and distressing images or sensations (this can even include physical sensations such as pain, sweating and trembling);
(ii) Avoidance and emotional numbing: avoiding certain people or places that remind you of the trauma, avoiding talking or engaging with people or in activities, or even avoiding feeling anything at all;
(iii) Hyperarousal or 'feeling on edge': constantly aware of threats and being easily startled, irritability, angry outbursts, sleeping and concentration problems (NHS, 2016).

PTSD diagnosis and clinical assessment is discussed further in the Methodology Chapter 2 (Section 2.3.2).

There is a general consensus in the trauma literature that traumatic memories are difficult to process (Kirmayer et al., 2007; Brewin & Holmes, 2003). When memories are of a particularly extreme nature (i.e. when they are traumatic), they are accompanied by a stress response which demands more hippocampal resources to encode the memory than "ordinary normative memories" might otherwise demand (Brewin, in Vasterling & Brewin, 2005; Van der Kolk et al., 1989). When this encoding has not happened (or is *yet to* happen), these uncontextualised memories of trauma can become disruptive to everyday cognitive functioning. The unprocessed experiences may have a sense of 'now-ness', they may be incongruous with our world view, be evocative, loaded with sensory information, and they may elicit the fear response or prompt environmentally inappropriate behaviour (Bisby et al., 2010; Dalgleish, 2004; Pearson et al., 2012). Essentially, individuals may respond to memory cues in the present in a way that is related to their past, unprocessed trauma memory. These memory processing deficits are synonymous with the collective term for the condition known as Post-Traumatic Stress Disorder or PTSD (Foa et al., 1995).

Research has long considered the impact of PTSD on an array of cognitive functions and human behaviours which are not included in the current DSM-V criteria (including attention, working memory, disturbed attachment patterns) and these can lead to many comorbid diagnoses (Teicher et al., 2013; Acheson et al., 2012; Quereshi et al., 2012; Brandes et al., 2002; Hart et al., 2008; Knauss, 2007; Thomaes et al., 2013; Vasterling et al., 1998). One less

researched behavioural trait is to do with how individuals find their way in the environment: travel anxiety, travel phobias and being less likely to want to explore or 'master' their environment have been recognised in children and adults with PTSD (Osofsky et al., 2010; Ehring et al., 2006; Lubit et al., 2003; Kowitz, 2011).

1.1.1 Key characteristics of PTSD

Some characteristics of PTSD are particularly relevant to this study, including: visual intrusions (or 'flashbacks'), the startle response, and associative styles of thinking. These characteristics are relevant by virtue of the neural circuitry which is said to be involved in those symptoms, i.e. the functionality (or dysfunctionality) of the hippocampus (Bisby et al., 2010; Brewin & Burgess, 2014; Smith et al., 2015; Miller & Wiener, 2014). The hippocampus is introduced more fully later (in Section 1.1.4 and 1.2.1). Other symptoms are less directly relevant to this study and these include those relating to avoidance, physical manifestations of the stress response and anger or irritability.

To provide a little more detail about the most relevant symptoms, a signature symptom of PTSD which is familiar to modern interpretations of trauma is the 'flashback'. Flashbacks are one type of visual intrusion which are thought to typify the uncontextualised (or 'unfiled') memory, and are often referred to in clinical studies of trauma (e.g. Bisby et al., 2010; Holmes et al., 2010). Brewin et al. (2010) describe these intrusions as being instances of *involuntary*, unbidden memory retrieval as opposed to voluntary memory retrieval; "their appearance in consciousness is spontaneous rather than following a deliberate effort or search" (Brewin et al., 2010). Intrusions tend to be repetitive, uncontrollable, and distressing and experimental research indicates that imagery may elicit stronger emotional responses than do corresponding verbal cognitions (Holmes et al., 2010). Intrusions can occur in different forms, such as dreams, nightmares, or unpleasant imaginings (Horowitz, 1986). Intrusions have often been used as a measure of trauma-related memory impairment and they feature in many studies (e.g. Bisby et al., 2010; Brewin et al., 2010; Glazer et al., 2013; Meyer et al., 2012). More information about visual intrusions and detailed examples are provided in Chapter 4 (Section 4.1.6).

The startle response is an index of trait anxiety which has been examined in many human and rodent studies about trauma (see Zhang et al., 2014; Andero & Ressler, 2012; Rattiner et al., 2004; Takei et al., 2011, Acheson et al., 2012; Rosas-Vidal, 2014, etc.). The startle response (which is also referred to as the startle reflex or the alarm reaction) is both a psychological and physiological response to a sudden unexpected stimulus. Such stimuli might be a flash of light, a loud noise or a quick movement near the face (Zhang et al., 2016). Abnormality of the startle response, which results from an elevated activation of the autonomic nervous system, is a core symptom of PTSD; hyperarousal (Zhang et al., 2016; Foa et al., 1995). In the human model and in PTSD, startle is typified by symptoms of hyperarousal. Examples of questions in PTSD screens pertaining to hyperarousal and the startle response include; "Being overly alert (for example, checking to see who is around you, being uncomfortable with your back to a door, etc..)" or "being jumpy or easily startled" (for example, when someone walks up behind you)

(Foa et al., 1995). 'Startle' is discussed in more detail in Chapter 7 in relation to PTSD and the BDNF gene.

Another key component of PTSD theory is the 'associative' nature of trauma memories. Individuals who have been exposed to trauma may: experience involuntary retrieval of associated memories; experience emotions about that trauma from a personal point of view; and may exhibit strong Pavlovian-like associations[1] between what they remember about a trauma and what they see in front of them (e.g. Lang et al., 1977; Foa & Rothbaum, 1998; Erwin, 2003; Le Doux, 2000; Maren, 2008). Associative thinking is central in much trauma literature (e.g. Eich et al., 2012; Lang, 1977, 1984; Erwin, 2003; Epstein, 1985; Horowitz, 1986; Janoff-Bulman, 1992; Foa & Rothbaum, 1998; Foa & Kozak 1986; Steel et al., 2005) and associative learning also features in neurological models of memory (e.g. Buckley et al., 2015; Morris in Andersen et al., 2007; Wiener et al., 2013). Associative thinking in PTSD typically involves associating a stimulus (places, objects, events) in the current environment with past events and the emotions experienced at that (now, past) time. A case of associative thinking is presented in Chapter 4 (Section 4.1.6.1) with reference to an article in the Guardian newspaper (2014). In this example, combat veterans recounted how bumper boxes of Christmas chocolates here in the UK could suddenly evoke vivid traumatic memories of earlier combat in Iraq and Afghanistan. The associative relationship in this instance was formed because in combat, plastic chocolate boxes were often used by insurgents to package Improvised Explosive Devices (IEDs). For these veterans, the chocolate box has an encoded association with combat, and the present day context of a family Christmas has no bearing on the individual's re-lived experience of that trauma. Associative thinking is addressed in more detail Chapter 4 (in Section 4.1.6).

1.1.2 Types of trauma

The breadth of human experience is extensive, and individuals may encounter any number of different traumas at any one time in their lives. Up to 29 different types of traumatic events are officially recognised by the World Health Organisation (WHO) who use a Composite International Diagnostic Inventory (CIDI) to categorise trauma exposures in World Mental Health (WMH) surveys (Atwoli et al., 2015). The classification of 'trauma type' in psychological literature is as diverse as the research questions therein. Commonly researched sources of trauma include terrorism, transport disasters, rape, child sexual abuse, domestic violence and war (Perrin et al. 2007; Sarapas et al. 2011; DiMaggio & Galea, 2006; Karunakara, et al. 2004; Tempesta et al. 2011; Ahmed, 2007; Filipas & Ullma, 2006; Lyoo et al., 2011; Sulivan & Holt, 2008).

There is one type of trauma which is particularly interesting for this exploration of the relationship between PTSD and navigation; Combat-Related PTSD or 'CR-PTSD'. Those with

[1] Pavlovian conditioning is a learning process in which an innate response to a potent stimulus (such as a traumatic event) comes to be elicited in response to a previously neutral stimulus (in the present day environment) and is named after Ivan Pavlov (1927).

experience of combat presented a useful population for this research to explore how traumatic stress might interact with the demand to perform well in navigation. Effective spatial processing, wayfinding and navigation skills are critical for many military roles, roles which may well (ironically) involve exposure to trauma and high levels of stress. CR-PTSD is discussed in more detail in Chapter 6.

1.1.3 Historical understanding of Combat-related PTSD (CR-PTSD)

To provide some background to the concept of CR-PTSD, how combat-related psychological stress has been acknowledged and accepted in social history provides some context for how neuropsychological research into CR-PTSD has been (and is) received. The neuropsychological effects of combat remained undefined until the First World War (1914-1918), only to be labelled after the armistice at best as "shell shock" (Myers, 1915) and at worst as "the just deserts of the morally feeble individual" (Gee, 2013). During the Second World War (1939-1945) the term "battle exhaustion" was used. In the Vietnam War (1965-1974) another war syndrome with unexplained medical symptoms was referred to as the "effects of Agent Orange". It was not until 1980 that Diagnostic criteria for Post-Traumatic Stress Disorder (PTSD) were introduced by the American Psychiatric Association and these criteria were met with much academic and public scepticism (Pitman et al., 2012). Even in 1991 the term was not in full use, and instead, the Gulf War brought with it a new phenomenon, "Desert Storm syndrome" or "Gulf War Syndrome" (Jones & Wessely, 2005, 2006). Since then, the King's Centre for Military Health Research (KCMHR) has been established and the prevalence and severity of traumatic stress in more recent combat with Operation Telic (namely Iraq and Afghanistan) is more closely monitored and researched (KCMHR, 2010).

A brief review of the combat literature was undertaken in parallel with consultation with various military professionals[2]. What was clear from the early review and consultation was that CR-PTSD was a still a subject matter rife with contention. Discourse about CR-PTSD was interlaced with references to 'fabrication, 'stigma', political impetus, and even to partiality in research due to funding arrangements (Poyner, 2010; Hoge, 2011; Palmer, 2012; Gee, 2013; Jones & Wessely, 2005, 2006). It was important to delineate what constitutes 'CR-PTSD', what constitutes 'PTSD' and what constitutes neither. Research bodies responsible for understanding combat related PTSD have been keen to stress that combat-related PTSD (or CR-PTSD) is not more prevalent (3.2%) than trauma arising from non-combat civilian incidents (2.7%, Gee, 2013; KCMHR, 2010; Atwoli et al., 2015). Yet distinguishing between CR-PTSD and non-combat related PTSD has still been highly valued (see Marmar et al., 2015; Richardson et al., 2010; Yehuda et al., 2005). This is reflected in recent calls amongst certain military leaders (APA,

[2] Those consulted included: interviews with Sir Prof Simon Wessely (director of the KCMHR and chair of the Combat Stress Ethics Committee), Prof Nicola Fear (KCMHR), Dr Walter Bussitil and Prof Ian Palmer (military psychiatrists), Milos Stancovic (former director of military research charity Braveheart and author), Kate Adie (war correspondent and author) and Captain Duncan Precious (psychologist in the British Army); and discussions with Combat Stress veterans, and serving personnel in British Military Fitness and Forces Fit initiatives.

2013) to introduce separate diagnostic criteria for CR-PTSD and to rename the 'disorder' to something which is "more in line with the language of troops" (APA, 2013).

Researchers developing models of PTSD have also argued that there needs to be an appreciation of the difference between a "stressful experience [in the past]" and a "stressful *military* experience, as evidenced by Weathers et al.'s development of separate civilian and military trauma assessments (the PTSD Check List or PCL in 1993). However, rarely are any details given as to what these differences are, and how their effects on cognition and behaviour can be measured. To maximise the credibility of research into CR-PTSD, research bodies dedicated to studying combat-related trauma also recommended that "*objective neuropsychological assessment*" be applied to research as much as possible (KCMHR, 2010).

1.1.4 The neural processing of trauma

PTSD occurs as an abnormal psychological phenomenon when traumatic experiences have not been (or have yet to be) sufficiently processed and contextualised in long term memory (i.e. contextualised in time and place). Whilst PTSD is inextricably linked to the stress response, the 'disorder' of the condition is arguably as much one of memory consolidation as it is one of stress-related behaviour (Zhang et al., 2016; Bisby et al., 2010; Bremner & Elizinga, 2002; Glazer et al., 2013). In order to understand PTSD in terms of memory consolidation, it is worth spending some time to briefly introduce the memory system involved in trauma processing, a system which is integral to cognitive models of PTSD; that of the hippocampus (Astur et al., 2006; Ehlers & Clark, 2000; Pitman et al., 2012; Admon et al., 2013).

The significance of the hippocampus on our understanding of human behaviour has a long history. The hippocampus was first named by the Bolognese anatomist Giulio Cesare Aranzi (circa 1564) because of the similarity of its shape to that of the seahorse (Andersen et al., 2007). In 1937, James W. Papez published an influential hypothesis that the hippocampus was part of a neural circuit responsible for emotional processing, later to be known as 'the Papez Circuit' (Andersen et al., 2007). The crucial role of the hippocampus in memory formation and consolidation then became clear in the 1950's with a seminal study of brain damaged patients by William Scoville and Brenda Milner in 1957 (Scoville & Milner, 1957). The most famous patient was H.M. who underwent surgery for severe epilepsy involving the removal of his hippocampus. This resulted in him being unable to form new memories (Andersen et al., 2007).

Being able to form new memories was not the only function of the hippocampus which proves relevant to PTSD. What has later emerged is that hippocampal memory consolidation also involves spatial encoding: by using viewpoint independent spatial encoding (which is referred to later as 'allocentric' spatial encoding) the hippocampus enables an individual to place events in a spatial context as well as a temporal one (Bisby et al., 2010; Brewin & Burgess, 2014). The relevance of the hippocampus for spatial memory is well recognised and the role the hippocampus plays in forming 'cognitive maps' was brought to the world's attention by John O'Keefe in 1971 (O'Keefe & Dostorovsky, 1971, and this is discussed again in Section 1.2.1).

The relationship between the spatial encoding function of the hippocampus and other domains of neural processing is of interest to both human and animal research (e.g. Arnold et al., 2013; De Araujo et al., 2001). What is interesting to this research, however, is how hippocampal dependent processing is integral to memory encoding and organisation (Bremner & Elzinga, 2002) and, more specifically, how hippocampal dependent spatial encoding assists the encoding of traumatic memories.

Traumatic memories are typically: 'persistent', have considerable emotional significance, are loaded with sensory information, and are incongruous with how we expect events to be- and yet they need to be organised episodically to be committed to long term memory to prevent them from causing disruption to our everyday life (Eichenbaum in Andersen et al., 2007; Kesteren et al., 2013; Dalgleish & Power, 2004; Bremner & Elzinga, 2002; Brewin & Burgess, 2014; Doidge 2007). By providing contextualisation of 'time and place', this encoding undertaken in the hippocampus enables an individual to modulate their stress responses to what they encounter in the present (Glazer et al., 2013; Brewin & Burgess, 2014; Rudy et al., 2004; Phelps 2004; Bremner & Elzinga, 2002; Gould in Andersen et al., 2007; Fanselow & Dong 2010; Acheson et al., 2012; Selden et al. 1991). Contextualisation of trauma memories is key to theories of PTSD (Brewin & Burgess, 2014) which argue that evocative, sensory memories from a traumatic experiences require there to be more 'structural' information about the context of what happened and where: information which is not dependent on the individual's personal perspective. This 'structural' contextualisation is not automatic and requires activation of the hippocampus (Hanson, 2011). When the hippocampus is down-regulated (as a result of stress from the trauma, for example), this encoding can be impaired: rendering the memories uncontextualised in space and time, and more likely to 'reappear' unbidden in response to environmental stimuli – and these appearances are referred to as 'intrusions' (Meyer, 2012; Bisby et al., 2010; Steel et al., 2005).

As was learned with patient H.M. (Scoville & Milner, 1957), the hippocampus also facilitates the consolidation of newly formed experiences. Newly formed experiences *of safety* in particular play a key role in alleviating the fear response and these new safe experiences are often called safety 'cues' (Soliman et al., 2010; Frankland et al., 1998; Elzinga & Bremner, 2002; Andero et al, 2012; Peters et al., 2010). Together, contextualisation and the formation of safety cues helps to organise our experiences and can prevent us from exhibiting environmentally inappropriate behaviour, behaviour which is 'out of context' to what is currently going on (Morris, 1981; Teicher et al. 2003; Pearson et al., 2012). In terms of PTSD, such behaviour might include a fear response to conditions which are not fearful, or a lack of a fear response when conditions present a genuine threat to life (Acheson et al., 2012). One could reason that the hippocampus is there to provide the 'order' post-trauma, which those who suffer from Post-Traumatic Stress *Dis*order (PTSD) essentially lack.

However, what is somewhat paradoxical in the relationship between the hippocampus and traumatic stress is that the hippocampus is also known to be an area of the brain which is

particularly *vulnerable to the effects* of stress (Vasterling & Brewin, 2005; Acheson et al., 2010; Sapolsky et al., 2010; Bremner et al., 2002; Conrad, 2006). This vulnerability underpins much research, including the most recent research into PTSD, genetics, epigenetics and DNA methylation (e.g. Zhang et al., 2006, 2014; Wang et al., 2015; Unternaehrer et al., 2012; Roth et al., 2011; Notaras et al., 2015). So far, this research has shown that acute psychosocial stress results in epigenetic modification and dynamic changes in the DNA methylation of BDNF (Roth, et al., 2011; Unternaehrer et al., 2012). The implications of the hippocampus' vulnerability to stress are discussed further in relation to the first experiment (see Chapter 3).

1.2 NAVIGATION

This study essentially investigates the relationship between trauma and navigation, and how exposure to trauma experiences may impair our ability to apply spatial processing techniques. The fact that PTSD can impair spatial processing has now been established (Smith et al., 2015). This study aims to investigate this impairment further by considering how spatial processing techniques are used in active navigation, i.e. finding one's way in an environment. This is also with a view to better understanding how it might be that PTSD can affect travel behaviour and willingness to explore the environment in trauma literature (e.g. Osofsky et al., 2010; Ehring et al., 2006; Ehlers et al., 1998; Kowitz, 2011; Lubit et al., 2003; Adler et al., 2009; Handley et al., 2009; Butler et al., 1999).

There are many ways to which finding one's way in the environment is referred in the literature reviewed for this study, and these included: navigation; spatial processing; spatial learning; wayfinding; spatial orientation; situational awareness (Wolbers & Wiener, 2014; Dudchenko, 2010; DSTL, 2014; Smith et al., 2015; Wiener et al., 2013).

Spatial orientation and *situational awareness* are terms which are often used to describe how individuals can identify where they are in space and how they may avoid getting lost or disorientation (Dudchenko, 2010; DSTL, 2014). These terms are found in contemporary military literature and more information about this situational awareness as a military priority can be found in Chapter 6 (Section 6.1.2).

This study mainly uses the terms *navigation* and spatial *processing*. For the purposes of this study, the way in which information is used to navigate is referred to as *spatial processing* (and this is later explained at section 1.1.2 as being either allocentric spatial processing or egocentric spatial processing). Spatial processing of information is differentiated from navigation in this study. Spatial processing (be it allocentric or egocentric) is regarded as being a cognitive component of the behaviour of active navigation. That is to say, that individuals undertake cognitive spatial processing to be able to actively orient and manoeuvre themselves in their environment. Spatial processing can also be undertaken from a static position, or in figural or vista frames of space, and this positioning can be represented on paper based or digitally (Section 4.1.2 discusses frames of space in more detail). In this study, the paper-based Four

Mountains task (Hartley et al., 2007) is considered to be a static test of allocentric spatial processing.

When spatial processing involves movement in environmental space (again, see Section 4.1.2 for more detail about frames of space), this is space which cannot be experienced from a single place but requires considerable movement (Wolbers & Wiener, 2014) and orienting in this way is referred to as *active navigation*. The paradigm that is used to assess active navigation in this study is one which involves way-finding and which requires spatial learning, the Alternative Route (AR) paradigm (Wiener et al., 2013). *Wayfinding* describes (as the phrase suggests) how individuals find their way in the environment, how they learn how to get 'from A to B'. The phrase *spatial learning* is used to describe the process of encoding spatial information which can be used to solve navigation tasks, such as learning a route, or creating a mental map of a given area. Spatial learning for navigation can be encoded in an egocentric or an allocentric reference frame (and this is discussed in more detail in Section 1.2.2 and in Chapters 3 and 4). Allocentric spatial learning is required for individuals to successfully find their way through and complete the AR paradigm in this study (and the paradigm is introduced more fully in Section 2.6.1.2).

1.2.1 Navigation and the hippocampus

Spatial learning has been of interest to psychology and neuropsychology since the beginning of the 20th Century (Dudchenko, 2010). Early behavioural studies of spatial cognition and learning typically involved rodents and mazes, with the first well-known study translated into a human model being that by Tolman in 1948. Tolman's work developed theories of spatial learning beyond those founded on stimulus and response learning, by introducing a new understanding of spatial learning around the concept of a 'cognitive map'; that is, that while running the maze, rats develop an overall representation of the maze. This representation granted the rats cognitive flexibility when faced with alternative configurations of the maze (Dudchenko, 2010). As mentioned earlier (in Section 1.1.5), the concept of having a mental representation of an environment was then developed further in the 1970's. O'Keefe & Nadel identified (1978) the hippocampus as the mammalian brain structure which was integral to the development of the cognitive map, which has featured heavily in much research since (e.g. Burgess et al., 2008; Wills et al., 2010; Arnold et al., 2013; Schinazi et al., 2013; and reviewed by O'Keefe, 2013). The notion of individuals building a cognitive map to navigate brings our attention to a form of spatial processing that is involved in using that map once it is established: allocentric processing.

1.2.2 Allocentric spatial processing

"While the widely studied allocentric spatial representation holds a special status in neuroscience research, its exact nature and neural underpinnings continue to be the topic of debate." (Erkstrom et al., 2014).

A key component of navigation and of hippocampal function is 'allocentric processing' (see Wiener et al., 2013; Smith et al., 2015; Bisby et al., 2010; Lövdén et al., 2011). The 'filing', encoding and modulating functions of the hippocampus involve allocentric processing (Brewin et al., 2010). Allocentric coding is said to occur when spatial information, such as the position of a landmark, is encoded with respect to other objects or locations in the environment, and this creates an allocentric reference frame (see Wiener et al., 2009). Allocentric representations are independent of the position of an observer in the environment and do not change (see Figure 1.2a). The allocentric reference frame features heavily in navigation and spatial processing research but is also described in terms of emotional and trauma processing (and this is explained further in Sections 1.2.3 and in Chapter 4 at Section 4.1.6).

The allocentric reference frame is 'viewpoint independent' which means, in terms of spatial processing, that an individual is able to identify an object's position (or direction) from a point of view or direction that is *not necessarily the one that they themselves hold* or are positioned in (which would be an egocentric perspective). Information about an object is encoded allocentrically when it is encoded relative to another object. Strategies involving this form of hippocampal dependent processing are also referred to as 'configural' (and the use of configural strategies is discussed further in Chapter 4 at Section 4.1.3). An example of a typical allocentric navigation strategy would be one where an individual builds a map-like representation of the area in which they are navigating. The individual then uses this 'mental map' as a guide to navigation to direct their way in the environment, regardless of their current location or the direction they are facing (e.g. see Furnman et al., 2014).

The egocentric reference frame is 'viewpoint dependent, which means that an individual identifies an object's position *only in relationship to their own location* (see Figure 1.2b). Egocentric processing is thought to involve other brain structures than the hippocampus; such as the parietal cortex, caudate nucleus and striatal circuits (see; Andersen et al., 2007; Campbell et al., 2009; Banner et al., 2011). Two examples of egocentric processing strategies are 'associative cue' or 'response-based' (e.g. Wiener et al., 2013; Banner et al., 2011) and again, these are discussed further in Chapter 4 Section 4.1.4. An individual would be using an egocentric strategy, for instance, if they were using local landmarks to remember a route, by associating a directional turn (left or right) with that landmark (on the basis that they would be facing the same direction when they came to repeat the route they were learning) (also see Taylor & Tversky, 1992).

a) Allocentric processing b) Egocentric processing

Figure 1.2: Examples of (a) allocentric and (b) egocentric spatial processing.
Image reproduced with permission, courtesy of Prof Kozhevnikov, Mental Imagery & Human-Computer Interaction Lab, Harvard Medical School, U.S.

1.2.3 Allocentric processing and PTSD

Once the domain of spatial processing and navigation literature, the phrase 'allocentric processing' only emerged as a specific term of reference relevant to the study of PTSD in 2010. Bisby et al. (2010) demonstrated that performance on an allocentric (hippocampal dependent) spatial processing task was related to the frequency of visual intrusions which participants experienced after being exposed to trauma footage (this study is discussed again in more detail in Section 4.1.6). On the basis of this research, the prominent theory of PTSD, the Dual Representation Theory (DRT, Dalgleish, 2004) was updated to include more detail about the how allocentric and associative neural systems become dysfunctional in cases of PTSD. DRT is based on the premise that sensory, evocative trauma memories need to be explicitly contextualised in space and time, using hippocampal dependent processing, to prevent them from being implicitly 'associated' with other (inappropriate) contexts and environmental stimuli. The application of allocentric type trauma processing approaches is not new to trauma research and they are being applied in clinical settings (Ehlers & Clark, 2000; Steel et al., 2005; Neuner et al., 2008; McIsaac & Eich, 2004; Kaur, et al., 2016). DRT and allocentric processing of trauma is discussed further in Chapter 4 (Section 4.1.6.2).

The conflict between the 'associative' thinking style characteristic of PTSD and the *allocentric* style processing required to contextualise unprocessed trauma has been the subject of research since 2010 (see Brewin & Burgess, 2014; Pearson et al., 2012). Meyers et al. (2012) have also shown that 'configural learning' (which uses allocentric processing) had the effect of reducing PTSD symptomology. They reported that individual differences in spatial configuration learning predicted the occurrence of intrusive memories in individuals who had been exposed to traumatic film footage in a laboratory (that is to say, participants who demonstrated better learning had fewer intrusions). Brewin & Burgess subsequently suggested that "above average allocentric spatial processing would confer protection against the development of PTSD" (Brewin & Burgess, 2014). Most recently, Smith et al. (2015) urged for future research to investigate the extent to which facilitating allocentric processing may reduce visual intrusions as a symptom of PTSD. This thesis goes some way to develop a more detailed understanding of PTSD and allocentric processing.

1.3 BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF)

The final chapter of this research into PTSD and navigation behaviour explored another influence over hippocampal functionality: the Brain-Derived Neurotrophic Factor (BDNF) gene. BDNF has been referred to as a 'model system' for examining gene by environment interactions (Casey et al., 2009) due to its essential role in development processes and the impact that its release has on behavioural and neuroanatomic changes that vary with age. The approach by Casey et al. (2009) recognised that BDNF gene variation may be a risk factor in some stages of development or under some conditions, and a protective factor in others. Studying the 'gene by environment' interaction (or the *G x E* interaction) has been undertaken in other areas of mental health (such as depression, Aguilera et al., 2009). Koenen et al. (2008) urged that *G x E* interaction be studied in relation to PTSD, the principle behind this being that "the effect of a genotype on a condition differs by the presence or absence of an environmental effect" (Koenen et al., 2008). The final study of this thesis (Chapter 7) explores the potential role of BDNF within our sample population to see if BDNF genotype may influence responses to environmental conditions: in terms of trauma processing, navigation behaviour or the relationship between the two.

1.3.1 The BDNF gene and its function

The BDNF gene provides instructions for making and releasing a protein which is also called BDNF, the highest concentrations of which are found in the hippocampus (Hofer et al., 1990). The BDNF protein promotes growth and survival of hippocampal neurons and helps regulate synaptic plasticity and long term potentiation (LTP; Szesko et al., 2005; Jia et al., 2008; Bastikova et al., 2008; Chaieb et al., 2014; Ninan et al., 2010; Doidge, 2007; Egan et al., 2003). To coin the infamous phrase "*neurons that fire together, wire together*", the growth factor of BDNF consolidates connections between (i.e. wires) neurons that fire together (Carla Shatz in Doidge, 2007). BDNF is considered to be a positive marker (or indication) of neuronal integrity in the hippocampus (e.g. Hariri et al., 2003).

1.3.2 Variations in BDNF genotype and their implications

There are variants of the BDNF gene and the release of the BDNF protein into the hippocampus differs between BDNF genotypes (Egan et al., 2003; Notaras et al., 2015). Two of the three variants of the BDNF genotype ('valval', 'valmet' and 'metmet') carry the 'met' allele (i.e. the valmet' and 'metmet' variants) and 'met carriers' equate to 30% of the Caucasian population (Petreyshen et al., 2010). The met allele is negatively associated with hippocampal integrity in terms of both vulnerability to stress and to navigation behaviour (e.g. Wang, 2015; Lövdén et al., 2011). As Notaras et al. (2015) conclude, "…taken as a whole, the conventional view is that the [val66met] polymorphism disrupts activity-dependent release of BDNF…potentially having consequences for psychological functions modulated by BDNF" (Notaras et al., 2015).
This study takes a tentative look at two such psychological functions; trauma processing and navigation behaviour. A brief introduction to the literature regarding the BDNF gene, PTSD and navigation is provided here, with more extensive discussion in Chapter 7.

1.3.3 BDNF and PTSD

To date, the evidence linking specific genes to PTSD has been mixed (Koenen et al., 2009; Schmidt et al., 2011; Skelton et al., 2012; Miller & Wiener, 2014). A recent review by Nievergelta et al. (2015) has identified 25 studies which aimed to link specific genes to the development, prevalence and or severity of PTSD; with “promising” but largely inconclusive findings (Nievergelta et al., 2015). Candidate genes have often been selected for PTSD research because they are already known to influence PTSD-type symptoms (such as ‘startle’, Zhang et al., 2014) and typically encompass the stress-response and fear-based traits (Suliman et al., 2013; Gottesman & Gould, 2003; Acheson et al., 2012; Rosas-Vidal, 2014). The startle response is typically used in studies relating to PTSD as it is a measurable indicator of the fear response in both human and rat models, and fear extinction is another known area of function attributed to the hippocampus, the integrity for which BDNF is considered responsible (Morgan et al., 1995; Zhang et al., 2014; Andersen et al., 2007). The BDNF gene has also been extensively investigated in terms of the stress response and more recently there has been epigenetic and DNA methylation research into PTSD and mental health (e.g. Murakami et al., 2005; Pizarro et al., 2004; Perroud et al., 2008). This extension is important as it suggests that an individual may not just be predisposed to PTSD because of their genetic profile, but that the effect of the traumatic experiences of one generation may be ‘transmitted’ onto the next (e.g. Roth et al., 2011; Uternaehrer et al., 2012; Fuchikami et al., 2012).

In 2013, Hemmings et al. summarised the state of play of knowledge about the influence of genetics on PTSD: “no gene variant has yet been reported as unequivocally involved in the development of this disorder [PTSD]” (Hemmings et al., 2013). However, less than a year later, this picture had changed and a recent study by Zhang et al. (2014) found that the allelic frequency of BDNF ‘met’ was twofold higher in those with probable PTSD, than those without PTSD. This was the first time that the BDNF gene had been unequivocally associated with PTSD. The BDNF and PTSD literature is reviewed more fully in Chapter 7, Section 7.1.2.

1.3.4 BDNF and navigation behaviour

To date, few genes have been identified as implicated in (hippocampal dependent) navigation. One gene is the *NMDAR1* (N-methyl-D-aspartate receptors) gene which was found in certain cells of the hippocampus that have a role in synaptic plasticity, absence of which impaired spatial memory in mice (Tsien et al., 1996). Other genes were the Arc, c-fos, and zif268 genes (genes associated with neuroplastic mechanisms), expression of which were reported after hippocampal dependent learning by Guzowski et al. (2001). Finally, a gene more recently researched is S100B, a variation of which was shown to affect how individuals selected visual scenes as being relevant to the navigation task which they are undertaking (Kong et al., 2016). However, none of these genes seems to have been researched any further with reference to active navigation in humans.

The gene most frequently investigated in relation to hippocampal dependent activity and spatial processing is the BDNF gene (see Sanchez et al., 2011; Ward et al., 2014; Lövdén et al., 2011;

Banner et al., 2011). As with PTSD, the connection between the BDNF gene and navigation has been by virtue of its impact on hippocampal dependent (and in the case of navigation, 'allocentric') processing. The rationale in much of the BDNF literature is that carrying the met allele (as 30% of the Caucasian population do) reduces BDNF secretion in response to hippocampal activity which is likely to have an impact on hippocampal plasticity and function (in Pretryshen et al., 2010; and, e.g. Notaras et al., 2015; Lövdén et al., 2011).

Many studies have demonstrated a disadvantage of carrying the BDNF met allele and these disadvantages include deficits in exploring new environments (e.g. Chen et al., 2006) and having greater rates of age-related decline in spatial skills (e.g. Sanchez et al., 2011; Erickson et al., 2010). In particular, there are two landmark studies from 2011 which are particularly pertinent to this thesis (Lövdén et al., 2011; Banner et al., 2011). Together, these studies have demonstrated that BDNF met carriers exhibited: lower levels of neurotrophin release in the hippocampus in response to navigation training (Lövdén et al., 2011); and less spontaneous uptake of hippocampal dependent strategies in a navigation task (Banner et al., 2011). These studies are particularly relevant in Chapter 7 as this study closes by addressing how BDNF may influence the application of allocentric processing to either navigation behaviour or trauma processing (or both).

2 METHODOLOGY

GENERAL APPROACH

The study sample consisted of 150 participants drawn from: a Bournemouth University research volunteer scheme, NHS treatment clinics, the veterans' charity Combat Stress treatment centre and Cambridgeshire and Dorset Police. Participants were screened for their exposure to traumatic events and those who had been exposed to trauma were assessed for clinical or probable levels of PTSD. The sample population were then categorised and grouped according to whether they were *Trauma Unexposed, Trauma Exposed with No PTSD,* or had *PTSD.*

Participants were administered a series of desk-top tests, including a static spatial processing test (the Four Mountains task), a virtual environment wayfinding paradigm (the Alternative Route paradigm) and three validated self-reported navigation questionnaires (the Santa Barbara Sense of Direction questionnaire, the Questionnaire of Spatial Representation, and the Fragebogen Räumliche Strategien).

Self-testing saliva kits were used to collect samples for DNA testing for the BDNF gene. The results of the spatial processing tests are reported in Chapter 3 (Section 3.3), the wayfinding paradigm results are reported in Chapter 4 (Section 4.3), the navigation questionnaire results in Chapters 5 and 6 (Sections 5.4 and 6.3), and finally in Chapter 7 (Section 7.3), the results from the tests are assessed in terms of BDNF genotype (grouped as *valval* homozygotes or *met* carriers).

2.1 PARTICIPANTS

2.1.1 Recruitment

A total of *n* = 150 participants were recruited to the study and Table 2.2.1 summarises the sources of recruitment for the current study.

Table 2.2.1: Recruitment source and sample population description (*n* =150).

Recruitment Source	**Population description**	***n***
Bournemouth University	Mainly healthy controls: trauma unexposed and trauma exposed.	77
Dorset NHS (Intensive Psychotherapy Treatment Service, IPTS)	Previous diagnosis of PTSD symptomology and some trauma exposed staff without PTSD	9
Camden and Islington NHS Traumatic Stress Clinic (TSC)	Diagnosis of PTSD, participants in previous study. Limited data sharing. Different demographic and clinical data collection.	10
Dorset and Cambridgeshire Police	Trauma exposure through police work, mainly healthy controls.	27
Combat Stress	Diagnosis of combat-related PTSD plus one healthy staff member	25
Military Fitness	Trauma exposure though military, healthy controls.	2
Total		150

Participants were recruited via:

(i) Bournemouth University Psychology Research Volunteer Scheme (*n* = 77) including staff, students, and members of the public. Advertisements were placed in the Psychology Volunteer Scheme newsletter and were circulated amongst post graduate research students.

(ii) The Intensive Psychotherapy Treatment Service (IPTS) at Dorset Health Care University Foundation Trust (DHCUFT) (*n* = 9) including two members of staff. Recruitment was conducted using poster advertising in the IPTS clinic (Branksome, Poole). Under the clinical supervision of Professor Sue Clarke (BU and IPTS), the project was awarded Clinical Research Network (CRN) "Portfolio Study" status by the National Institute of Health Research (NIHR) in 2013 (reference #120945).

(iii) University College London (*n* = 10) through the participant pool from a previous NHS study (later published as Smith et al., 2015) in collaboration with Professor Chris Brewin at University College London (UCL). These ten participants were originally recruited through the Traumatic Stress Clinic, Camden and Islington NHS Foundation Trust with permission granted through the NHS Integrated Research Application System (IRAS). Consent to contact and recruit former participants was granted through the IRAS system and was undertaken by email via UCL researcher Kirsten Smith.

(iv) Dorset Police and Cambridgeshire Police (*n* = 27). Recruitment for these participants was facilitated by Trauma Risk Management (welfare) officers and Police Federation representatives. The study was advertised online through General Orders (a daily morning email alert) and was authorised by the office of the Dorset Police and Crime Commissioner. Participants from Cambridgeshire Constabulary were recruited through the researcher's own professional network with authorisation from the acting Chief Superintendent.

(v) The military charity Combat Stress (Ex Services Mental Welfare Society Registered Charity # 206002) (*n* = 25). Recruitment was conducted through the PTSD Rehabilitation course (Tyrwhitt House, Leatherhead, Surrey) for which the researcher ran a series of seminars on 'The Brain and PTSD'. Referral to the programme was made by psychiatrists and clinical psychologists at Combat Stress often after referral from General Practitioners (GPs). Recruitment was authorised by the Combat Stress medical director and chair of the Combat Stress Ethics Committee (and Director of the King's Centre for Military Health Research, London). A sample recruitment poster is provided in Appendix A (Section B).

(vi) British Military Fitness and Forces Fit military fitness programmes (*n* = 2). Recruitment of these participants was undertaken through UK Armed Forces fitness groups based in Bournemouth and Winchester.

2.1.2 Exclusions

Five further participants were excluded during recruitment. One participant disclosed having (regularly) lost consciousness for more than one hour due to frequent and treatment-resilient epileptic and non-epileptic Medial Temporal Lobe (MTL) seizures. Two participants were excluded on the basis of their direct genetic relationship to two other participants (this hereditary influence would be a confounding variable in analysis of BDNF and PTSD prevalence). One

participant was excluded after disclosing being under the influence of recreational drugs at the time. A further recruit was excluded mid-screen due to reporting a previous head injury.

2.2 ETHICS

A comprehensive review of the ethical issues involved in this trauma study is provided in Appendix A along with supporting documentation of the ethics approvals.

The principal ethical considerations for this study relate to the vulnerability of those participants recruited with mental health issues (including PTSD) and the collection of human tissue (saliva samples) for DNA extraction. These issues were managed by ensuring that those with clinical or probable levels of trauma impact (that is, Post-Traumatic Stress Disorder) were given information and contact details for advice and support, and were assurances in writing that all participants data was depersonalised, stored securely, and that DNA samples would be destroyed when the study had closed.

Ethical approval comprised:

(i) BU Graduate School Ethics Board approval (including Hazard and Activity Trawl and Risk Assessment) at their meeting of the 22nd November 2012, contingent on obtaining NHS ethical approval (see Appendix A).

(ii) Combat Stress Research Ethics Committee (chaired by Professor Sir Simon Wessely of the KCMHR, London) approval on 16th April 2013 (see Appendix A).

(iii) NHS Ethical approval was obtained from the South West (Cornwall and Plymouth) Research Ethics committee on 6th March 2013, reference #13/SW/0041 (see Appendix A).

(iv) The study was awarded National Institute for Health Research (NIHR) Clinical Research Network (CRN) Portfolio Study status in March 2013, reference #81/2012/2013 (see Appendix A).

2.3 ASSESSING TRAUMA

The main focus of this thesis was to explore differences in navigation skills between those with different experiences of trauma in their lives (and later between those with different variations of the BDNF gene). Essentially, participants were asked to scan through life events for those which may have been traumatic; to recall the severity of any incidents brought to mind; and to reflect on the nature of their responses to the incidents at the time, compared to how they feel now. This was achieved using several tools to assess trauma exposure, trauma impact and clinical levels of trauma (these are introduced in Section 2.3.1, are discussed again where applies in Chapters 3 to 7, and can be found in Appendix F).

2.3.1 Trauma Exposure

Whether an individual had been traumatised by an event in their life was assessed by considering individuals' descriptions of the event and the extent to which subsequent behaviours suggested that they had (or had not) been affected by the traumatic event. This process of understanding whether an individual had been exposed to a potentially traumatic event (or events) and the extent to which it had affected them was supported with the use of

established checklists, screens and diagnostic scales (all of which are provided at Appendix F). These comprised:

(i) **The Life Events Checklist (LEC, Blake et al., 1995).** This provides a simple list of experiences in life which are typically outside the parameters of everyday life experience, and which are of a nature which could be deemed 'traumatic'. The lists ranges from domestic violence, to witnessing fatalities, to earthquakes. The LEC is used as a prompt to enable participants to reflect on whether they think they have been exposed to a traumatic incident which may fulfil APA criteria for a trigger to PTSD (i.e. exposure to actual or threatened death, serious injury or sexual violation). In practice, individuals are usually aware of whether they have experienced something which was traumatic or not, but the list was helpful for those who were unsure of their own perception of what they experienced (either because they may have experienced these events as part of their job, or if they were avoiding discussing the experiences). In terms of the sample population, the n = 125 participants who reported trauma exposure reported a range of incidents from domestic violence and road traffic collisions, to witnessing infant rape and experiencing mock execution.

(ii) **The Diagnostic and Statistical Manual version five (DSM-V criteria)** (Bedard Gilligan & Zoellner, 2008). This describes how experiences may be classified as 'traumatic' in their impact. The diagnostic criteria require that the trauma exposure must result from: directly experiencing the traumatic event; witnessing the traumatic event in person; learning that the traumatic event occurred to a close family member or close friend (with the actual or threatened death being either violent or accidental); or experiencing first-hand repeated or extreme exposure to aversive details of the traumatic event (not through media, pictures, television or movies, *unless work-related*, DSM-V, 2015).

(iii) **The Brief Trauma Screen (BTS, Brewin et al., 2002).** This is a 'light-touch' series of ten questions which describe what it is like to feel traumatised by an incident. This helps to give an early indication that individuals have found an event to be traumatic, even if such an event did not appear on the LEC (Blake et al., 1995).

The aim for the study sample was for it to include individuals who had not been exposed to trauma as well as individuals who had. While some studies, such as that by Smith et al., (2015) have focussed on whether individuals can successfully process trauma they have been exposed to (and therefore only include trauma exposed participants), the intention for this study was additionally to consider individuals who had no trauma exposure to process. Comparison of trauma exposure cases versus cases of no trauma exposure has been undertaken in previous research but not in conjunction with cases of PTSD nor in the same design, or in the context of spatial navigation (Yehuda et al., 2005; Lyoo et al. 2011; Zhang et al. 2014; Lee et al. 2006; Duke & Vasterling, 2005; Valente et al. 2011; Karunakara et al., 2004). By including participants with no self-reported experience of trauma alongside those who reported trauma experiences (with and without PTSD), this enables a consideration of the potential disruption that *any* trauma exposure might have on healthy individuals' navigation behaviour, irrespective of PTSD status.

The criteria for data which was relevant to this study was: for participants to have been unexposed to trauma (i.e. reporting no exposure to any incidents on the LEC, Blake et al., 1995), *or* to have been exposed to trauma (i.e. such as listed on the LEC) and *either* to be clinically unaffected (i.e. to not score at clinical or probable levels of PTSD as a result, on the PDS scale by Foa et al., 1995) *or* to be affected (i.e. scoring at clinical or probable levels of PTSD on the PDS).

The three experimental groups therefore comprised the following: individuals who self-reported no exposure to trauma; those who reported being exposed to trauma but who were not adversely affected; and those who reported being currently negatively affected by trauma exposure, experiencing symptoms of Post-Traumatic Stress Disorder (PTSD). These groups are described in more detail later in Section 2.3.3. Grouping sample populations by trauma exposure and PTSD status is typical for trauma studies in the wider literature (e.g. Smith et al. 2015; Bisby et al. 2010, 2015; Wang, 2015)[3].

2.3.2 Post-Traumatic Stress Disorder (PTSD)

Studies which have investigated the neuropsychological impact of trauma typically compare groups on the basis of whether participants have a clinical diagnosis (or probable levels of) Post-Traumatic Stress Disorder (PTSD) or not (Sheerman & Zimmerman, 2002; Yehuda et al., 2005; Lee et al., 2006; Hemmings et al., 2009; Tempesta et al., 2011; Smith et al., 2015). By way of a reminder, Post-Traumatic Stress Disorder (PTSD), the condition, features in the psychiatric manual the DSM-V (APA, 2013) and is said to comprise "a history of exposure to a traumatic event ...that meets specific stipulations and symptoms from each of four symptom clusters: intrusion, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity" (APA, 2013). In the current study, PTSD diagnosis was classified using the PTSD Diagnostic Scale (or PDS) by Foa et al. (1995). This can be found in Appendix F. The PDS was favourable in comparison to other measures which were also reviewed (see Table 2.3.2 overleaf).

PTSD was classified using the standard severity threshold of 'moderate to severe' which equates to a score equal to or over 21 on the PDS (Foa et al., 1995; Griesel et al., 2006). The PDS thresholds comprise: 1–10 (mild), 11–20 (moderate), 21–35 (moderate to severe) and >36 (severe). The threshold of 21 was also employed by Smith et al. (2015) in their similar study of the effects of PTSD on spatial processing. An alternative threshold of 27 (recommended by Sheerman & Zimmerman, 2002) was discounted on the basis that this would only include the most severe cases of PTSD, rather than 'probable' levels of PTSD which was the focus of this study.

[3] Alternative trauma groupings were also considered and more information can be found at Appendix D.

Table 2.3.2: Comparative means of assessing the impact of trauma to the PTSD Diagnostic Scale (Foa et al., 1995).

Alternative trauma screen	**Comparison to PDS (Foa et al., 1995)**
Davidson Trauma Scale (DTS) (1997).	The DTS offers detail about trauma impact which were superfluous to this study which would have incurred unnecessary financial expense.
Structured Clinical Interview (SCID) for the DSM- IV (First, et al., 1997)	The SCID offers extensive detail about comorbidity as well as trauma impact, information which would be superfluous to this study. There was also a substantial training commitment for delivering the SCID which would have delayed the data collection considerably.
Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV)	Satisfaction of DSM-IV criteria would not provide impact scales and would require professional psychiatric assessment.
PTSD Symptom Scale Interview (PSS-I) (Foa, 1995)	The PSS-I was comparable to PDS but includes frequency and intensity ratings which were deemed unnecessary for the study.
Clinician-Administered PTSD Scale (CAPS) (Weathers et al., 2013)	The CAPS included details of functional impairment, onset, severity, and impact etc. which were deemed unnecessary for this study.

PDS scores were used to assess trauma impact in the here and now, rather than retrospective trauma impact at the time of the incident in question. This was to ensure that participants were being examined for their capacity to *process* and to have processed trauma, rather than the extent to which they were immediately affected by the extreme nature of a traumatic incident. For those with both previous childhood trauma and more recent adult trauma, current PDS scores were taken for both childhood and adulthood trauma experiences and the higher of the two PDS scores was used in analysis.

Participants were allocated to one of three experimental groups:

(i) Those unexposed to trauma (i.e. those who reported no experiences of trauma, having seen the Life Events Checklist by Blake et al., 1995), referred to as the '*Trauma Unexposed'* group;

(ii) Those exposed to trauma with no PTSD, i.e. a score of 0 or below 21 on the PDS, referred to as the '*Trauma Exposed No PTSD'* group; and

(iii) Those with clinical or probable levels of Post-Traumatic Stress Disorder (PTSD) with a score of 21 or over on the PDS, referred to as the '*PTSD'* group (and these participants are by default trauma exposed).

This three-way grouping was used as the between-groups measure for the main body of the analysis, as presented in Table 2.3.3 below.

Table 2.3.3: Overview of experimental group structure in the sample population (*n* = 150): *Trauma Unexposed vs Trauma Exposed No PTSD vs PTSD*.

Experimental group		
Trauma Unexposed	Trauma Exposed No PTSD	PTSD
n = 33	*n* = 60	*n* = 57

2.3.3 Trauma type

Finally, specific types of trauma were also considered in the design of the current study, namely childhood trauma and combat-related trauma. Firstly, childhood trauma and the timing of trauma exposure during critical periods of development is often a key consideration in trauma studies and studies pertaining to hippocampal processing (Teicher et al., 2012; Bremner et al., 1997; Andersen et al., 2008; Kirmayer et al., 2007; Frodl et al., 2010; Carrion et al., 2001; Gee et al., 2013; Brewin et al., 2000; Vasterling & Brewin, 2005; McGowan & Szyf, 2010; Carballedo et al., 2013; Frodl et al. 2010; Doidge, 2007; Bagot et al., 2007). Childhood trauma impact was recorded using Brewin's (2002) adaptation of Bernstein and Fink's (1998) Childhood Trauma Questionnaire (CTQ). Brewin's (2002) version of the CTQ only comprised 10 items which was deemed favourable to the original by Bernstein and Fink (1998) which comprised 28. This was because the initial intention for this study was to gain some indication of the extent to which adult participants may or may not have been effected by childhood trauma, rather than to measure in detail the manifestation of that trauma. However, adults' recall of previous childhood trauma was inconsistent and many participants reported not feeling confident in assessing trauma impact in hindsight as an adult- this effected the quality of the data. Furthermore, for the effects of childhood trauma to be fully investigated, the study would ideally have recruited a sample group with *only* childhood trauma (as opposed to childhood trauma in addition to adult trauma) and this was unachievable in the time frame for the study[4].

Secondly, combat-related trauma was also considered in the design of the study. The Combat Stress (registered military charity) sample population (*n* = 25) provided a clinically diagnosed sample of participants with PTSD. However, their profile differed to non-military participants, predominantly because their trauma had been experienced in a professional capacity, but also because of the likely navigation training that accompanies military training in the UK (for more information about this, see Chapter 6 Section 6.1.2[5]). The aim for the current study was to control for any such effect of trauma being 'work-related' and so exposure from non-military occupations was also represented (e.g. see Asmundson et al., 1998). To this effect, Police officers (*n* = 26) were recruited to the sample from Cambridgeshire and Dorset constabularies, all of them reporting trauma exposure from incidents experienced in a professional capacity. Further differences in the profile of those with combat-related PTSD compared to non-combat PTSD are explored in Chapter 6 (Sections 6.1.2 and 6.4.2).

[4] The prevalence of adult PTSD in those who have had unrelated childhood trauma in addition to adult trauma exposure is such that recruiting participants who are adults who have *only* had childhood trauma is notoriously difficult. See Brewin & Holmes (2003), KCMHR (2010), Bremner et al. (1993).

[5] Evidence and examples of navigation training in the military include: Phase One Initial Training; Manual Annual Training Test (MAAT); Marines Commando training.

2.4 BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF)

2.4.1 BDNF genotypes

Exploration of the role of the Brain-Derived Neurotrophic Factor (BDNF) gene in the relationship between PTSD and navigation was introduced to the study in its second year after the literature review. The influence of the BDNF gene on the relationship between PTSD and navigation was assessed by using saliva to determine BDNF genotype (as being either *valval, valmet* or *metmet*). This method was distinct from some other studies which have measured neurotrophic proteins which are *associated* with BDNF genotypes (e.g. Banner et al., 2011; Lövdén et al., 2011) or the presence of secreted BDNF in blood (e.g. Unternaehrer et al., 2012) or plasma (e.g. Rakofsky et al, 2011; Van de Heuvel et al., 2016).

The BDNF homozygote '*metmet*' is carried by less than 4% of the population and in this study the sample size of this group was *n* = 7. Studies of this sample size (where there are fewer than ten individuals of the *metmet* BDNF genotype) typically combine *valmet* and *metmet* groups (e.g. Egan et al., 2003; Hariri et al., 2003; Pezawas et al., 2004; Dempster et al., 2005; Van de Heuvel et al., 2016). This was the approach taken in this study. This meant there were two main BDNF groups: valval homozygotes and met carriers. Again, the observed populations were as expected from the wider population, as presented in Table 2.4.1.

Table 2.4.1: Observed vs expected (Frielingsdorf, Petryshen et al., 2010) BDNF populations (n = 150) with valval homozygotes (70%) and met carriers (30%).

BDNF genotype	Valval homozygotes	Met carriers
Sample population (Observed)	*n* = 104, 69.3%	*n* = 46, 30.7%
Caucasian population (Expected)	*n* = 105, 70%	*n* = 45, 30%

2.4.2 BDNF population sample size

The introduction of the BDNF gene into this research study in 2013 rendered the study a 'candidate gene study', and this brought with it the need to achieve an adequate sample size to be able to demonstrate a significant effect of the gene. Achieving a viable sample size was also part of the scientific criteria by which the study was granted clearance through the IRAS system and by which the study was able to achieve NIHR 'CRN Portfolio Study' status. The sample size (*n* = 150, *n* = 57 with PTSD) was comparable with sample sizes from recent and similar studies into the same gene (BDNF) and the genetic profile of the sample proved to be proportionate statistically to the genetic profile of the wider population.

Examples of comparable studies' sample sizes include studies by: Zhang et al. (2013) who tested 49 Special Operation veterans with PTSD, and 491 without; Hemmings et al. (2012) who studied 150 'at risk' (trauma exposed) participants and found statistical differences in PTSD development on the basis of the BDNF genotype and another candidate gene, DRD2 Taq1A; Hemmings et al. (2013) who demonstrated an interaction between BDNF and childhood trauma for Obsessive Compulsive Disorder (OCD) in a sample of 134 patients (*n* = 188 controls); and, finally, Gatt et al. (2009) analysed brain imaging data from only 89 participants and found statistical differences between BDNF genotypes.

With regard to proportionality with the wider Caucasian population, the BNDF gene has three variations (i.e. genotypes or 'polymorphisms'; 'valval', 'valmet' and 'metmet') and ideally the study's sample should replicate the proportions of these genotypes found in the wider population. Based on established Caucasian population data (e.g. Frielingsdorf et al., 2010; Petreyshen et al., 2010) the expected BDNF genotype proportions were as follows: 70% for 'valvals', 26% for 'valmets' and 4% for 'metmets'. Chi-square revealed that there was no significant difference between observed and expected BDNF populations in this study (n = 150), $\chi^2 = 0.37$, $p = 0$ .83. Table 2.4.1 and Figure 2.4.1 below illustrate the distribution of BDNF genotypes compared to expected populations and across the experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*).

Table 2.4.1: Observed vs expected (Frielingsdorf, Petryshen et al., 2010) BDNF populations (n = 150).

BDNF genotype	Valvals	Valmets	Metmets
Sample population (Observed)	n = 104, 69.3%	n = 39, 26%	n = 7, 4.7%
Caucasian population (Expected)	n = 105, 70%	n = 36, 26%	n = 9, 4%

2.5 DEMOGRAPHIC AND CLINICAL FACTORS

Previous research (which is summarised in Table 2.5) suggests that age and gender may systematically affect hippocampal processing and navigation skills. These variables were considered across the sample population (Tables 2.5.1 and 2.5.2). More detail about the bearing of specific factors to specific research questions and experiments is provided in the relevant chapters (3 to 7).

Table 2.5: Summary of research indicating that age and gender may have a bearing on hippocampal processing and navigation.

Demographic Factor	Literature reviewed
Age	Hippocampal dependent processing (Smith et al., 2015; Daugherty et al.,2015; Rosenweig & Barnes, 2003; Raz et al., 2009; Moffat et al., 2001, 2009; Wiener et al., 2012, 2013; Daugherty et al. 2015); Virtual navigation (Driscoll et al., 2005); mobility and navigation (Burns, 1999); spatial cognition (Klencken et al., 2012); age, sense of direction and driving (Turano et al., 2009) Navigation strategy use (Rodgers et al., 2012; Nicolle et al., 2003); Self-reported navigation confidence (De Beni et al., 2006; Borella et al., 2014); age, genetics and working memory (Nagel et al, 2008) Hippocampal activation in PTSD with age (Carrion et al., 2010); PTSD therapy and age (Duax et al., 2013); BDNF, hippocampal volume and aging (Erickson et al., 2010).
Gender	Hippocampal size (Luders et al., 2015); Self-reported navigation confidence (Furnman et al., 2014; Lawton et al., 1994; Münzer & Stahl, 2011 Navigation strategy (Schmitzer-Torbert, 2007; Meneghetti et al., 2010; Daugherty et al.,2015)

Table 2.5: Summary of research indicating that age and gender may have a bearing on hippocampal processing and navigation.

2.5.1 Demographic factors

Tables 2.5.1 and 2.5.2 provide information about the distributions of both age and gender across the sample (*n* = 150) by experimental group (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) and by BDNF groups (*valval homozygotes, met carriers*).

Table 2.5.1: Mean age (in years) in sample (*n* = 150) stratified by both experimental group *(Trauma Unexposed, Trauma Exposed No PTSD, PTSD)* and BDNF genotype.

	Trauma Unexposed	**Trauma Exposed No PTSD**	**PTSD**	**Group comparison**
Age	32.5 ± 10.4	38.7 ± 10.3	39.1 ± 9.9	F (2, 147) = 5.04, p < 0.01**
	Valvals	**Met carriers**		t (148) = -1.20, p = 0.23
	36.8 ± 10.6	39 ± 10.0		

Table 2.5.2: Distribution of gender in sample (*n* = 150, 69 females) stratified by both experimental group *(Trauma Unexposed, Trauma Exposed No PTSD, PTSD)* and BDNF genotype.

	Trauma Unexposed	**Trauma Exposed No PTSD**	**PTSD**	**Group comparison**
Gender	Females (*n* = 21) 64%	Females (*n* = 32) 53%	Females (*n* = 16) 28%	$\chi 2$ = 12.8 p < 0.01**
	Valval	**Met carriers**		$\chi 2$ = 4.79 p = 0.03*
	Females (*n* = 54) 52%	Females (*n* = 15) 33%		

The PTSD group was significantly older than the *Trauma Unexposed* group and females were underrepresented in the *PTSD* group (likely due to the all-males sample of ex-military participants with *Combat-Related PTSD*, *n* = 27). Females were also underrepresented in BDNF met carriers. Both age and gender were therefore considered in later statistical analysis.

2.5.2 Clinical factors

Previous research has shown that the experience of pain, medication, sleep disturbance and depression can affect either hippocampal processing or navigation skills (see Table 2.5.3 overleaf).

Table 2.5.3: Summary of literature examining clinical factors (pain, medications, sleep and depression) which may have a bearing on hippocampal processing and navigation skills.

Clinical factor	Literature reviewed
Pain	Spatial memory in rats (Cardoso-Cruz et al., 2013) Low hippocampal BDNF in rats (Duric & McCarson, 2005, 2006).
Medications	SSRI's increase hippocampal neurogenesis and plasticity (Anacker et al., 2011; Bath et al., 2012; Engel et al., 2013) BDNF and antipsychotics (Autry et al., 2012); Antipsychotics supress hippocampal neurogenesis (Luo et al., 2005) Opiates and hippocampal long term potentiation (Pu et al., 2005).
Sleep disturbance	Hippocampal neuroplasticity (Doidge, 2007; Gorgoni et al., 2013); hippocampal-dependent memory consolidation (Albouy et al., 2013); PTSD symptomology and navigation (Tempesta et al., 2011).
Depression	Co-morbidity with PTSD (Campbell et al., 2007; Smith et al., 2015). Trauma therapy and depression (Hemmy-Asamsama et al., 2015);

Data about pain was collected via the standard Numerical Rating Scale (NRS, Jensen et al., 1986), which is presented in Table 2.5.4.

Table 2.5.4: Numerical Rating Scale (NRS) for pain (Jensen et al., 1986).

Rating	Pain Level
0	No Pain
1 – 3	Mild Pain (nagging, annoying, interfering)
4 – 6	Moderate Pain (interferes significantly)
7 – 10	Severe Pain (disabling)

A number of participants were taking medications that had the potential to interfere with hippocampal-dependent memory systems: two were taking Mirtazopine (Engel et al., 2013); 13 were taking opiates (Pu et al., 2005); and one was taking Quetiapine (Luo et al., 2005). The majority (14 out of 16) of the participants taking either opiates or antipsychotics were in the *PTSD* group.

Sleep disturbance was measured in the current study using the Pittsburg Sleep Quality Index PSQI-Addendum for PTSD by Germain et al., (2005) which consists of seven items that focus on the frequency of seven disruptive nocturnal behaviours in the preceding month. A score of 5 or over is taken as an indicator of sleep disturbance.

Co-morbidity of PTSD with depression is common in clinical (Hemmy-Asamsama et al., 2015; Vasterling & Brewin, 2005) and experimental psychology (Campbell et al., 2007) and higher depression scores (using the Becks Depression Inventory BDI, Beck et al., 1996) were expected in the PTSD sample. In their similar study, Smith et al. (2015) only controlled for depression by excluding one control participant (out of n = 30 control participants) who scored

moderately on the BDI. In the current study none of the control participants scored in the moderate range (or above) on the BDI and BDI score was therefore not included as a covariate in further analysis.

2.5.3 Clinical Index

For reference purposes, Table 2.5.3 below presents a basic 'clinical index' (CI) of the extent to which clinical influences are represented across experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD,* PTSD) and BDNF genotypes. As with demographics factors, more detail about the bearing of specific clinical factors to specific research questions is provided in the relevant chapters.

The Clinical Index (CI) comprised of a score of 1 point per clinical factor, i.e. any score on the NRS pain scale (i.e. a score of more than zero); the taking of either SSRIs (Selective Serotonin Reuptake Inhibitors), benzodiazepines, opiates or antipsychotics; any sleep disturbance score on the PSQI-A; and any score on the depression index (BDI). The maximum score was 7. Data validity was limited due to missing values for the *n* = 10 participants from UCL from whom data on medications and sleep quality were not collected.

Table 2.5.3: Mean Clinical Index (CI) score in sample of participants (*n* = 150) as a function of experimental group (*Trauma Unexposed, Trauma Exposed No PTSD,* PTSD) and BDNF genotype (*valval homozygotes, met carriers*).

Group			**Group comparison**
Trauma Unexposed (*n* = 33)	**Trauma Exposed No PTSD** (*n* = 60)	**PTSD** (*n* = 57)	*F* (2, 147) = 31.4, *p* <0.001**
0.73 ± 0.98	1.12 ± 1.01	2.60 ± 1.54	
Valval (*n* = 104)	**Met carriers** (*n* = 46)		*t* (148) = 0.52, *p* =0.58
1.63 ± 1.50	1.50 ±1.39		

Pairwise comparisons showed significantly more clinical factors are present in the *PTSD* group than both the *Trauma Unexposed* group and the *Trauma Exposed No PTSD* group. The Clinical Index did not significantly differ between the *Trauma Exposed No PTSD* and the *Trauma Unexposed* group. The Clinical Index did not significantly differ between BDNF genotypes.

2.5.4 Excluded factors

2.5.4.1 ALCOHOL CONSUMPTION

An original intention of the study was to collect data pertaining to participants' weekly units of alcohol consumption. Low levels of alcohol consumption had been identified as a positive influence on the number of PTSD-related visual intrusions individuals experience and a negative influence on hippocampal dependent spatial processing in a study by Bisby et al. (2010; 2015). Alcohol consumption was also considered in clinical settings to be specifically disruptive to trauma recovery (Combat Stress, 2012) and so alcohol intake was identified as a possible variable to control for in this study. A review of related literature revealed that it is not uncommon for self-reported alcohol intake measures to be unreliable (Whitford et al., 2009). Consistent with this unreliability in the current study there were also relatively high levels of missing data (14%) in relation to alcohol consumption. In addition, there were concerns about

the pressure on combat veterans to self-report 'no alcohol intake', given that this was an inclusion criteria for the PTSD rehabilitation programme they were undertaking with Combat Stress.

2.5.4.2 IQ, VISUO-SPATIAL ABILITY AND EDUCATION

Controlling for IQ (Intelligence Quota), visuo-spatial ability and education was not undertaken in the current study, but was in a study which was published by Smith et al. in 2015 (which assessed differences in allocentric spatial processing in those who had PTSD and those who did not have PTSD after trauma exposure). The rationale for not considering IQ in the current study had been based on the fact that IQ had not featured as a confounding variable in the literature about hippocampal processing reviewed for this study. For example, Vasterling et al. (1998) found that sustained attention and initial learning (on a battery of tests including the Stroop colour test, and the Wisconsin card-sorting test) was affected by PTSD but that this was *independent of intellectual functioning*. Brandes et al. (2002) found no impairment in verbal recall and learning (in numerous tests such as the digit span test, and picture completion tests in Weschler's Adult Intelligence Scale and Memory Scales) *despite lower IQs* in those with PTSD compared to those without. Lastly, Knauss (2007) presented a case that visuo-spatial reasoning (such as that tested by Smith et al. in 2015) was one cognitive function that was *'least* likely' to be affected by PTSD. Nonetheless, Smith et al. (2015) controlled for visuo-spatial ability using IQ tests of verbal functioning and Raven's Advanced Progressive Matrices (RAPM) and the implications of this are discussed in Chapters 3, 4 and 8.

2.5.4.3 NAVIGATION EXPERIENCE AND PTSD TREATMENT

Participants were asked descriptive questions about previous navigation experience (either specific training or undertaking navigation as part of their everyday employment) and previous PTSD treatment (therapy). These questions are provided in Appendix I. This information was sought so that one could establish if some participants had had extensively more opportunities to either improve their own performance in hippocampal dependent navigation or to actively engage in trauma processing. The quality of these data however was limited due to missing values (at 21.3%) which precluded their inclusion in statistical analysis. However, the question of access to navigation training is considered further in Chapter 6.

2.6 MATERIALS

2.6.1 Spatial processing and navigation paradigms

The research required reliable means of assessing differences in allocentric and egocentric navigation behaviour which could be attributable to group influences. Two tests were used:
a) A simple, quick, easily applied static paper-based test of allocentric spatial processing (Hartley, Bird and Chan, 2007); and
b) A more involved and 'active', virtual environment (VE) task that would provide more rich data about allocentric and egocentric navigation performance and strategy use (Wiener, de Condappa, Harris and Wolbers, 2013).

2.6.1.1 THE FOUR MOUNTAINS TASK

A review of the spatial processing literature was undertaken to identify a static, paper-based spatial processing test which could be used to quantify allocentric spatial processing abilities. Many spatial processing tests were discounted either due to uncertainty over their ability to test allocentric processing, or because of a lack of ecological validity. More information about the review can be found in Chapter 3, Section 3.1

The Four Mountains task by Hartley et al. (2007) is a static paper-based topographical test of spatial memory and which is thought to require allocentric processing (Hartley et al., 2007; Bird et al., 2010; Hartley & Harlow, 2012). The task (depicted in Figure 2.6.1) requires an individual to be able to apply perspective taking to a topographical scene after having committed a visual representation of the scene to short term memory. The test is described in more detail in Chapter 3, Section 3.2.3.

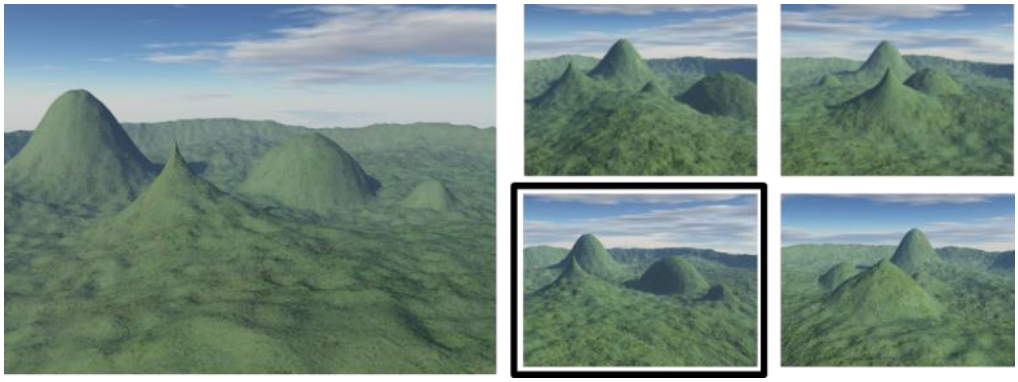


Figure 2.6.1: Image extracted from the Four Mountain spatial memory test (Hartley et al., 2007). The highlighted box indicates the correct answer for this match-to-sample test.

2.6.1.2 THE ALTERNATIVE ROUTE

Virtual Environment (VE) and Virtual Reality (VR) task paradigms (becoming increasingly ecologically valid) are popular in the testing of allocentric spatial processing and navigation. They have already been used in studies similar to the present one, some of which have involved trauma processing (such as that by Tempesta et al., 2011) and others the BDNF gene (such as that by Banner et al., 2011). A review of the spatial processing literature was undertaken to identify a more involved and 'active', Virtual Environment (VE) task that would provide richer data about allocentric and egocentric navigation performance and strategy use. The outcome of that review is provided in Chapter 4 (Section 4.1.8). The paradigm deemed most appropriate for the purpose of this investigation into trauma group differences in hippocampal dependent (allocentric) and *in*dependent (egocentric) spatial processing performance and strategy use was the Alternative Route (AR) paradigm introduced by Wiener et al. (2013).

The AR paradigm was designed to assess age-related differences in allocentric and egocentric navigation strategy use and performance (Wiener et al., 2013). The AR paradigm's sensitivity to age-related processing bias for egocentric navigation (Wiener et al., 2103) was something which could be highly relevant for this investigation of trauma exposure and PTSD. Wiener et

al.'s (2013) hypothesis was that spatial processing impairment may manifest in older persons (who would potentially be suffering from age-related hippocampal atrophy) and that these older persons would exhibit a "maladaptive bias" for a hippocampal *in*dependent (i.e. egocentric) navigation strategies. In turn, the current study sought to test the hypothesis that trauma exposed participants, (*potentially* suffering from hippocampal dependent processing deficits, as in Bisby et al., 2010; Smith et al., 2015) would also exhibit a 'maladaptive bias' for egocentric navigation strategies. This is explained in more detail in Chapter 4.

With regards to the potential role of the BDNF gene, Banner et al. (2011) demonstrated a maladaptive bias toward a hippocampal *in*dependent (egocentric) navigation strategy amongst 'met' carrying BDNF genotypes using a similar experimental model to the AR paradigm. This will also be addressed in the research and this is explained in more detail in Chapter 7.

By way of introduction, the AR paradigm (Wiener et al. 2013, pictured below at Figure 2.6.2) is a novel route-learning paradigm designed to test hippocampal dependent (allocentric) and hippocampal *in*dependent (egocentric) navigation performance and to identify the application and type of spatial processing strategies used. The objective of the task is to commit a route to memory over 24 minutes so that the route can be used flexibly when participants are tested on it throughout the task. Figure 2.6.2 provides a screen shot of the virtual environment, an illustration of the training route that needed to be learned on the task, and an example of tests on the route (coming from same and different directions). More information about how the AR paradigm assessed navigation performance can be found in the Materials Section 4.2.3. The Alternative Route paradigm produced complex and highly detailed data. More detail about AR performance measures used in this study are provided in Chapter 4, in the Materials section 4.2.3. Further information about the performance measures which were discounted for use in this study can be found in Appendix G.

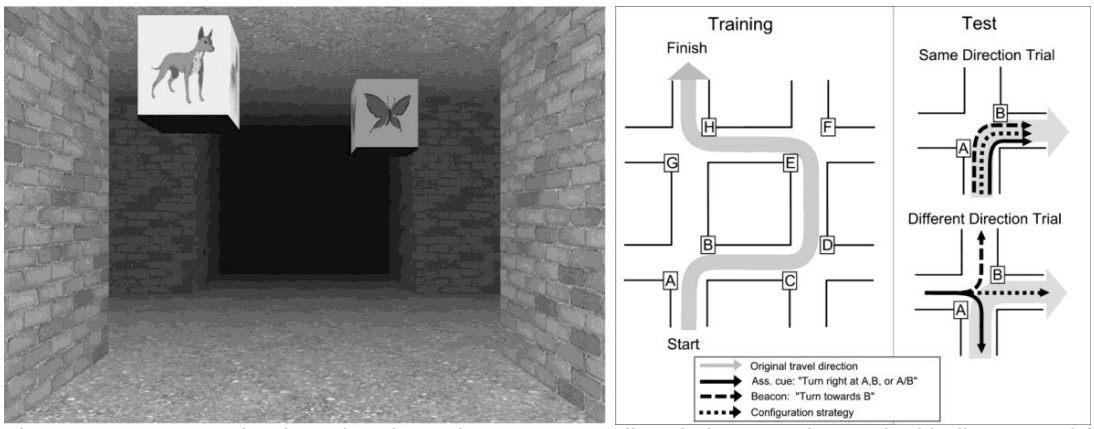


Figure 2.6.2: Screen shot from the Alternative Route Paradigm (Wiener et al., 2013) with diagrams of the training route and test intersections.

2.6.2 Navigation questionnaires

An important element of this study into trauma, BDNF and navigation behaviour is to better understand individual's application of allocentric and egocentric processing in everyday life. Self-reported navigation questionnaires can provide important additional insights into individuals' navigation behaviours and beliefs about navigation competence. The three most prominent in the literature reviewed for this study were:

(i) The Santa Barbara Sense of Direction (SBSOD) by Hegarty et al. (2002);
(ii) The Questionnaire of Spatial Representation (QSR) by Pazzaglia & De Beni (2001);
(iii) The "Fragebogen Räumliche Strategien" (FRS, translated as the 'questionnaire on spatial strategies') by Münzer & Hölscher (2011).

These questionnaires measure individuals' awareness of their navigation competence vs rating one's navigation competence and questions refer to perceptions of general confidence in 'sense of direction'; preferences for -and likelihood of using- certain navigation strategies in certain scenarios; and likelihood of responding successfully to navigation demands. The three questionnaires assess general confidence as well as confidence in specific navigation styles or strategies which can be characterised as egocentric (route-based and landmark based strategies) or allocentric (map- based strategies) or those using cardinal or 'compass' directions. Questions are scored on a Likert-type scale. (For a full list of questions in each survey, see Appendix C.)

These questionnaires have extensively been applied in research into hippocampal dependent spatial processing, performance and strategy use (Schinazi et al., 2013; Epstein et al., 2005; Nilsson, 2012; Janzen et al., 2008; Halko et al., 2014; Pazzaglia et al., 2011; Furnman et al., 2014).

The diversity of the questions in the three questionnaires made it possible to compare participants' self-reported awareness of (and confidence in) both allocentric and egocentric information processing in navigation. In Chapters 5 and 6, egocentric and allocentric question scores were correlated with data from the Four Mountains task and the Alternative Route paradigm, i.e. allocentric (hippocampal dependent) and egocentric (hippocampal *in*dependent) spatial processing performance (Sections 5.4.1 and Section 6.3.1). This was to ascertain how 'aware' individuals were of their own egocentric and allocentric navigation competence. Assessment was undertaken in different experimental groups within the sample population (based on trauma exposure in Chapters 5 and 6, and based on BDNF genotype in Chapter 7) to see how self-reported confidence correlates with performance, in those who have had different experiences of trauma, and who are of different BDNF genotypes.

Full copies of the questionnaires are provided in Appendix C and the validity of the questionnaires and their allocentric and egocentric subsets of questions are explained in greater detail in Chapter 5, Section 5.2.

2.7 PROCEDURE

Summary

Table 2.7 below describes the study's experimental procedure, including: the taking of consent, collection of demographic and clinical data, trauma screening, navigation questionnaires, the Four Mountains Task, the Alternative Route paradigm and the collection of DNA (BDNF) saliva samples.

Table 2.7: Summary of procedures in sequential order for study participants.

ASSESSMENT	PROCEDURE
RECRUITMENT	
Consent	Information Sheets sent online and Consent forms completed by hand (at time of testing)
Demographics and clinical information	Online demographic and clinical survey (including navigation experience and treatment status)
TRAUMA ASSESSMENT	
Trauma exposure status	Life Events Checklist (Blake et al.,1995) (including early separation question) sent by email.
Childhood trauma screen	Online Childhood Trauma Questionnaire (Brewin et al., 2002)
Trauma impact (current)	Online PTSD diagnostic Scale (Foa et al., 1995)
NAVIGATION PERFORMANCE	
Self-reported navigation competence	Three online navigation questionnaires: SBSOD (Hegarty et al., 2002); QSR (Pazzaglia & De Beni, 2001); FRS (Münzer & Hölscher, 2011).
Spatial processing task	The Four Mountains task (Hartley et al., 2007) in laboratory.
Navigation paradigm	The Alternative Route Paradigm (Wiener et al., 2012) in laboratory.
DNA SCREEN	
BDNF genotype test	DNA Genotek Orangene™ self-test saliva kit in laboratory or by post.

2.7.1 Consent

Information sheets were sent (and / or given) to all participants and consent was obtained from all participants (*n* = 150, see Appendix A). Email addresses were collected with consent forms for correspondence purposes and to provide those participants willing to complete data collection online with a unique identification code and a confidential link to an online version of the research surveys (in SNAP™) hosted securely by the Market Research Group (MRG) at Bournemouth University.

Recruited participants were asked if they were willing to provide demographic data and complete trauma screens and navigation questionnaires in advance over email or if they wished to complete them at the beginning of the experimental session. Those willing to complete them in advance were sent the link over email. Trauma unexposed (control) participants were given the option to complete surveys at the experimental session (rather than online) and were asked to allow 45 minutes to complete them *in situ* at the BU laboratory. Laboratory completion of

questionnaires prior to testing was not deemed appropriate for participants with trauma exposure. This was due to the potential risk of re-exposing these participants prior to testing which could cause individuals unnecessary distress and could negatively bias navigation test data, reducing its validity.

All participants were assured that they were free to stop the experiment at any time and to withdraw from the study at any point without needing to give an explanation.

2.7.2 Demographic and clinical data

Participants completed a confidential demographic and clinical survey using their unique identification code. Data were saved in an encrypted folder on a Bournemouth University secure server. One password protected copy was retained by the researcher on a personal computer for back-up purposes. No data which could identify a participant to an external party were included in the research dataset.

2.7.3 Trauma screening

Participants were given the Life Events Checklist (Blake et al., 1995 which can be found in Appendix B, and which was introduced in Section 2.3) and were asked to indicate if they had been exposed to a traumatic life event: those who reported no exposure to a traumatic event proceeded to complete the navigation questionnaires; those who reported previous trauma exposure to a traumatic event were asked if this was in childhood, adulthood or both.

Participants with childhood trauma were given the Childhood Trauma Questionnaire (CTQ, Brewin et al., 2002 which can be found in Appendix B, and which was also introduces in Section 2.3) to complete, recalling (as best they could) what their responses were at the time of the incident. These participants were then asked to complete the standard adult Post-Traumatic Stress Disorder Diagnostic Scale (PDS, Foa et al., 1995, which can be found in Appendix B, and which was also introduced in Section 2.3) to ascertain the extent to which this childhood trauma still affected them. If participants indicated that they were only exposed to trauma in adulthood, they were given the adult PDS (Foa et al., 1995) and were asked to complete it with two different time anchors: namely, basing their responses on a) how they recalled feeling at the time of the event and b) how they feel about the event now. Only current total PDS scores (from either childhood or adult trauma -or both) were used in in the main analysis.

Participants were also asked if they were separated from their biological parents at an early age (under the age of 5 years old) for a substantial time (such as hospitalisation or social care), so as to give an indication of *potential* childhood trauma which may not have been consciously recalled as being such by the adult in the present day. These data were recorded for control purposes but substantial levels of missing values (30%) precluded inclusion in the main analysis (see Section 2.8.8.2 for more information on their exclusion).

Data were either collated electronically using SNAP™ software (survey software for designing and hosting online questionnaires) and converted into SPSS or were manually inputted directly into the research dataset.

2.7.4 The Four Mountains task

Participants were given verbal instructions for the Four Mountains Task (Hartley et al. 2007) and were provided with a 'practice' version of the task to ensure that the instructions were understood. The ten minute task was undertaken by hand and timed under the supervision of the researcher. Data was collected using a standard response sheet which was scanned for back up purposes and then manually entered into the research dataset for analysis.

2.7.5 The Alternative Route paradigm

Participants were given hard copy instructions for the Alternative Route Paradigm (Weiner et al. 2013) and verbal (scripted) instructions were provided by the researcher. A five minute demonstration version of the paradigm was presented to each participant to ensure all participants were familiar with the onscreen layout and the controls before proceeding with the 24 minute task. Data were saved in the BU psychology laboratories, processed using specialist software and integrated into the main research dataset by the researcher using double data entry. Data quality checks were conducted for 10% of the dataset at each data upload session.

2.7.6 Navigation questionnaires

Participants were provided with either electronic or hard copies of the three navigation questionnaires. Data was either collated electronically using SNAP™ software and converted into SPSS or manually inputted directly into the research dataset.

2.7.7 DNA (BDNF) saliva samples

DNA was collected using self-administered saliva sample Orangene™ DNA kits (produced by DNA Genotek, Ottawa, Canada, ISO 13485:2003) which have been used in similar studies (such as Lövdén et al., 2011). The process required participants to spit into a test tube which was sealed and anonymously coded by the researcher and stored at Bournemouth University. Samples were collated and posted to DNA Genotek extraction services in the United States. Genomic DNA was then extracted from the buccal mucosa on a cotton swab for TaqMan SNP genotyping for BDNF using PicoGreen fluorescent quantification, A260/A280 and running of an agarose gel. Results were emailed back to Bournemouth University in the form of an Excel spreadsheet with the depersonalised codes and genotype results alongside (i.e. whether the participant was 'valval', 'valmet' or 'metmet').

2.8 ANALYSIS AND STATISTICS

All statistical analyses were performed using SPSS version 22 (SPSS, IBM Corp. in Armonk, NY) and G Power™ software (Faul et al., 2007). Regression analysis was only undertaken where viable with the number of variables being assessed, compared to the sample size (Mayers, 2013).

ANALYSIS BY GROUP

Table 2.8 presents the format of the analysis by group for each chapter.

Table 2.8: Participant group structure for analyses in Chapters 3- 7: by experimental group (*Trauma Unexposed, Trauma Exposed No PTSD,* PTSD) and by BDNF genotype.

Chapter	Group		
3	Trauma Unexposed	Trauma Exposed No PTSD	PTSD
4	Trauma Unexposed	Trauma Exposed No PTSD	PTSD
5	Trauma Unexposed	Trauma Exposed No PTSD	
6	Combat-Related PTSD	Non-Combat PTSD	
7	BDNF valval homozygotes (70% of the Caucasian population)	BDNF met carriers (30% of the Caucasian population)	

MISSING VALUES

There were two variables for which missing values were interpreted as a negative response: one for the taking of Selective Serotonin Reuptake Inhibitors (SSRIs) and one for pain. Those who did not complete the SSRI and pain score question were assumed to not be taking SSRIs and not to be in pain. Missing values were common (up to 30%) for background questions (such as those about navigation training, trauma therapy and early life separation) and precluded these data from being used statistically in analysis (see Section 2.5.4). A possible explanation for these missing values is that the wording of these questions may have seemed somewhat vague and disjointed from the highly structured questions of the full clinical screens and surveys, such as the PDS (Foa et al., 1995) and the navigation questionnaires.

3 PTSD AND THE FOUR MOUNTAINS TASK

ABSTRACT

PTSD theory states that successful trauma processing relies on contextualisation of sensory and traumatic memories which is undertaken by the hippocampus (Bisby et al., 2010; Smith et al., 2015). The hippocampus' capacity for allocentric processing (i.e. taking a non-egocentric, objective perspective) is considered necessary for successful trauma processing and yet is at risk of impairment *by* that trauma (Brewin & Burgess, 2014; Smith et al., 2015).

The first experiment of this study measured performance on a paper-based, static test of topographical perspective-taking (the Four Mountains task by Hartley et al., 2007) which is considered to be allocentric (and one infers from that; hippocampal dependent). Performance was assessed between groups of: those who reported not having been exposed to trauma (*a Trauma Unexposed* group); those who reported having been exposed to trauma but who had not developed clinical levels of PTSD (a *Trauma Exposed No PTSD* group); and those who had clinical or probable levels of PTSD (a *PTSD* group).

Results demonstrated significant impairment of perspective taking in those with clinical or probable levels of PTSD. This effect was independent of clinical and demographic covariates which are known to influence hippocampal dependent spatial processing, including: age, gender, depression, the taking of anti-depressants, benzodiazepines or opiates, pain and sleep disturbance.

These findings provide initial data to support the hypothesis that clinical levels of unprocessed trauma significantly impairs the hippocampus' capacity to apply allocentric processing to a static perspective-taking task. The findings present a case for further investigation of the impact of PTSD and trauma exposure on navigation behaviour, with a view to unfolding the seemingly inextricable link (explained in Section 1.1.4) between trauma, the hippocampus and allocentric processing.

3.1 INTRODUCTION

"The exquisite vulnerability of the hippocampus to the ravages of stress is one of the key translational neuroscience discoveries of the 20th century" (Teicher et al., 2012).

3.1.1 Trauma and hippocampal processing

The relationship between PTSD and the hippocampus is fundamental to the study of the effect of PTSD and trauma on spatial processing and navigation (Smith et al., 2015). A healthy hippocampus plays a critical role in the active organisation of new information within the context of previous experience (Eichenbaum, 2000). It alters the nature, persistence and organisation of memory representations synthesising episodic, declarative memories with sensory representations of emotional significance (Eichenbaum, 2006; Bremner & Elzinga, 2002; Brewin & Burgess, 2014; Byrne et al., 2007). To do this, it uses allocentric (non-egocentric)[6] perspective to 'contextualise' memories, encoding them in both time and space (Brewin & Burgess, 2014).

The detrimental effect of chronic stress on the human brain, and in particular, the hippocampus is integral to our understanding of the impact of PTSD on hippocampal dependent processing and behaviour (O' Keefe & Nadel, 1978; Van Gerven et al., 2016; Andersen et al., 2007; Dunman & Monteggia, 2006; Gray & Mc Naughton, 2003). Van Gerven et al. (2016) have recently articulated the complexity of studying the relationship between *acute* stress and allocentric processing (their findings this year demonstrated surprisingly positive effects of acute stress[7] on the uptake of hippocampal dependent strategy in human navigation). The focus of this study, however is on *chronic stress* from self-reported historical trauma exposure and its relationship to hippocampal dependent processing. Stress-related hippocampal atrophy (and lack of maturation) has explained why a reduction in hippocampal volume has been observed in those with PTSD (Sapolsky, 2000; Gilbertson et al., 2002; Apfel et al., 2011; Teicher et al., 2012; Lindauer et al., 2004, 2006; Rao et al., 2010). As well as reduced volume and cell diminution, dentritic retraction in hippocampal neurons has also been observed in chronically stressed rats- and this dentritic retraction is associated with spatial memory deficits (Conrad, 2006). In rat and human models, chronic stress has been shown to directly impair hippocampal dependent spatial processing (Schwabe et al., 2008). PTSD is understood to impair hippocampal dependent 'context memory' and PTSD-related symptoms (namely visual intrusions and sleep disturbance) have been associated with hippocampal dependent spatial processing impairments (Acheson et al., 2012; Bisby et al., 2010; Tempesta et al., 2012, Meyer et al., 2012). The negative effect of trauma on the hippocampus, and the spatial processing for which it is responsible is evident from previous research (reviewed by Miller & Wiener, 2014).

[6] To clarify, 'allocentric' processing describes the non-egocentric, observer, objective or field perspective which an individual applies to process the relationship between two objects or occurrences, independent of their own viewpoint or position. See Chapter 1 Section 1.2.2.
[7] Van Gerven et al. (2016) exerted stress on participants using the Paced Auditory Serial Addition Task (PASAT); measured stress through blood pressure, salivary cortisol concentration and self-reported anxiety (using the State-Trait Anxiety Inventory, STAI) and assessed strategy use in a human model of the Morris water maze. See Chapter 4 Section 4.1.7 for more detail.

Conversely, what is also increasingly understood in the neuropsychological literature, is the *positive role* that the hippocampus plays in the *successful processing* of trauma, (Astur et al., 2006; Bisby et al., 2010; Brewin & Burgess, 2014). A diverse literature presents several hippocampal functions that are key to managing symptoms synonymous with PTSD. Examples include the hippocampus contextualizing the fear response, dealing with visual intrusions and challenging sensory associations (Jeansok & Fanselow, 1992; Philips & Le Doux, 1992; Bisby et al., 2010; Brewin et al., 2010).

3.1.2 Dual Representation Theory (DRT)

More specifically, the function of allocentric spatial processing is now considered fundamental to the processing of trauma. Allocentric processing has been integrated into existing theories of PTSD such as Dual Representation Theory (DRT, Dalgleish, 2004; Bisby et al., 2010; Brewin & Burgess, 2014). DRT is a theory which purports that the objective 'perspective taking' quality of allocentric memory systems helps to contextualise evocative sensory and egocentric representations of trauma: encoding them in space as well as in time. Dual Representation Theory (DRT) has been revised (DRT-R, Brewin et al., 2010) to incorporate a neurobiological model of intrusive memories (Bisby et al., 2010; Kaur et al., 2016) and explains that some individuals' contextual encoding and representation of an extremely traumatic or stressful event is disrupted, but that sensory and affective representations of the event are not disrupted. Sensory representations are referred to as S-Reps (which are situationally accessed memories, SAMs) and contextually encoded representations as C-Reps (which are verbally accessed memories, VAMs). Over time, the fact that sensory representations are not sufficiently encoded, impairs the individual's ability to apply allocentric processing to effectively contextualise past trauma, and this results in symptoms of PTSD. What is striking about this theory of PTSD is that presents PTSD as a result of dysfunction of a dual memory encoding system. This stands out from other theories which present PTSD as being the result of an issue within a single memory system; a system which is either in a reactive state (with associative, fear-based, stress-responses, e.g. Horowitz, 1986), or a system which has a longer term disadvantage relating to the schemas from which individuals may process emotions differently to others (e.g. Janoff-Bulman, 1992; Epstein, 1985; Foa & Rothbaum, 1998; Rauch & Foa, 2006). There has been little negative critique of the DRT-R (Brewin et al., 2010), perhaps because the explanatory power of the model has been externally validated using neural imaging and other measures of hippocampal functionality (Bisby et al., 2010; Smith et al., 2015). However, arguably, there is the observation that DRT-R does not discuss how schema may play a role in the dual memory system of applying (allocentric) contextualisation to sensory (traumatic) information (Baker et al., 2013).

3.1.3 Allocentric perspective taking and PTSD

The value of the allocentric perspective is not new to psychological interventions for trauma. Many therapies draw upon 'associative network' theories of trauma and aim to the challenge egocentric and associative biases which were first identified as synonymous with trauma exposure by Sigmund Freud (Eich et al., 2012; Lang, 1977, 1984; Erwin, 2003). Challenging the egocentric bias comprises encouraging the individual to conscientiously apply more *allocentric,*

objective, ‘observer’ viewpoints to their recollection of trauma, therefore rendering the memories less personalised, less intrusive and less impacting on their experience of the present (Steel, 2005; Neuner, 2008; McIsaac & Eich, 2004). An example of this application of allocentric processing to trauma therapy is provided in the Discussion Chapter 8 (see Figure 8.3). At the time of submission of this thesis, a case study was published (Kaur et al., 2016) which narrated the application of allocentric-type processing to combat trauma processing, based on the DRT-R model. Results have indicated that adapting trauma focussed cognitive behavioural therapy to have a stronger emphasis on allocentric processing may be helpful for patients with high levels of dissociative and avoidance-based PTSD symptoms.

A tension which underlies this study is that: it is clear that hippocampal integrity is at risk from the chronic stress of unprocessed trauma (or PTSD), but at the same time, the hippocampus is required to adequately process the very trauma to which the individual is experiencing a prolonged stress response, often resulting in that disorder (or, to put it another way, is developing symptoms of Post-Traumatic Stress Disorder). This potentially cyclical relationship between traumatic stress, PTSD, hippocampal functionality and spatial processing has yet to be disentangled and is now being investigated in an emerging (and somewhat ‘niche’) domain of neuropsychology (Acheson et al., 2012; Bisby et al., 2010; Tempesta et al., 2012; Pitman et al., 2012; Miller & Wiener, 2014; Meyer et al., 2012; Smith et al., 2015).

In order to start to untangle this complex relationship (i.e. between trauma, the hippocampus, and allocentric processing), it would be useful to ascertain if there is a difference between the effects of traumatic stress and the effects of *clinical levels of PTSD* on an individual’s ability to apply the very perspective taking which is required to process trauma. To do this, this study will assess perspective taking ability between: those who report not having been exposed to trauma (i.e. they have had no trauma which would require processing); those who report having been exposed to trauma and who have processed it (i.e. they do not report clinical or probable levels of PTSD); and those who report having been exposed to trauma and have not processed trauma (i.e. they report clinical or probable levels of PTSD). This assessment may give some indication as to whether allocentric perspective taking ability is proportionate to the *impact* of unprocessed trauma and may be a first step towards a better understanding of the relationship between trauma, the hippocampus and allocentric processing.

The rationale for this study is that PTSD occurs after trauma exposure partly due to an inability of the hippocampus to apply an allocentric perspective to encode experiences effectively. (It is also noted that there may be other areas of neurocognitive function aside from the hippocampus which play a part in the development of PTSD, but the focus here is on the hippocampus). This lack of allocentric encoding results in the stress response continuing, which interferes further with memory encoding, and potentially exacerbates hippocampal impairment to the point at which hippocampal dependent spatial processing is adversely effected. To extend this rationale to cases of trauma exposure without PTSD, the suggestion is that these individuals have been able to an apply allocentric perspective to sufficiently process trauma (unlike those with PTSD) and subsequently their stress response can diminish, leaving

hippocampal dependent processing sufficiently intact to maintain the contextualisation of trauma (preventing PTSD) and to maintain spatial processing performance.

The aim of this first phase of the study was to identify a simple measure for allocentric spatial perspective taking and to compare performance on the test between groups of participants with different experiences of trauma (as described above).

3.1.3 The Four Mountains task (Hartley et al., 2007)

This first phase of the study required the use of an allocentric spatial processing (and more specifically, a 'perspective-taking') task. Ekstrom et al. argued in 2014 that finding a task to test "pure" hippocampal dependent processing was likely unachievable, given that multiple brain regions contribute necessary functions to allocentric memory (Ekstrom et al., 2014; see also Gerlai, 2001).

A review of spatial processing literature was undertaken which presented several static, paper-based spatial processing tests which could be used to quantify hippocampal dependant (or 'allocentric') spatial processing impairment. Many spatial processing tests were discounted either due to there being some uncertainty over their ability to test allocentric processing, or because of the tests' incongruity with the type of navigation behaviour one expects to engage in in everyday life (that is, their ecological validity).

Paper-based spatial processing tasks which were discounted because their allocentric nature had been brought into question included: Warrington's Camden Spatial Memory Test (1996, critiqued by Hartley & Harlow, 2008); Simons & Wang's object location test, (1998, critiqued by Burgess et al., 2005); the Ray Osterich configural drawing task (used by Moffat et al. in 2009) and Gilbertson et al.'s mental rotation test (2002, critiqued by both Erkstrom et al., 2014; and Smith et al., 2015 and with reference to Farah & Hammond, 1988; King et al., 2002). Other paper-based tests were discounted because their presentation did not complement the everyday 'navigation' theme of this research and lacked relevance to the notion of finding one's way around an environment (see also Deadwyler et al., 1996; Ganis & Keivit, 2015; Otto & Eichenbaum, 1992; Wraga et al., 2005). A well-known example of such a test is Shephard & Metzler's (1971) three-dimensional drawing of blocks and cubes. Other scene recognition tests considered and discounted were King et al.'s (2004) episodic spatial memory test which was based on Virtual Reality rather than being paper-based and Konkle et al.'s scene test (2010) which focussed on memory capacity for visual scenes (rather than the allocentric processing of spatial relations and perspective taking within those scenes).

The task which was selected for the first part of this study is The Four Mountains task by Hartley et al. (2007) which is a static topographical (allocentric) test of spatial memory (Hartley et al., 2007; Bird et al., 2010; Hartley & Harlow, 2012). The task essentially requires an individual to be able to apply perspective taking to a topographical scene after having committed the image to short term memory. Another component of the experiment is a test of perception (as a opposed spatial memory). Five patients with hippocampal damage (such as MTL lesions and as confirmed by fMRI, MRI and extensive radioneurological investigations) were significantly

impaired on the topographical memory task, with all scores which would have placed them below the 3rd percentile of the normal population (Hartley et al, 2007). Not all of the participants (i.e. *n* = 2) showed impairment in the perception task. Topographical spatial memory performance on the Four Mountains Task has since been positively correlated with hippocampal volume (Hartley & Harlow, 2012). Given that lower hippocampal volumes have previously been associated with PTSD (Gilbertson et al., 2002; Apfel et al., 2011), the Four Mountains task seemed particularly relevant for this study's population.

The Four Mountains task (Hartley et al., 2007) had also been used in a contemporary study which had investigated the direct relationship between PTSD on spatial processing (by Smith et al., 2015) and its findings were relevant to our research. Smith et al.'s (2015) findings showed that PTSD impaired overall spatial processing (i.e. the perception and spatial memory task combined) compared to a control group of participants who had been trauma exposed but who had not developed PTSD. There was significant main effect of group (F (1, 55) = 6.18, p = .02, η_p^2 =.10) reflecting a poor performance on overall spatial processing (perception and memory based processing) of the *PTSD* group. The differences and parallels between the studies and their findings are addressed in more detail later discussion (see Section 3.4.1).

3.1.4 Experimental groups

Experimental groups for the Four Mountains Task were categorised on the basis of trauma exposure:

i) Those who reported not having been unexposed to trauma (to be known as the *Trauma Unexposed* group)
ii) Those who reported having been exposed to trauma but who did not report clinical or probable levels of PTSD (the *Trauma Exposed No PTSD* group)
iii) Those with clinical or probable levels PTSD (to be known as the *PTSD* group).

All participants recruited through Bournemouth University (*n* = 140) were given the Life Events Checklist (LEC, Blake et al., 1995) which was supplemented by DSM-IV (APA, 2013) criterion for traumatic incidents to ascertain if participants had or had not been exposed to traumatic experiences. Those who confirmed no trauma exposure were assigned to the *Trauma Unexposed* group. All those who did report exposure to traumatic trauma exposed were assessed using the PTSD Diagnostic Scale (Foa et al., 1995) and all participants who undertook the assessment scored on the scale. Those who scored below the cut off for probable (or clinical) PTSD constituted the *Trauma Exposed, No PTSD* group, and those who scored at or above the cut off, the *PTSD* group. (More information about the PDS scale and trauma screening is provided in the Methodology Section 2.7.3).

3.1.5 Demographic and clinical influences

Demographic and clinical variables identified in the literature as pertinent to Chapter 3 and the Four Mountains task include: age; the taking of SSRIs and other medications, pain and sleep disturbance.

Age has long been shown to have a negative impact on various forms of spatial memory which rely on the hippocampus (e.g. Daugherty et al., 2015; Rosenweig & Barnes, 2003; Raz et al., 2009; Moffat et al., 2001, 2009; Wiener et al., 2012, 2013). More directly relevant to PTSD, age has been associated with reduced hippocampal activation in PTSD (Carrion et al., 2010) and with the efficacy of trauma processing interventions. Age also featured in the recent study by Smith et al. (2015) which assessed the impact of PTSD on participants' score on the same perspective-taking test of topographical memory as this study does, the Four Mountains task (Hartley et al., 2007). With a similar age range (18 to 65 years) to this study, that by Smith et al. (2015) highlighted the importance of controlling for age by demonstrating a unique contribution of age to performance on the Four Mountains task. For these reasons, age is a principal demographic factor to analyse in Chapter 3.

The Four Mountains task was selected as a test of allocentric (hippocampal dependent) processing and so literature was reviewed for other clinical influences over hippocampal function. These are summarised in the Methodology (Section 2.5) and comprise: pain, which has been shown to effect spatial memory in rats (Cardoso-Cruz et al., 2013); the taking of Selective Serotonin Reuptake Inhibitors (SSRI's) which have been said to increase hippocampal neurogenesis and plasticity (Anacker et al., 2011; Bath et al., 2012; Engel et al., 2013), and, conversely antipsychotics and opiates which have been said to supress hippocampal neurogenesis and Long Term Potentiation (LTP, Luo et al., 2005; Pu et al., 2005). A study by Tempesta et al. (2011) also demonstrated that PTSD-related sleep disturbance interfered with hippocampal dependent spatial processing and for that reason, sleep disturbance will also be considered.

Hypotheses and predictions

i) **'The *PTSD* group would demonstrate significantly poorer performance in perspective taking on the Four Mountains task than the *Trauma Unexposed* group'.** This prediction was made on the basis of there being impairment in allocentric spatial processing caused by clinical levels of unprocessed trauma (which was found in the study by Smith et al., 2015). The dependent variable (*DV*) being Four Mountain score out of 15.

ii) **'The *Trauma Exposed No PTSD* group's performance on the Four Mountains task would be better than that of the *PTSD* group'.** This prediction was made on the basis of this group not having clinical levels of unprocessed trauma to disrupt allocentric spatial processing (already demonstrated in the study by Smith et al., 2015). The dependent variable (*DV*) being Four Mountain score out of 15.

iii) **'The *Trauma Exposed No PTSD* group would perform more poorly on the Four Mountains task than the *Trauma Unexposed* group**'. This prediction was made on the basis of there being some degree of impact from trauma exposure on spatial processing, albeit at subclinical levels of PTSD. This was based on the principals of allocentric processing being used to process both traumatic information and spatial information (e.g. Bisby et al., 2010). The dependent variable (*DV*) being Four Mountain score out of 15.

3.2 METHODS

3.2.1 Participants

Participants were a subset of 138 (61 females) of the total sample population (*n* = 150) who undertook the Four Mountains task. Participants were recruited via:

(i) Bournemouth University (*n* = 76) including staff, students, and members of the public through the Psychology Research Volunteer Scheme.

(ii) Intensive Psychotherapy Treatment Service (IPTS) at Dorset NHS (*n* = 8).

(iii) Dorset Police and Cambridgeshire Police (*n* = 27).

(iv) Combat Stress (a military charity) PTSD Rehabilitation course at Tyrwhitt House Treatment Centre, Leatherhead, Surrey (*n* = 25).

(v) British Military Fitness and Forces Fit military fitness programmes (*n* = 2).

Participants were offered a £10 financial reimbursement for their time. Those recruited through Combat Stress received £20 reimbursement to cover their additional travel costs. The study was approved by: the BU Graduate School Ethics Board; the Combat Stress Research Ethics Committee; and the NHS South West (Cornwall and Plymouth) National Research Ethics Service (NRES).

Table 3.2.1 below presents the demographic and clinical data by experimental group and illustrates that there are significant group differences across all variables (represented by chi square calculations, χ^2).

Table 3.2.1: Descriptive and inferential statistics for demographic and clinical data: means and standard deviations by experimental group (Trauma Unexposed, Trauma exposed No PTSD, PTSD) (n = 137). Other medications = benzodiazepines and opiates. $p < 0.05$*, $p < 0.01$**.

Demographic or clinical factor		***Trauma Unexposed*** (*n* = 32)	***Trauma Exposed No PTSD*** (*n* = 58)	***PTSD*** (*n* = 47)	**Significant group differences**
Mean age (years) *(SD)*		32.7 *SD* ± 10.6	38.9 *SD* ± 10.3	38.2 *SD* ± 9.6	*F* (2, 137) = 4.27, *p* = 0.02*
Gender (%)	Male	37.5%	46.5%	78.7%	χ^2= 16.3, *p* < 0.01**
	Female	62.5%	53.5%	21.3%	
SSRIs (%)	No	100%	94.1%	71.1%	χ^2 = 17.7, *p* < 0.01**
	Yes	0%	5.9%	28.9%	
Other medication (%)	No	100%	96.5%	72.3%	χ^2 = 20.7, *p* < 0.01**
	Yes	0%	3.5%	27.7%	
Sleep disturbance (Mean PSQI score, *SD*)		0.41 *SD* ± 1.39	1.02 *SD* ± 2.41	8.11 *SD* ± 6.17	*F* (2, 133) = 50.3, *p* < 0.01**
Pain (Mean SNR score, *SD*)		0.44 *SD* ± 1.37	0.86 *SD* ± 1.94	3.15 *SD* ± 3.70	*F (2, 136) = 13.9, p < 0.01***
PTSD (PDS score, *M, SD*)		0	7.06 *SD* ± 6.62	35.3 *SD* ± 9.46	*F (1, 96) = 289, p < 0.01***

3.2.2 Procedure

Informed consent was sought from all participants (*n* = 138).

As explained in Section 3.1.4, participants completed a screen for trauma exposure using the Life Events Checklist (LEC, Blake et al. 1995). Those who reported no exposure trauma were assigned to the *Trauma Unexposed* group (*n* = 32). Those who self-reported trauma exposure were given the Post-Traumatic Stress Disorder Diagnostic Scale (PDS, Foa 1995) to ascertain the present day impact of the trauma previously experienced. Those with self-reported PDS scores above threshold of 21 were allocated to the *PTSD* group (*n* = 47). Those with self-reported PDS scores below the threshold of 21 were allocated to the *Trauma Exposed No PTSD* group (*n* = 58).

Participants completed clinical measures for depression (Beck's Depression Inventory, BDI, Beck et al. 1996), pain (standard Numerical Rating Scale, NRS, Jensen et al. 1986) and sleep quality, (the Pittsburg Sleep Quality Index Addendum for PTSD, PSQI-A, Germain et al., 2005).

Participants were then administered a practice trial of the Four Mountains task to familiarise them with the layout of the test and to ensure that instructions were understood. Participants then undertook the Four Mountains task (Hartley et al. 2007) which took 10 minutes to complete. Further information about the task is provided in the Materials section below.

3.2.3 Materials

The Four Mountains task (Hartley et al., 2007) is a match-to-sample test of short term memory for the topographical aspects of visual scenes, which is considered in the literature to be hippocampal dependent or 'allocentric' in nature (Hartley et al., 2002; Hartley & Harlow, 2012; Bird et al., 2010).

The test itself comprises an A4 paper booklet of 15 separate computer-generated landscapes (the stimuli), each containing 4 mountains. The participant is shown the first stimuli for ten seconds (see the figure below) and is asked to *memorise* the scene. The researcher then turns the page and then a blank page is presented for two seconds. The participant is then presented with a new page of four images. Three of those images are variations of the stimulus, with its spatial and non-spatial features independently varied. A fourth image is the original scene (from the stimulus) but depicted from a different perspective (this is highlighted in black in Figure 3.2.3.1 below). The task is for the participant to identify, within 30 seconds, which of the four images is the original scene depicted from a different perspective. The participant marks their response on a separate response sheet with a cross which corresponds with the selected image in the task. This is repeated 15 times with different scenes, so the participant has 15 images to correctly identify, given them a total possible score of 15 out of 15.

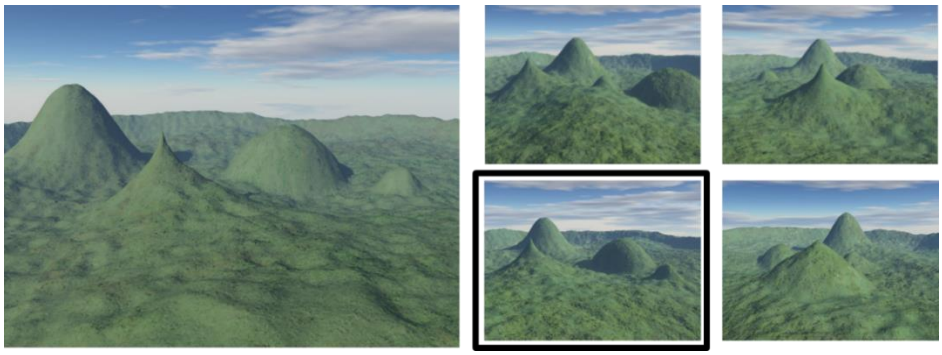


Figure 3.2.3.1: Image extracted from the Four Mountain task (Hartley et al., 2007). The highlighted box indicates the correct answer (the original scene but depicted from a different perspective).

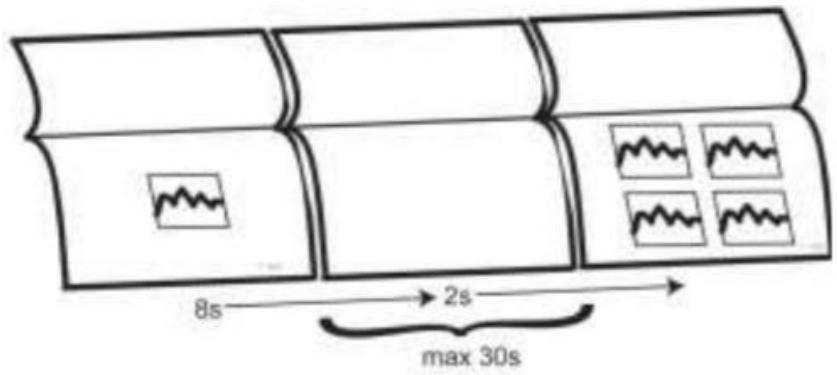


Figure 3.2.3.2: The Four Mountain task A4 booklet as produced by Hartley et al. (2007).

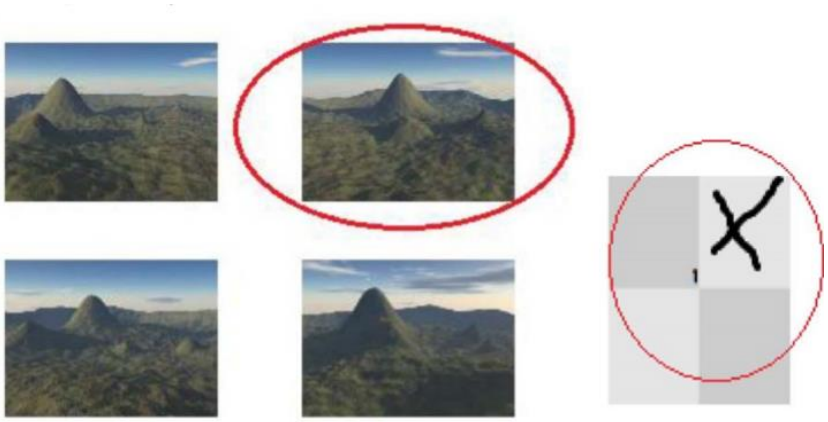


Figure 3.2.3.3: The Four Mountains task response sheet: the selected image with the corresponding answer box selected.

3.3 RESULTS

Statistical analyses were performed using SPSS version 22 (SPSS, IBM Corp. in Armonk, NY).

3.3.1 The Four Mountains task

A univariate ANOVA was conducted with the between factor experimental group (*Trauma Unexposed, Trauma exposed No PTSD, PTSD)* and the dependent variable Four Mountains score and this revealed a significant main effect on topographical (allocentric) spatial memory of experimental group, F (2, 136) 7.49, $p < 0.01$, $\eta_p^2 = 15.0$.

Table 3.3.1: Descriptive statistics for the analysis of variance in Four Mountains Score by experimental group (*Trauma Unexposed, Trauma Exposed No PTSD and PTSD*) (n = 137).

Experimental Group	**Mean score**	**Std. Deviation**	***n***
Trauma Unexposed Group	11.3	*SD* ± 2.31	32
Trauma Exposed No PTSD Group	10.8	*SD* ± 2.47	58
PTSD Group	9.3	*SD* ± 2.25	47

Figure 3.3.1 overleaf presents the distribution of performance scores on the Four Mountains task by experimental group (*Trauma Unexposed, Trauma Exposed No PTSD and PTSD*). The figure illustrates that the *PTSD* group has a lower mean score than both the other groups. *Trauma Unexposed* and the *Trauma Exposed No PTSD* groups have a comparable mean score.

Pairwise comparisons revealed a significant difference in performance on the Four Mountains task between the *PTSD* group and both the *Trauma Exposed No PTSD* group, *mean difference (MD)* = -1.42, *SD* ± 0.46, $p < 0.01$, and the *Trauma Unexposed* group, *MD* = *-1.91*, *SD* ± 0.54, $p < 0.01$. This shows *PTSD* to have a significant negative effect on performance on the Four Mountains test.

There was no significant difference in the Four Mountains score between the *Trauma Exposed No PTSD* and the *Trauma Unexposed* group, *MD* = .491, *SD* ± 0.52, $p = 0.35$. In the *Trauma Exposed No PTSD* group, all participants score something on the PTSD Diagnostic Scale (PDS by Foa et al. 1995) –albeit at subclinical levels of PTSD. According to these data, trauma exposure at these subclinical levels was not sufficient to significantly impair short term topographical, allocentric spatial processing (perspective-taking)[8].

[8] G Power analysis shows that for Four Mountain task performance between the *Trauma Unexposed* group and the *Trauma Exposed No PTSD* group, the effect size is small at 0.21. To demonstrate a significant main effect of 'trauma exposure' on this task, a sample size of n = 984 would be required. This suggests that this task is not particularly sensitive to the effects of trauma exposure, but is sensitive to the effects of PTSD. G Power calculated the effect size of *PTSD* (comparing performance with the *Trauma Exposed No PTSD*) at 0.63 and power at 0.94.

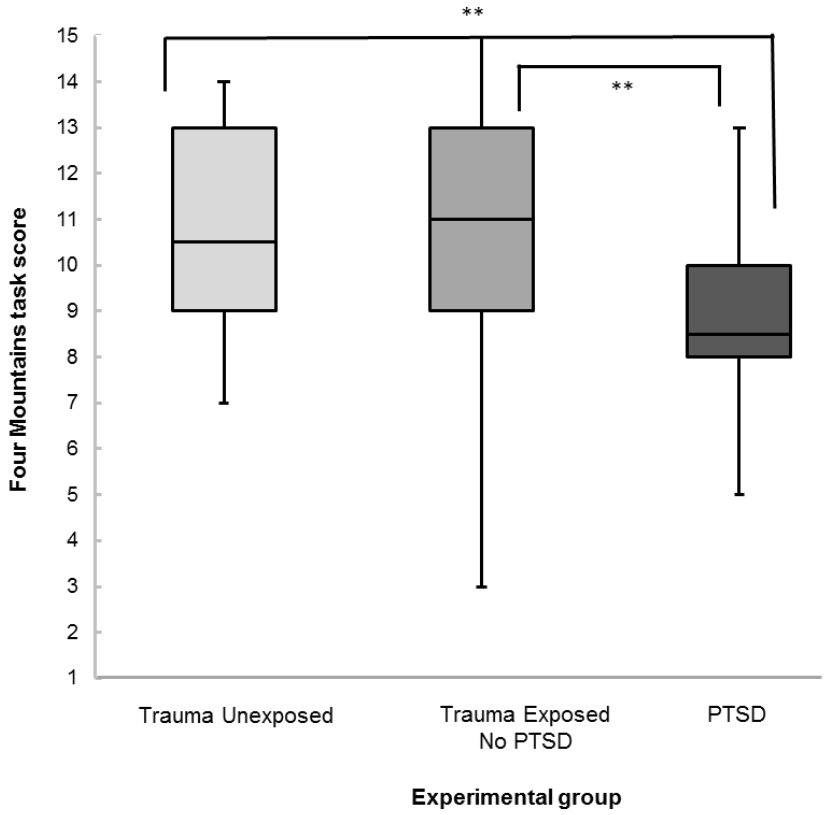


Figure 3.3.1: Box plot presenting the analysis of variance in the Four Mountains task scores by experimental group (*Trauma Unexposed, Trauma Exposed No PTSD and PTSD*) (*n* = 137) with 95% CI error bars.

3.3.2 Demographic and clinical variables

Potentially confounding clinical and demographic variables were entered into a hierarchical linear regression. Age, gender, the taking of SSRIs, benzodiazepines and opiates, sleep disturbance score and pain score were entered at step 1, and experimental group (*Trauma Unexposed, Trauma Exposed No PTSD and PTSD*) was entered at step 2, with the Four Mountains score as the dependent variable. At step 1, the clinical and demographic variables did not explain a significant amount of variance in Four Mountains task score, F (6, 130) = 0.66, p = 0.68, r^2 = 0.03, Adjusted r^2 = -0.15. At the second step, experimental group accounted for a significant additional proportion of the variance, F (7, 129) = 2.87, p < 0.01, r^2 = 0.14, Adjusted r^2 = 0.09. In the final equation, only experimental group provided a unique contribution to the Four Mountains tasks score, b (-1.36) = - 4.06, p < 0.01. (Given that the other variables showed no effect on the Four Mountains score, no further post hoc tests were conducted.)

These results demonstrate that of the variables considered only ‘experimental group’ (*Trauma Unexposed, Trauma Exposed No PTSD and PTSD*) contributed uniquely to performance on the Four Mountains perspective-taking test of topographic spatial memory and this was independent of the other potentially confounding variables (such as age, gender, the taking of medications, pain and sleep disturbance).

3.4 DISCUSSION

3.4.1 PTSD and the Four Mountains task

These findings fit with the predictions of this experiment and demonstrate that clinical levels of PTSD have a significant negative effect on topographical (allocentric) spatial memory. They support the hypothesis that once unprocessed trauma reaches 'clinical levels' of 'PTSD', the ability to use an allocentric perspective is significantly impaired. This is in line with findings from previous studies which have demonstrated performance deficits in hippocampal-dependent spatial processing in participants with specific trauma-related symptomology; namely, visual intrusions (Bisby et al., 2010) and sleep disturbance (Tempesta et al., 2012).

Moreover, the negative influence of PTSD also appears in this data to be independent of other clinical and demographic covariates (including age, gender, the taking of SSRIs, benzodiazepines and opiates, sleep disturbance and pain) which are known to also have a detrimental effect on allocentric spatial processing.

However, it important to note that our clinical and demographic covariates did not include intellectual and visuospatial processing (measured using Raven's Advanced Progressive Matrices, RAPM) which Smith et al. (2015) showed to contribute to variance in Four Mountains. Smith et al. (2015) tested for RAPM on the basis that Gilbertson et al. (2002) found general visualisation ability to be associated with performance on a visuo-spatial working memory task (a static 'Paper and Cube' task). Given that was no other indication in the literature reviewed that variation in intellectual and visuospatial processing would influence allocentric processing (Brandes et al., 2002; Knaus, 2007; Vasterling et al., 1998), which the Four Mountains task is said to test (Hartley et al., 2007) and this finding by Smith et al. (2015) is worthy of consideration.

Without being able to repeat this experiment, controlling for RAPM, the differences between the two studies need to be understood, before any conclusions can be drawn. Firstly, unlike our study, the Smith et al. (2015) study used a combined score from *two versions* of the Four Mountains task: one for short term topographical *memory* (which is considered hippocampal dependent) and one for *perception* (the hippocampal dependent nature of which is questioned by the authors, Hartley et al., 2007[9]). The experiment which was undertaken in this study only measures performance on the *topographical memory* version of the task in order to retain a preliminary focus on hippocampal dependent spatial processing. Hartley et al. (2007) indicate that the perception score could be a less accurate a measure of hippocampal dependent processing and this measure is not used in the current study. Secondly, the Smith et al. (2015) compares PTSD impact within the trauma exposed, whereas the current study compared PTSD impact and trauma exposure impact (using a control group of *Trauma Unexposed* participants).

[9] Hartley et al. (2007) report that only the topographical memory test demonstrates a specific role of the hippocampus, whereas the perception test "can allow for successful alternative strategies, possibly based on less flexible parahippocampal representations". The authors also note that performance deficits in the perception task was only evident in two of the four hippocampally impaired participants.

These design differences mean that it is not determinable if the contribution of RAPM (visuospatial ability) to impaired Four Mountains performance is: a) specific to cases of *trauma exposure* or not (as both of Smith et al.'s groups were trauma exposed); or b) specific to the 'perception' element of the Four Mountains task (which is not part of the current study). For these reasons, comparability between this study and that by Smith et al. (2015) is limited.

3.4.2 Trauma Exposure and the Four Mountains task

Those with trauma exposure but without PTSD (the *Trauma Exposed No PTSD* group) did not perform significantly more poorly on the Four Mountains task than the *Trauma Unexposed* group, contrary to predictions. Looking more closely at the findings from this preliminary experiment, there may be two explanations as to why the trauma exposed (no PTSD) participants did not show significant performance differences to the unexposed participants in the Four Mountains task. The first explanation is based on a rationale that individuals who can apply allocentric processing can do so to both trauma and spatial processing. So, in these results, who can apply allocentric processing spatially (as shown by their performance on the Four Mountains task) may have been able to do so in trauma processing, thereby protecting them against PTSD (and rendering them in the *Trauma Exposed No PTSD* group). The second explanation as to why the trauma exposed (no PTSD) participants did not show significant performance differences to the unexposed participants in the Four Mountains task, is that the Four Mountains task in isolation is not sensitive to the impact of sub-clinical trauma exposure, and is only sensitive to PTSD.

With regard to the first explanation, it is not possible to accurately assess the extent to which individuals can apply allocentric processing to trauma (as well as spatial processing) without either: including trauma exposure and trauma processing in the experiment itself (e.g. Bisby et al., 2010); or relying on individuals' subjective recall of what they have deemed traumatic and what they have personally processed in the past (Vasterling & Brewin, 2005; Brewin et al., 2000; Horowitz, 1999; Koenan et al., 2009; Mac Manus et al., 2014). Therefore, this line of enquiry could not be pursued further in this study.

However, the second explanation does invite further enquiry which is feasible for this study. The second explanation for these results is that the Four Mountains task may not be sensitive to the impact of sub-clinical trauma on allocentric processing, because it is not a test which is uniquely sensitive to allocentric processing. This explanation is made on the basis that one assumes the Four Mountains task to be a perspective-taking task that may be solved using some forms of mental rotation, and on the basis that it is a simple, static task. There have been suggestions in the literature that tasks which can be solved using mental rotation may not be specifically hippocampal dependent. The first indirect suggestion is by Smith et al. (2015) who critique Gilbertson et al.'s (2002) Cube and Paper test on the basis that mental rotation tasks may not require hippocampal dependent processing (making reference to Farah & Hammond, 1988 and King, et al., 2002 in the wider literature). The second suggestion is by Lambrey et al. (2012) who state that the hippocampus does not support spatial processing which involves the mental rotation of an object or configuration in front of an observer (as opposed to viewer-point,

imagined, mental rotation of an observer around an object or an environment). A final suggestion comes from Wolbers & Wiener (2014) who explain that spatial processing in situations which "can involve a single snapshot which could in principle be rotated by body repositioning" (be it mentally or physically) can to be solved non-allocentrically (Wolbers & Wiener, 2014, referring to Simons & Wang, 1998).The static nature of the task could also imply some independence of hippocampal processing, given Erkstrom et al.'s (2014) assertion that static relational processing between landmarks in locations which 'do not need to be integrated across time' could rely more predominantly on other brain regions (such as the retrosplenial cortex, for example).

These considerations notwithstanding, the results from this first experiment presents an important starting point for the work which follows. What has been established is that, first and foremost, PTSD has a deleterious impact on a measure of spatial processing (The Four Mountains task) which is not explained by other clinical and demographic factors. Additionally, those who have processed trauma experiences sufficiently not to have developed PTSD (the *Trauma Exposed No PTSD* group) perform significantly better on the task than those who have developed clinical or probable levels of *PTSD*.

The aim of the next part of this study (Chapter 4) is therefore to introduce a navigation paradigm which has the capacity to reveal more information about participants' capacity for spatial processing in active navigation, and how trauma exposure may effect that capacity in everyday life.

4 PTSD AND NAVIGATION

ABSTRACT

Post-Traumatic Stress Disorder (PSTD) has been shown to impair spatial processing performance by virtue of the negative impact that stress has on the hippocampus. Findings reported in Chapter 3 (Section 3.3.1) demonstrated such an impairment in a static topographic (allocentric) spatial memory test. Chapter 4 examined whether or not this impairment would manifest in other more 'active' forms of spatial processing such as route learning and wayfinding. Crucially, for the first known time, the research considered if trauma exposure in *healthy populations* also impairs navigation.

The current experiment measured spatial processing, navigation performance and strategy use in a Virtual Environment (VE) paradigm, the Alternative Route (AR, by Wiener et al., 2013). Performance was assessed between three experimental groups, namely:

i) Those who reported not having been unexposed to trauma (to be known as the *Trauma Unexposed* group)
ii) Those who reported having been exposed to trauma but who did not report clinical or probable levels of PTSD (the *Trauma Exposed No PTSD* group)
iii) Those with clinical or probable levels PTSD (to be known as the *PTSD* group).

Results support previous findings that PTSD-related symptoms impair spatial processing in navigation. Similar findings were reported in Chapter 3 (Section 3.3.1) and have also been reported in the wider literature (Bisby et al., 2010; Tempesta et al., 2012, Meyer et al., 2012). Furthermore, these findings demonstrate that this impairment affects the kind of spatial processing (allocentric processing) that takes place in active way-finding and route learning, *and* that this impairment is experienced in healthy people, who have been exposed to traumatic incidents in the past.

The results from the Alternative Route (AR) paradigm also offer new evidence that there is an associative bias in navigation amongst those with clinical or probable levels of PTSD. This is a markedly different bias from the maladaptive bias for a 'beacon' strategy in older persons (assumed to be a consequence of aging) which has been shown in a previous study using the AR paradigm (Wiener et al., 2013). The parallels between these associative biases in navigation and those observed in trauma psychology are striking. The results reported in Chapter 4 indicate for the first time that an associative bias in those with PTSD may be directly transferable to other areas of cognition, and this bias may have very practical implications for the ways in which those with PTSD navigate and find their way around in everyday life.

4.1 INTRODUCTION

"The neuroscience of spatial cognition is emerging as an exceptionally integrative field which provides an ideal test-bed for theories linking neural coding, learning, memory and cognition" (Hartley et al., 2013).

4.1.1 Background

That Post-Traumatic Stress Disorder (PTSD) may have a detrimental effect on the capacity of the hippocampus to apply allocentric processing to spatial processing tasks is supported by an increasingly well-evidenced literature in this area (Acheson et al., 2012; Bisby et al. 2010; Tempesta et al., 2012; Pitman et al., 2012; Miller & Wiener, 2014; Meyer et al., 2012). Within this literature, a tension has emerged and this has been clearly articulated in numerous papers (O' Keefe & Nadel, 1978; Andersen et al., 2007; Sapolsky, 2000; Gilbertson et al. 2002; Apfel et al., 2011; and to which this thesis has already referred in Section 1.1.4 and in the Abstract of Chapter 3). The tension arises from the fact that while hippocampal integrity is at risk from chronic stress (including, as it is now clear, the kind of stress which emanates from unprocessed trauma), it is, at the same time critical for successful trauma processing (Eichenbaum, 2006; Bremner & Elzinga, 2002; Brewin & Burgess, 2014).

This presents a challenge for the current research. Whilst the experiment reported in Chapter 3 confirmed a negative impact of PTSD on allocentric (hippocampal dependent) processing (Hartley et al., 2007; Bird et al., 2010; Hartley & Harlow, 2012), these results were only in the context of a static spatial processing, perspective taking task. While understanding influences over perspective taking is valuable (e.g. Lambrey et al., 2012; Simons & Wang, 1998; Wraga et al., 2005), what was still unknown at this stage was that if those with PTSD were only *i*mpaired in static perspective taking type spatial processing, or whether they were also impaired in more active navigation. Furthermore, what was also unknown was if it was the stress response of PTSD that impairs performance in allocentric processing, or if it is simply the fact that individuals have had any trauma to process and manage *at all* that was preventing full hippocampal resources from being applied to active navigation.

The experiment employs an active navigation paradigm (the Alternative Route by Wiener et al., 2013) to measure egocentric and allocentric navigation performance between the experimental groups (the *Trauma Unexposed* group*, Trauma Exposed No PTSD* group and the *PTSD* group*)*. A particular advantage of using the Alternative Route paradigm is that its design makes it possible to distinguish between different types or styles of navigation strategy. These strategies are categorised as either hippocampal dependent, (allocentric) or hippocampal *in*dependent (egocentric). When strategies are disproportionately favoured, this is referred to as 'bias'. One of these hippocampal *in*dependent strategies is associative in nature and this will be interesting to investigate in PTSD: the literature about PTSD and trauma psychology is replete with references to those with PSTD having a characteristic associative bias in the way they process information (e.g. Brewin & Holmes, 2003). Whether or not this associative processing in PTSD

also applies to associative processing in navigation behaviour is a key question addressed in this chapter.

The concepts of active navigation, spatial information processing biases, and the relevance of 'associative' information processing bias to PTSD are discussed here in more detail.

4.1.2 Active navigation

Investigating more active spatial processing makes this study more relevant to understanding the impact of trauma exposure on an individual's ability to navigate and find their way in the environment- be it in everyday civilian life, or as part of their job. This is because most navigation is not static and requires movement (Gheysen et al., 2010, and see Lövdén et al., 2011; Stackman et al., 2002) and exploration (Kaplan et al., 2014) through environmental space. Wolbers & Wiener (2014) point out that a fundamental characteristic of spatial processing is the frame of reference and scale of space in which it takes place (see also Evans et al., 2015).

The Four Mountains task is essentially a static paper and pen test, set in figural or vista space: that is, in the space of pictures of scenes, which can be "visually apprehended from a single location without movement", (Wolbers & Wiener, 2014 and see Campbell et al., 2009). The Four Mountains task may reliably inform us about hippocampal dependent perspective taking in this static, figural or vista frame of reference (as demonstrated in Chapter 3 and by Smith et al., 2015), but the task in isolation does not tell us much about how participants might engage in hippocampal dependent spatial processing when actively navigating and moving through the environment. Using virtual environments (VE) or virtual reality (VR) paradigms for understanding navigation behaviour is valuable (see Halko et al., 2014; Palermo et al., 2012) and Smith et al. (2015) also assessed allocentric spatial processing using a VE paradigm (called the Town Square Task). However, this was set in a 'vista' frame of reference and did not require active navigation, moving through the environment.

So far, the impact of PTSD and trauma exposure on hippocampal dependent (or allocentric) navigation in an environmental space (requiring movement), is relatively unexplored in the literature. In this investigation of the impact of trauma on hippocampal dependent navigation behaviour, it is important to be clear about what this is likely to comprise. As Erkstrom et al. (2014) remind us, finding a definitive task to test 'pure' hippocampal dependent processing is likely impossible, given the multiple brain regions which contribute to allocentric memory functionality (see the General Introduction Chapter 1, Section 1.2.1). Their description of the key elements of active hippocampal dependent navigation is useful for this study, i.e.

> "…acquiring and storing environmental information, configuring a mental representation of the environment, and making decisions about when to use this map allocentrically" (Erkstrom et al., 2014).

4.1.3 Spatial information processing biases

A key point that Erkstrom et al. (2014) make is that individuals 'make decisions' about how (and if) to navigate allocentrically. This highlights an important element of how individuals navigate in everyday life: our navigational style. The importance of this is clearly noted in the literature:

"**Understanding individual differences in navigational styles, as well as the degree to which individuals can flexibly engage different styles and strategies, will offer substantial insights into how humans accomplish the difficult task of learning about environments and responding to navigational challenges**" (Furnman et al., 2014).

How individuals make decisions about how to navigate and find their way around in daily life has been addressed by navigation studies which assess participants' use of navigation styles, preferences, strategies or 'biases' (e.g. Viard et al., 2011 and for a review, see Shelton et al., 2013). Navigation strategies (or biases) are generally depicted in spatial processing research as one of two kinds: those which either typically rely on *allocentric processing* (cognitive map, place or configural strategies) and involve the hippocampus; or those which typically rely on *egocentric processing* (route, landmark and response strategies) and involve the parietal cortex, caudate nucleus and striatal circuits (Wiener et al., 2013; Furnman et al., 2014; Banner et al., 2011). Hippocampal dependent, allocentric and configural strategies are deemed explicit, declarative and knowledge based, and hippocampal *in*dependent egocentric strategies as associative and implicit, and are more based on habit and response learning (Iaria et al., 2003; Banner et al. 2011; Furnman et al., 2014; Barrash et al., 2000). (The differentiation between declarative and implicit memory systems is addressed in more detail later in the discussion Section 5.5. of Chapter 5, Self-Reported Navigation).

Allocentric styles of navigation have been described in many ways, using terms such as: cognitive map strategy; spatial strategy (wherein participants build relationships between landmarks and the environment); place learning; survey strategy; and configural strategy (Lövdén et al., 2011; Furnman et al., 2014; Banner et al., 2011; Wiener et al., 2013; Janzen et al., 2008). By way of example, an allocentric, *configural* and place-based strategy might refer to a mental map or overhead view of an area to find an alternative route or shortcut.

Egocentric styles of navigation have also been described in many ways, using terms such as: cue-dependence; cue-response; response strategy; response learning; route strategy; schema dependent; associative cue strategy; and beacon strategy (Frankland et al., 1998; Selden et al., 1991; Van Kesteren et al., 2013; Lövdén et al., 2011; Banner et al., 2011; Furnman et al., 2014; Wiener et al., 2013). An egocentric *beacon strategy* might be one that uses 'heading towards' landmarks to take a person from one salient point to another, such as "head towards the library". An egocentric *associative cue* strategy is likely to involve the encoding of a directional turn with a specific landmark as a frame of reference, such as "turn right at the pub".

4.1.4 Identifying strategy use

How strategy preferences are quantified in navigation research depends very much on the spatial processing paradigms and performance measures used. In rodent research, neuroimaging techniques have been used to assess how the hippocampus may be used to encode spatial information (e.g. Kerner et al., 2008). In humans, another means of assessing navigation preferences is by asking participants to learn a route and assess whether they have built a cognitive map of the area while learning the route, or whether they continue to use egocentric strategies (learning turns and directional changes associatively).

Two prominent means of ascertaining if participants adopt allocentric processing techniques or retain egocentric techniques is to assess how participants use shortcuts and distal cues when route learning in virtual environments. Examples of such experiments are provided in Figure 4.1.4 (below) which first depicts Furnman et al.'s (2014) virtual environment and secondly depicts Banner et al.'s (2011) Four-on-Eight Virtual Maze (4/8 VM) based on Bohbot et al.'s (2007) eight arm radial maze.

An example of shortcut assessment is the study implemented by Furnman et al. (2014), presented first in Figure 4.1.4 below. Participants are tested on wayfinding or route learning and then asked if they used shortcuts when re-tested. Taking shortcuts would have required an allocentric strategy, whereas maintaining the familiar path (rather than using a short cut) would only require retaining an egocentric strategy. With regard to using distal cues, both paradigms below incorporate mountain ranges in the background environment to serve as distal cues.

Figure 4.1.4: Screen shots from other VE paradigms used to asses strategy use in other studies. The first image is the desktop virtual environment paradigm to assess strategy use in Furnman et al. (2014) and the second image is from Banner et al.'s virtual environment (2011), based on Bohbot et al.'s maze (2007).

The paradigm used by Banner et al. (2011) was able to determine if participants had mainly used these distal cues to form a cognitive map of the area (using allocentric processing) or if they had, instead, learnt to associate immediate landmarks with names and numbers (using egocentric processing). Participants were also asked at the end of the task to report how they solved it. Based on whether participants' responses to this question included references to the distal cues or to the counting or labelling landmarks, participants were respectively categorised as being either 'spatial' (allocentric) learners or 'response' (associative) learners.

4.1.5 The dual solution model

Understanding that individuals may employ different types of strategy to solve a navigation task provides a finer level of detail for this study into the impact of trauma on navigation behaviour; detail which may reveal biases for and changes in strategy use between groups.

This tradition of distinguishing between navigation strategies dates back to Tolman's pioneering development of the T-Maze in which rats learn space in terms of either place or response strategies (Tolman, 1948). Differentiation between the two solutions has persisted in the development of spatial paradigms (Wolbers & Wiener, 2014). Another prime example of a such a navigation paradigm featured heavily in the recent study by Furman et al. (2014, as detailed in Section 4.1.4) and was aptly named 'The Dual Solution' paradigm (produced by co-author Marchette, in Marchette et al., 2011; Bohbot et al., 2007).

While this distinction *between* allocentric and egocentric spatial processing is key it is also important to consider different types of *egocentric* strategies. Most studies do not typically distinguish between egocentric strategies based on coded associations (associative cue strategies) or those based on heading towards a general direction in the environment (beacon strategies). This distinction was, however, made by Wiener et al. (2013) who explained its relevance in terms of neuropsychology. Wiener et al. (2013) proposed that different areas of the brain may be employed for configural, associative cue and beacon strategies: that is, the hippocampus, the dorsal dorsolateral stratum, and the ventral dorsomedial stratum, respectively. One can see here that delineating different egocentric strategies in this manner provides a more comprehensive account of spatial processing. These issues were borne in mind when selecting an appropriate paradigm and are discussed in more detail later in this chapter (see Section 7.1.7.2).

Finally, gaining insights into understanding *maladaptive bias* may be as relevant for PTSD as for research into aging (Wiener et al., 2013). The dual model of allocentric and egocentric spatial processing can help unpick why spatial processing is not successful in some situations. When an individual persists in using an inappropriate strategy in a spatial task (rather than taking up an appropriate strategy for the task), this is referred to as a 'maladaptive bias'. Wiener et al. (2013) demonstrated a maladaptive bias in older persons; namely, a tendency to use a beacon strategy rather than an allocentric processing one. The inference from Wiener et al.'s study (2013) was that deficits in allocentric strategy use were due to age-related hippocampal atrophy in older participants, and that a beacon strategy was adopted in preference to an associative cue strategy (as this has also been associated with age-related atrophy in the dorsolateral stratum). In turn, this study in intended to consider if PTSD-related hippocampal impairment may result in different use of allocentric and egocentric strategies.

The relevance to this study of looking at how and why individuals *change their strategy* in navigation is summed up by Bohbot et al. (2013) in their investigation of navigation strategy use in cases of drug addiction. In their introduction, they clearly state that the use of navigation strategies is a "biologically adaptive mechanism". Bohbot et al. (2013) argue that there are some key drivers which, over time, determine a shift from allocentric to egocentric strategies:

"repetition that normally occurs during the formation of habits, stress and reward" (Bohbot et al., 2013). Research reviewed by Weber (2008) also discussed how trauma can affect individuals' capacity for attention to stimulus and how this can result in abnormal information processing. This study will look more closely at how trauma exposure (as well as PTSD) may influence or bias the strategies individuals use to navigate.

4.1.6 Information processing biases and trauma

When it comes to trauma psychology, the most prominent reference to information processing biases is to those that are associative in nature. The notion of associative bias is central to the trauma literature and features (to some degree) in all the theories of PTSD which were reviewed in this study.

4.1.6.1 ASSOCIATIVE BIAS IN THEORIES OF PTSD

The 'associative' bias of PTSD has a long history, but remains relevant to present day theory. Associative biases were thought to be first identified in cases of trauma exposure by Sigmund Freud where patients used egocentric schema from which they viewed the world and processed emotional responses to trauma based on that schema (Eich et al., 2012; Lang, 1977, 1984; Erwin, 2003; Epstein, 1985; Horowitz, 1986; Janoff-Bulman, 1992; Foa & Rothbaum, 1998; Foa & Kozak, 1986; Steel et al., 2005). The onus on 'association' in understanding PTSD is reflected in both schema and emotional processing theories of PTSD and is reflective of theories of classical conditioning. Central to the rationale of many theories of PTSD is that individuals who experience traumatic events develop Pavlovian-like associations[10] between past trauma and fears, and present day environmental cues (Maren, 2008; Krystal et al. in Horowitz, 1999; Rudy et al., 2004; Acheson et al., 2012; Jacobs & Nadel, 1985). This results in inescapable fear conditioning and indelible associations (Lang, 1987, 1994; Le Doux, 2000; Maren, 2001, 2008, 2011; Kirmayer et al., 2007). Theories based on this associative conditioning phenomenon came to be known as 'conditioning theories' (Brewin & Holmes, 2003).

A useful way of illustrating how associative information bias is pertinent to PTSD is to consider the widely recognised phenomenon of 'flashbacks' (as introduced in the General introduction, Section 1.1.1). A signature symptom of PTSD is the flashback, which is also referred to as visual intrusion. Visual intrusions and flashbacks are types of memory that involve intense reliving of a trauma, in an associative response to a cue in the present environment (Vasterling & Brewin, 2005). Associations result from insufficient contextualisation of the experience at the time and place where is occurred. The intrusions typically arise unprompted, without conscious awareness of what the association is between the stimulus in the current environment and the memory of the past event. Some contemporary examples of environmental cues and associations are well described in a podcast about combat-related PTSD (CR-PTSD), published online by the Guardian[11] (mentioned earlier in Section 1.1.1). In this example, combat veterans

[10] Pavlovian conditioning is a learning process in which an innate response to a potent stimulus (such as a traumatic event) comes to be elicited in response to a previously neutral stimulus (in the present day environment) and is named after Ivan Pavlov (1927).
[11] http://www.theguardian.com/society/video/2014/dec/19/trigger-point-ptsd-video

recount how, for instance, bumper boxes of Christmas chocolates here in the UK will suddenly evoke vivid traumatic memories of combat in Iraq and Afghanistan. The associative relationship here was formed because in combat, plastic chocolate boxes were often used to package improvised explosive devices (IEDs) by insurgents. The chocolate box has an encoded association with combat, and the present day context of a family Christmas has no bearing on the individual's re-lived experience of that trauma.

Interestingly, memories of trauma that are contextualised (one assumes by the hippocampus) are experienced as far less distressing. A practical example of this is provided in research reviewed by the King's Centre for Military Health in their 2010 report which showed that explicit and dramatic *reconstructions of trauma* do not trigger flashbacks in combat veterans, as one might typically assume they would (KCMHR, 2010). This can be explained: traumatic association arises from disparity between (or a disconnect between) sensory stimulus in the present (e.g. a box of chocolates at Christmas) and a traumatic memory from the past (e.g. the IEDs in combat in Iraq). In these videos, however, the context for what is happening is provided through dramatic reconstruction, and there is no such disconnect. What is being seen is being presented in the *appropriate context for what occurred*. Through this example, one can already see that the associative bias in trauma is not the only form of information processing that is important to PTSD: lack of allocentric contextualisation also plays a part in the experience of trauma memory.

In trauma theory, 'associative' and 'conditioning' theories of PTSD have been shown to have shortcomings and more integrative theories have been called for. This has mainly been on the basis that associative theories do not offer a comprehensive framework to understand individual difference and psychopathology (Brewin & Homes, 2003), nor do they offer predictive power (Dalgleish, 2004). Appeals have been made for neurological research to demonstrate how *different* types of memory systems are used to process trauma (for reviews, see Brewin & Holmes, 2003; Dalgleish, 2004; cf. Bucci, 1997; 2001). Theories which are more comprehensive and which do include different memory systems have been referred to as information processing theories (Brewin & Holmes, 2003). These theories are said to provide a "cognitive architecture" by which one can understand trauma processing:

"The central idea is that there is something special about the way the traumatic event is represented in memory and that if it is not processed in an appropriate way, psychopathology will result. Like social-cognitive theories, this approach emphasizes the need for information about the event to be integrated within the wider memory system" (Brewin & Holmes, 2003).

4.1.6.2 ALLOCENTRIC INFORMATION PROCESSING IN PTSD

A prime example of an information processing theory is Dual Representation Theory (DRT), originally developed by Dalgleish in 2004. This theory is based on the premise that a healthy memory of an event comprises two closely linked representations. One is an image-based, sensory representation which is reliant on the viewpoint of the person remembering it (an egocentric, associative representation), implicit, and is supported by the amygdala. The other is a contextualised representation in time and space, independent of viewpoint (an allocentric

representation), explicit and is supported by the medial temporal lobe (and in particular, the hippocampus). In healthy normal memory, the two representations (egocentric and allocentric) are well-linked and retrieval of the sensory representation is contextualised by the spatial temporal allocentric memory. Sensory representations are implicit, situationally accessed memories: they are associative in nature and, when *un*contextualised by the explicit allocentric memory, they can be re-experienced, unbidden, and out of spatial and temporal context (for example, as flashbacks).

In 2005, Vasterling & Brewin suggested direct application of allocentric processing techniques in trauma therapy may be therapeutically helpful for PTSD. From a review of other trauma literature, there is much evidence of efforts being made in clinical psychology to deter individuals from inhabiting the post-trauma egocentric self-referential perspective (Ehlers & Clark, 2000). These efforts to deter the egocentric mind-set involved applying 'observer' and 'field' perspectives to trauma memories, which is suggestive of allocentric style processing.

An example of how this might work in practice would be for trauma exposed individuals to be encouraged in the clinical setting to: revisit traumatic memories from an 'overhead view; recall traumatic events from different spatial viewpoints; and to consider the other contextual information about the time and place of the trauma. A working example of this application of allocentric processing to trauma is illustrated in the Discussion Chapter 8 in Figure 8.3.

Literature from clinical psychology certainly suggests that allocentric-type processing is already common to therapeutic practice, such as in exposure therapy (Steel et al., 2005; Neuner et al., 2008). References to this kind of approach can be found in trauma literature as far back as in Freudian psychoanalysis and as recent as 2015 (Smith et al. 2015; McIsaac & Eich, 2004; Eich et al., 2011, 2012; Steel et al., 2005; Neuner et al., 2008). However, until 2010, these trauma processing methods were not articulated in terms of *allocentric versus egocentric* processing (such terms being the reserve of the domain of navigation literature).

The relevance of allocentric processing to trauma processing was illustrated in a study by Bisby et al. (2010, introduced in Section 1.2.3). In a double-blind independent group design, participants were administered alcohol or a placebo and on a virtual environment paradigm which assessed object location memory (the same Town Square task as later used by Smith et al., 2015). Where deficits in allocentric memory were observed, these were proportionate to the prevalence of PTSD-related visual intrusions. Findings from this study demonstrated how the dual memory system worked in relation to the specific PTSD-related symptom of visual intrusions. Subsequently, the application of allocentric processing to trauma processing has been strongly advocated, and, in light of these findings, Dalgleish's original (2004) Dual Representation theory of PTSD was updated in 2010 (Bisby et al., 2010; Brewin & Burgess, 2014; Smith et al., 2015). Furthermore, at the time of submission of this thesis, Kaur et al. (2016) published an exploratory case study which trialled the application of allocentric-type processing to combat trauma processing. The results showed improvement in PTSD symptoms in two cases (see Section 3.1.3).

4.1.7 Determining 'associative' bias in PTSD and navigation

Whilst associative bias can be demonstrated clearly in navigation tasks (Wiener et al., 2013), how it plays out *within PTSD symptomology* is not something which this study into PTSD and navigation can address. Despite the clear relevance of associative information processing to PTSD, there is little clarity in trauma literature about *which* PTSD symptoms provide the most accurate measure of associative thinking. Some studies have focussed on particular PTSD symptoms but these were not explicitly identified as being particularly "associative". These include: visual intrusions (Bisby et al. 2010); sensory data and physical sensations (Brewin et al. 2010); startle response (Meyer, 2012); and reliving (or 'increased now-ness') (Glazer et al. 2013). Attempts to deconstruct PTSD symptoms into those which specifically reflect associative thinking and those which do not would be fraught with theoretical and clinical complexities. The American Psychological Association in the DSM-IV and DSM- V has deconstructed PTSD into clusters of symptomology (including re-experiencing, avoidance and hyper-arousal) has but none of these clusters have been directly attributed to specific associative thinking biases (APA, 2013). What is more, the term 'disassociation' in contemporary trauma psychology refers to a very specific *subtype of PTSD i*nvolving specific symptoms of depersonalisation and derealisation and these 'dissociative' symptoms should not be misinterpreted as constituting the 'opposite' of the associative type thinking being discussed here (Lanius et al., 2012; Teicher et al., 2003). Therefore, there are no established acceptable 'measures' by which specifically associative style thinking symptoms can be validly assessed. The only option available to this study is to use an individual's PTSD severity as a marker of their likely associative bias; that is, participants' total score on PTSD diagnostic scales (such as the PDS by Foa et al. 1995).

4.1.7.1 ASSESSING INFORMATION PROCESSING BIASES IN BOTH TRAUMA AND NAVIGATION

Investigating the application of associative and allocentric navigation processing biases in the context of trauma is novel and required a robust navigation paradigm. While theoretical and clinical links between *spatial processing* and *trauma processing* strategies are starting to be identified and developed by those interested in the application of allocentric processing to the context of stress and trauma, this is still a relatively young field of research (Dalgleish, 2004; Bisby et al., 2010; Vasterling & Brewin 2005; Smith et al. 2015; Brewin & Burgess 2014; Meyer et al., 2012, Schwabe et al., 2008). Up until 2016 (Van Gerven et al., 2016), there has been no investigation in navigation literature into the effects of stress on navigation strategy. As explained in Section 3.1.1, Van Gerven et al. (2016) published surprising results from a recent experiment[12] which showed that participants who had experienced recent acute stress (using a PASAT paradigm) switched navigation strategy (on a human model of the Morris Water maze) from egocentric to allocentric. These findings, however, were based on the effects on navigation behaviour of *acute* stress imposed on participants in the experiments, not on the effects of *previous traumatic experiences* and the longer term implications this may have for individuals'

[12] Van Gerven et al. (2016) used the Paced Auditory Serial Addition Task (PASAT) and measured its impact on blood pressure, salivary cortisol concentration and self-reported anxiety using the State-Trait Anxiety Inventory (STAI)

approach to using allocentric processing (e.g. Smith et al., 2015). Neuropsychological research had therefore yet to examine the dynamic between hippocampal dependent and *in*dependent memory systems in the context of active navigation behaviour in earlier traumatised populations. What is more, investigating 'dual solutions' to navigation tasks (Marchette, 2007), amongst populations with 'dual representations' of trauma memories (Dalgleish, 2004; Bisby et al. 2010) in *one experiment* was a new challenge for this study.

The requirements of the task were considered in detail so that a review could be undertaken of the navigation paradigms which would be most suitable. The challenge required a navigation experiment that could detect and differentiate between dual solutions (i.e. associative and non-associative egocentric biases *and* allocentric biases) as well as measure overall task performance.

4.1.7.2 REVIEWING VIRTUAL ENVIRONMENT (VE) NAVIGATION PARADIGMS

A review of spatial processing literature was undertaken to identify a more involved and 'active', VE task that would provide more rich data about allocentric and egocentric navigation performance and strategy use. The review of contemporary VE paradigms (see Table 4.1.7 overleaf) took into consideration: the level of detail provided by the navigation paradigms (such as whether they were able to measure strategy use as well as performance); the practical feasibility of the tasks (some tasks required the use of a treadmill, for example); the nature of the task (some were more focussed on route learning than navigating around an environment); and the ecological validity (e.g. use of environmental space rather than 'vista' space; and the evocative nature of the material- given trauma exposed participants' potential sensitivity).

Table 4.1.7: A review of alternative virtual environment experiments considered for this study.

Author(s)	Research Approach	Relevance of methodology and spatial tests
Banner et al. (2011)	4 / 8 radial maze based on Bohbot et al. (2007)	This task provided more detail on strategy uptake, and less detail on hippocampal dependent spatial performance. Single-question approach to navigation preferences.
Furman et al. (2014)	VE with novel vs familiar path uptake and navigation questionnaires.	Strategy uptake was not measured. SBSOD and QSR questionnaires were used but not the FRS. (Publication also post-dated data collection).
Lövdén et al. (2011)	Unnamed VE training task with allocentric training outcomes and assessment measures.	This used a treadmill and included realistic footage of wild animals, which was not appropriate for those in the current study's population who were trauma exposed and who included those with impaired mobility.
Tempesta et al. (2012)	Un-named VE route-planning task based on cognitive map building.	This test focussed more on route planning than navigation and there was also insufficient detail as to its ecological validity. Strategy uptake was not identified or assessed.
Polmero et al. (2012)	VE cognitive map formation / identification of shortcuts.	This test focussed more on route planning than navigation and was very gender sensitive.
Kirmayer et al. (2007)	Human adaptation of Morris Water Maze.	This 'escape learning' paradigm was not deemed appropriate for study populations with high anxiety levels.
Moffat et al. (2009)	Age and spatial memory: VE using hallways	This 'escape learning' paradigm was not deemed appropriate for study populations with high anxiety levels and was highly sensitive to age.
Bisby et al. (2010) Smith et al. (2015).	Town Square Task (VE)	This perspective taking task tested spatial memory more than active navigation, was set in 'vista' space and did not did not facilitate the assessment of strategy uptake.
Wiener et al. (2013)	The Alternative Route (AR) VE paradigm	This way-finding and route learning paradigm had been used to demonstrate age-related hippocampal impairment in navigation. Performance data included strategy use.

4.1.8 The Alternative Route (AR) paradigm (Wiener et al., 2013).

The Alternative Route (AR) paradigm, developed by Wiener et al. (2013) was selected as the most relevant to this study. The VE paradigm encompasses key elements of allocentric navigation (as described by Ekstrom et al., 2014) including: acquiring and storing environmental information, configuring a mental representation of the environment, and making decisions about when to use this map' allocentrically'. The AR paradigm was also capable of demonstrating performance differences in active navigation involving hippocampal dependent spatial processing (as distinct from hippocampal *in*dependent processing). The AR paradigm was ecologically valid in its use of environmental space[13], which is more attuned to everyday navigation than purely 'vista' space' which does not require active navigation moving through the environment (Wolbers & Wiener, 2014), such as with the Four Mountains task.

[13] Figural, vista and environmental frames of space are introduced at Section 1.2. and discussed in more detail at Section 4.1.2.

What is more, the AR paradigm was deemed 'PTSD-Friendly' in so far as:

i) The AR did not require the use of a treadmill (which would otherwise preclude those with mobility impairment from partaking in the research);
ii) The AR did not include evocative or powerful imagery (such as wild animals) which may have been inappropriate and detrimental for those with high anxiety levels or PTSD;
iii) The AR did not involve "escape learning" which could also be inappropriate and detrimental for those with high anxiety levels or PTSD;
iv) The AR was not gender-sensitive which could have been problematic for performance analysis of all-male combat trauma exposed participant groups.

The Figure 4.1.8 below illustrates a typically 'immersive' virtual reality navigation training paradigm such as is used in the UK military, compared to the less evocative material of the Alternative Route paradigm.

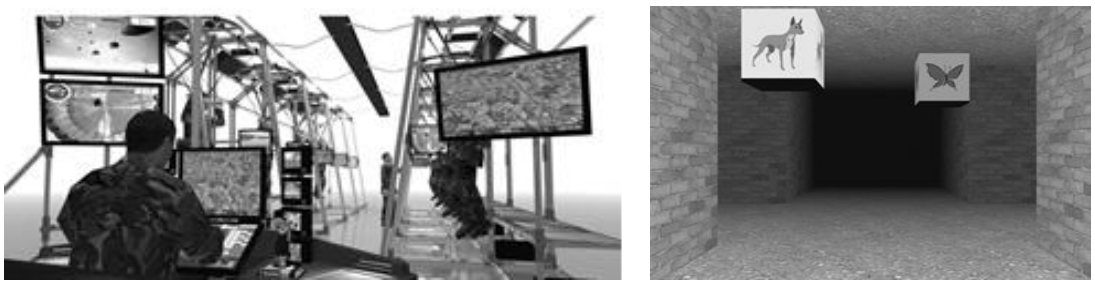


Figure 4.1.8: Comparing the ecological validity and immersion of virtual reality navigation paradigms used in UK MOD[14] parachute training, and in neuropsychological research (Wiener et al. 2013).

The AR paradigm comprises key elements of active allocentric navigation (as described earlier by Erkstrom et al., 2014) including: acquiring and storing environmental information, configuring a mental representation of the environment, and making decisions about when to use this map allocentrically'.

'Strategy use' is key to this investigation of the impact of PTSD on navigation. In their study of the effect of aging on navigation performance, Wiener et al., (2013) designed and employed this novel route-learning paradigm to test allocentric and egocentric navigation performance, but, importantly, Wiener et al. (2013) designed the AR to identify preferences (biases) for different navigation (spatial processing) *strategies*. These information processing biases included: the allocentric 'configural' strategy; the egocentric 'associative cue' strategy (akin to the 'associative' thinking styles described in trauma literature and inferred by participants' landmark-based decisions); and another egocentric strategy called the 'beacon strategy' (which did not involve encoding of associations).

The objective of the AR task was to commit a route to memory and to use it flexibly. Participants were repeatedly exposed to a route through a virtual environment which they learned over a period of 24 minutes. During the 24 minutes, participants were regularly 'tested' on the route (participants were presented with intersections from the route and were asked to select in which

[14] Courtesy of the Ministry of Defence. See: https://www.defencetalk.com/new-virtual-reality-parachute-trainers-for-armed-forces-25250/

direction they would turn at this test intersection in order to re-join the route). The test intersections were sometimes presented to participants from a different direction to those already presented in the learning trials. This means that purely egocentric hippocampal *independent* strategy would not have been sufficient to solve these intersection tests. Neither a beacon strategy (of generally 'heading towards' landmarks), nor an associative cue strategy (of turning in a direction that is encoded with a landmark) would suffice – as the direction of travel was different. Only the allocentric configural strategy (of mentally mapping the route, so that it could be applied from any directional orientation) would result in a correct answer. On these 'different direction' trials, participants could either adopt either an allocentric configural strategy (and this resulted in a correct answer) or could maintain a maladaptive egocentric strategy (and be incorrect).

It is clear from this initial description of the task that the demands of the AR closely reflect the key elements of allocentric navigation described by Erkstrom et al., 2014): acquiring and storing environmental information (the training route), configuring a mental representation of the environment (which enables participants to solve different direction trials), and making decisions about when to use this map allocentrically (participants' uptake of a configural strategy rather than maintaining egocentric strategies).

The Alternative Route paradigm produces quantifiable performance data on allocentric spatial processing (*different direction* trials, as compared to *same direction* trials) as well as strategy preference (*configural, associative cue and beacon*), and produces both *overall* performance data and *block-by-block* performance data. More detail about the AR paradigm and the performance measures it produces can be found in the Materials Section 4.2.3.

4.1.9 Demographic and clinical factors

Demographic and clinical variables identified in the literature as pertinent to Chapter 4, the Four Mountains task and the Alternative Route paradigm, include: age, gender, pain, the taking of medications and sleep disturbance.

Despite that fact that age was not found to influence performance on the Four Mountains task in Chapter 3 (Section 3.3.2), age has been shown to have a negative impact on spatial memory which relies on the hippocampus (e.g. Smith et al., 2015; Daugherty et al., 2015; Rosenweig & Barnes, 2003; Raz et al., 2009; Moffat et al., 2001, 2009; Wiener et al., 2012, 2013). Age has also been associated with reduced hippocampal activation in PTSD (Carrion et al., 2010) and with the efficacy of trauma processing interventions (Duax et al., 2013). With regard to the Alternative Route paradigm age has also been negatively associated with navigation performance in virtual environments (Driscoll et al., 2005) and has been assessed in relation to strategy use in navigation (Rodgers et al., 2012).

Despite the fact that in Chapter 3 (Section 3.3.2), none of the potentially confounding clinical variables were found to influence perspective-taking performance on the Four Mountains task, the same variables were still included in analysis in Chapter 4. This was on the basis that the Alternative Route paradigm (Wiener et al., 2013) was intended to provide a finer level of detail

about hippocampal dependent spatial processing and strategy use, which had the potential to be more sensitive to clinical influences. By way of a reminder, these clinical factors were:

i) Pain, which has been shown to effect spatial memory in rats (Cardoso-Cruz et al., 2013);
ii) The taking of Selective Serotonin Reuptake Inhibitors (SSRI's), antipsychotics and opiates - which have been said to interfere with hippocampal neurogenesis and plasticity (Anacker et al., 2011; Bath et al., 2012; Engel et al., 2013; Luo et al., 2005; Pu et al., 2005);
iii) Sleep disturbance, which has been shown to effect hippocampal dependent processing in cases of PTSD, in study by Tempesta et al. (2011).

Hypotheses and predictions

Given the literature reviewed, the recent findings by Smith et al. (2015) and the findings from Chapter 3, the following hypotheses were formulated.

(i) 'PTSD negatively impacts hippocampal dependent active navigation performance.' This hypothesis followed observations in the literature of PTSD-related impairments in hippocampal dependent spatial processing (Acheson et al., 2012; Bisby et al. 2010; Tempesta et al., 2012; Pitman et al., 2012; Miller & Wiener, 2014; Meyer et al., 2012; Smith et al., 2015). This was also based on the initial findings reported in Chapter 3 which demonstrated hippocampal dependent perspective taking impairments in those with PTSD (the *PTSD* group). The prediction was that the *PTSD* group would demonstrate significantly lower scores for hippocampal dependent performance measures than the *Trauma Unexposed* group. The *DV* for this prediction was different direction trial accuracy at each of the six blocks of the AR paradigm.

(ii) 'Subclinical levels of unprocessed trauma will impair navigation performance.' The rationale behind this hypothesis was that even in cases where trauma had not result in clinical or probable levels of PTSD symptomatology, unprocessed trauma would still deplete hippocampus resources and thereby compromise its ability of the hippocampus to apply allocentric processing to solve spatial navigation tasks. The prediction was that the *Trauma Exposed No PTSD* group's performance would not be poorer than that of the *Trauma Unexposed* group's (due to there being some degree of impact from trauma exposure on spatial processing, albeit subclinical levels of PTSD). The prediction was made on the premise that the level of detail that the Alternative Route paradigm (Wiener et al., 2013) would facilitate a more sensitive test of trauma exposure impact than the Four Mountains task (Hartley et al., 2007 which is described in full in Chapter 3, Section 3.1.3). The *DV* for this prediction was different direction trial accuracy at each of the six blocks of the AR paradigm.

(iii) 'Associative bias in PTSD will present in navigation behaviour.' This hypothesis was based on recognised links in the literature between PTSD and associative thinking styles and the need to apply 'corrective' non-egocentric (allocentric) processing styles to counteract trauma symptomology (Erwin, 2003 with reference to Freud; Eich et al., 2012; Lang, 1977, 1984; Vasterling & Brewin, 2005; Brewin & Burgess, 2014; Smith et al., 2015; Miller & Wiener,

2014). Neurobiological models of associative and allocentric processing which were referred to in the reviewed literature also support this hypothesis (Byrne et al., 2007; Featherstone & McDonald, 2004, 2005 in Wiener et al., 2013; 6012; Vasterling & Brewin, 2001; 110; Shin et al., 2011; Shenton & Turetsky, eds., 2010; and Rauch, 2006 in Brewin, 2014). The prediction was that the *PTSD* group would demonstrate significantly higher uptake of hippocampal *in*dependent navigation strategies, with a particular preference for associative cue strategy, given the evidence that associative biases are more likely following trauma exposure (that is, *PTSD*). The *DVs* for this prediction was associative cue strategy use in each block (1 to 6) over the AR paradigm.

4.2 METHODS

4.2.1 Participants

The experiment included 138 participants (62 females) of the total sample population (*n* = 150). Healthy controls (*n* =78) were recruited from Bournemouth University (staff and students and the general population) through the Psychology Research Volunteer Scheme. Bournemouth University (BU) recruited 78 healthy controls including staff, students, and members of the public. Nine participants with symptoms of Post-Traumatic Stress Disorder (PTSD) were recruited through the Intensive Psychotherapy Treatment Service (IPTS) at Dorset NHS. Twenty-four participants with trauma exposure were recruited from Dorset and Cambridgeshire Police. Twenty-five military veterans were recruited from Combat Stress's rehabilitation programme (Ex Services Mental Welfare Society Registered Charity No. 206002, Surrey). Two healthy combat trauma exposed participants from the UK Armed Forces were recruited through British Military Fitness and Forces Fit military fitness programmes.

Participants were offered a £10 financial reimbursement for their time. Those recruited through Combat Stress received £20 reimbursement to cover their additional travel costs. The study was approved by: the BU Graduate School Ethics Board; the Combat Stress Research Ethics Committee; and the NHS South West (Cornwall and Plymouth) National Research Ethics Service (NRES).

The experimental groups were categorised on the basis of trauma exposure in the same manner as described in Chapter 3. Of the total 138 participants, 47 had PTSD, 58 were Trauma Exposed but had no PTSD, and 33 were not Trauma Exposed and had no PTSD. By way of a reminder, the typical threshold used to diagnose probable PTSD on the PDS is a score of 20 or greater (Foa et al., 1995).

Demographic and clinical data were collected from the 138 participants. These demographic and clinical variables had been identified in the literature as pertinent to hippocampal dependent spatial processing and included: age (in years), gender (male or female), depression, the taking of anti-depressants (Selective Serotonin Reuptake Inhibitors or SSRIs) and benzodiazepines or opiates, pain and sleep disturbance. Table 4.2.1 below illustrates that there were significant group differences for all variables, requiring each to be controlled for in subsequent analyses.

Please note that clinical and demographic data in the table below are different from those presented in Chapter 3 (Section 3.2.1) due to one more participant providing data.

Table 4.2.1: Descriptive and inferential statistics for demographic and clinical data: means and standard deviations by experimental group (Trauma Unexposed, Trauma Exposed No PTSD, PTSD) (n = 138). Other medications = benzodiazepines and opiates.

Demographic or clinical factor		***Trauma Unexposed*** (*n* = 33)	***Trauma Exposed No PTSD*** (*n* = 58)	***PTSD*** (*n* = 47)	**Group comparison**
Mean age in years *(± SD)*		32.5 *SD* ±10.4	38.9 *SD* ±10.3	38.2 *SD* ± 9.6	F (2, 135) = 4.61, p = 0.01*
Gender (%)	Male	36.4%	46.6%	78.7%	χ^2= 17.0, p < .01**
	Female	63.6%	53.5%	21.3%	
SSRIs (%)	No	100%	94.1%	71.1%	χ^2 = 17.7, p < .01**
	Yes	0%	5.9%	28.9%	
Other medication (%)	No	100%	96.6%	72.3%	χ^2= 20.7, p < .01**
	Yes	0%	3.5%	27.7%	
Sleep Disturbance: Mean PSQI score (± *SD*)		0.41 *SD* ± 1.5	1.02 *SD* ± 2.43	8.11 *SD* ± 6.17	F (2, 135) = 50.3, p <.01**
Pain: Mean SNR score (± SD)		0.42 *SD* ± 1.37	0.86 *SD* ± 1.94	3.15 *SD* ± 3.70	F (2, 130) = 14.2, p < .01**
PTSD: Mean PDS score (± *SD*)		0	7.06 *SD* ± 6.62	35.3 *SD* ± 9.46	F (1, 94) = 290, p <.01**

4.2.2 Procedure

Informed consent was obtained from all participants (*n* = 138). All participants were assured that they were free to stop the experiment at any time and to withdraw from the task at any point without needed to give an explanation. Participants completed a screen for trauma exposure using the Life Events Checklist (LEC, Blake et al., 1995). Those who self-reported no trauma exposure were assigned to the *Trauma Unexposed* group (*n* = 33). Those who self-reported trauma exposure were given the Post-Traumatic Stress Disorder Diagnostic Scale (PDS, Foa 1995) to ascertain the present day impact of the prior trauma. Those who self-reported PDS scores at or above the threshold of 21 (as typically used by Foa et al., 1995) were allocated to the *PTSD* group (*n* = 47). Those who self-reported PDS scores below the threshold of 21 were allocated to the *Trauma Exposed No PTSD* group (n = 58).

Participants completed clinical measures of depression using the Beck Depression Inventory (BDI, Beck et al., 1996), pain using the standard Numerical Rating Scale (NRS, Jensen et al.,1986) and sleep, using the Pittsburg Sleep Quality Index Addendum for PTSD (PSQI-A, Germain et al., 2005).

Participants were then given written instructions for the Alternative Route (AR) paradigm and once participants had read these the experimenter summarised them verbally. A demonstration of the AR was shown to all participants and a practice run was undertaken, showing the participants how to use the controls and to advise participants about format and timing of the task. The participants then undertook the AR which took 24 minutes to complete.

4.2.3 Materials

The Alternative Route paradigm

The Alternative Route (AR) paradigm (Wiener et al., 2013, pictured below at Figure 4.2.3) is a novel route-learning paradigm designed to test hippocampal dependent (allocentric) and hippocampal *in*dependent (egocentric) navigation performance and to identify the application of spatial processing strategies.

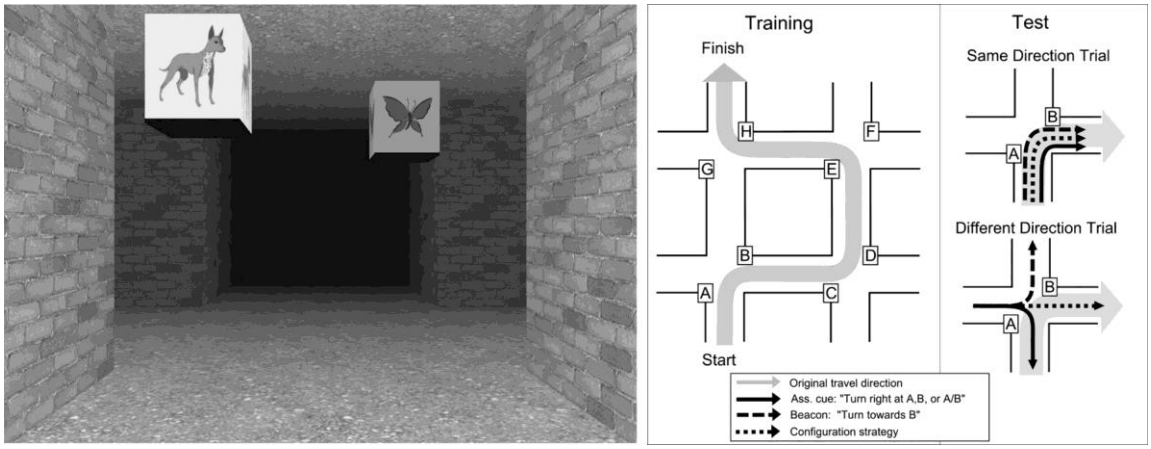


Figure 4.2.3: Screen shot from the Alternative Route Paradigm (Wiener et al., 2013) with diagrams of the training route and test intersections.

In the AR task participants were trained to learn a route comprising four intersections. They were then continually tested on how well they were learning the route by being asked to re-join the route from different directions (sometimes from the same direction that they learned the route, sometimes not). Where the participants were tested on the route from a different direction, their decisions could be analysed and the strategy that they used could be identified.

As depicted in Figure 4.2.3 above, intersections along the route were characterized by two unique landmarks located in diagonally opposite corners, unambiguously identifying the intersection as well as the direction from which it was approached. A black fog effect was used in the virtual environment to ensure that only one intersection was visible at any time.

The process of being shown the route and being tested on that route was repeated six times over 24 minutes. Each of the six experimental sessions (or 'blocks') comprised a training phase (in which participants were passively transported along the route of two left turns and two right turns) and a subsequent test phase. In the test phase, participants approached the four intersections within the route and were asked to indicate the direction needed to follow (or- pick up) the original route by pressing the left, right, or up (i.e., straight) arrow key. These responses were recorded but participants received no feedback about correctness of their responses to prevent learning from feedback. The four intersections were approached from every direction with the exception of the direction of travel to pick up the route. This meant that 12 tests were presented to the participants (in a randomised order to prevent participants detecting a pattern of directional turns for each junction).

Performance was assessed at 12 tests in each of the six blocks. The test intersections were approached from either:

1) The same side in the same order as presented in the training route;
2) The same side in a different order from that presented in the training route;
3) A different side, but in the same order, as that presented in the training route; or
4) A different side and a different order from that presented in the training route.

Same direction (type 1) trials tested participants' ability to replicate the route in the same way in which it was learned in training, i.e. to replicate the direction changes experienced during the learning phase. These trials can be solved using any strategy (be it associative cue, configural or beacon strategy) but performance in 'same direction' trials are generally accepted in the study by Wiener et al. (2013) as being a reliable indicator of egocentric spatial processing. Different direction trials (types 2 and 3) tested participants' ability to construct an allocentric representation of the route. The different direction trials can only be solved using the allocentric configural strategy. Performance on different direction trials is a measure of allocentric spatial processing[15].

The paradigm has been developed (by Wiener et al., 2013) in such a way that at type 3 trials, the direction of travel selected by the participant will reveals which strategy the participant has employed (be it associative, configural or beacon). The number of times an individual uses each strategy can be assessed and therefore this can produce a mean 'associative', 'configural' and 'beacon' score for each participant. The mean can be calculated for the whole experiment or by block.

The Alternative Route (AR) paradigm therefore produces performance data on egocentric and allocentric spatial processing as well as strategy uptake. The paradigm produces overall performance data (as a means for the whole task) but also performance data on a 'block-by-block' basis, which is useful to show how participants improve (or not) and also how they change their use of different strategies. A summary of the AR performance measures used in this experiment is provided below:

i) Egocentric performance: mean correct same direction trials (type 1 trials) as a percentage in each block (i.e. % correct in block 1, % correct in block 2, % correct in block 3, etc..).
ii) Allocentric performance: mean correct different direction trials (type 3 trials) as a percentage in each block (i.e. % correct in block 1, % correct in block 2, % correct in block 3, etc..).
iii) Associative strategy use (an egocentric strategy, akin to the associative bias reported in PTSD literature by Vasterling & Brewin, 2005, Eich et al., 2012, etc.): the number of times a participant uses associative cue strategy at type 3 trials. This is calculated as a percentage in each block (i.e. % use in block 1, % use in block 2, % use in block 3, etc.).

[15] Type 4 trials can be solved egocentrically as well as allocentrically and therefore are not included in measures of different direction performance (Wiener et al., 2013).

iv) Configural strategy use (an allocentric strategy, which is required in order to solve different direction trials): the number of times a participant uses configural strategy at type 3 trials. This is calculated as a percentage in each block (i.e. % use in block 1, % use in block 2, % use in block 3, etc.).
v) Beacon strategy use (an egocentric strategy, which was the strategy for which older persons adopted a maladaptive bias in Wiener et al.'s study of aging in 2013): the number of times a participant uses beacon strategy at type 3 trials. This is calculated as a percentage in each block (i.e. % use in block 1, % use in block 2, % use in block 3, etc.).

There were also several performance measures which were discounted in consultation with the designers of the paradigm (Wiener et al., 2012, 2013) primarily because the additional measures offered no more clarity or accuracy when compared with the selected measures for group differences. Further information comprising of a table of comparative data using these alternative AR performance measures can be found in Appendix G.

4.3 RESULTS

4.3.1 Design

Performance and strategy use in the Alternative Route (AR) paradigm analysed by experimental group. All statistical analyses were performed using SPSS version 22 (SPSS, IBM Corp. in Armonk, NY).

MISSING VALUES

The AR task was timed so that responses needed to be given within 6 seconds for each of the 72 trials (this is explained in Chapter 4 in more detail). There were six instances (one instance per row in six rows out of 9864 rows of data) of missing trial data among the 150 participants. This could have occurred randomly due to human error (such as distraction or lack of concentration) or because of the time pressure of the paradigm. Due to the small number of instances of missing responses (at less than 0.01%), the trials in which the responses were not given were removed (see the study by Wiener et al., 2013 for a similar treatment of missing AR data).

PERFORMANCE

Navigation performance on the Alternative Route paradigm (Wiener et al., 2013) was assessed between the respective experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD and PTSD*). A repeated measures 6 x 3 analyses of variance (ANOVA) was used to assess experimental group differences (*Trauma Unexposed, Trauma Exposed No PTSD* and *PTSD)* on measures of egocentric and allocentric performance (same direction and different direction trial accuracy at each of the six blocks). The comparison between different (allocentric) and same (egocentric) direction spatial processing performance has been used by Smith et al. (2015) in their study of PTSD and allocentric processing, King et al.'s (2004) study of focal hippocampal damage, Bisby et al.'s (2010) study of visual intrusions and spatial processing, and Wiener et al.'s (2013) study of aging and allocentric processing (which also uses the Alternative Route paradigm).

Demographic and clinical variables were then entered separately into the 6 x 3 ANOVA as covariates. Linear regression analysis was then undertaken for allocentric performance using all demographic and clinical variables. This model was also implemented in the study by Smith et al. (2015) which assessed different view performance differences between PTSD and non-PTSD groups. Post hoc t-tests with the dependent variable of allocentric performance were also conducted to examine specific demographic and clinical group differences more closely.

STRATEGY USE

Navigation strategy use in the Alternative Route paradigm (Wiener et al., 2013) was assessed between the respective experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD and PTSD*). This is first presented graphically. Statistical analysis was then conducted using a repeated measures 6 x 3 ANOVA design to assess experimental group differences (*Trauma Unexposed, Trauma Exposed No PTSD* and *PTSD)* in associative cue, then configural and then beacon strategy use. Demographic and clinical variables were entered into a linear regression analysis for mean configural strategy use (as a mean % over the six blocks) and then for associative cue strategy use (as a mean % over the six blocks).

4.3.2 Navigation performance

Experimental group differences (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) in egocentric performance and then allocentric performance were assessed to ascertain if there is any particular impairment in hippocampal dependent (allocentric) processing which is unique to PTSD or trauma exposure.

4.3.2.1 EGOCENTRIC PERFORMANCE

The first analysis compares egocentric navigation performance (mean % *same direction* trial correctness) between the experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) (*n* = 138) over each of the six experimental sessions (blocks) of the task.

A repeated measures 6 x 3 ANOVA with the between factor *group* (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) and the within factor *block* (1 to 6) revealed a significant main effect of *group*, F (2, 135) = 7.50, $p < 0.01$, $\eta_p^2 = 0.94$. Pairwise comparisons (with Bonferroni correction) demonstrated that the *PTSD* group performed significantly worse (M = 0.75, SD ± 0.02) than both the *Trauma Unexposed* group (M = 0.86, SD ± 0.03, *PTSD* vs *Trauma Unexposed* group p <0.01) and the *Trauma Exposed No PTSD* group (M = 0.86, SD ± 0.02, *PTSD* vs *Trauma Exposed No PTSD* group, p <0.01). There was no significant difference between the *Trauma Exposed No PTSD* group and the *Trauma Unexposed group* (p = 1.00). There was no significant main effect of block, F (4.51, 135) = 0.53, p = 0.74, $\eta_p^2 = 0.01$. Performance at block 1 was 81% (SD ± 2.1%) which only increased to 83% at block 6 (SD ± 2.1%*).* There was no significant interaction between block and group, F (9.03, 135) = 0.14*,* p = 0.10, $\eta_p^2 = 0.41$).

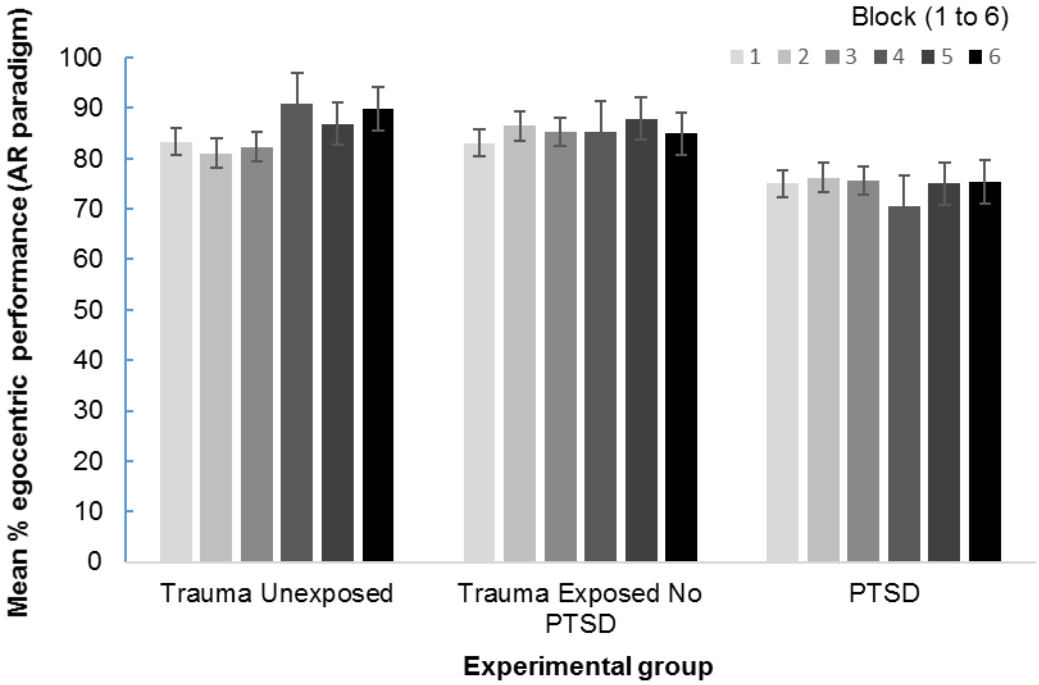


Figure 4.3.2.1: Mean (%) egocentric performance in the AR paradigm by experimental group (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) for same direction trials by block (1 to 6) (*n* = 138) with standard error bars.

The overall egocentric navigation performance is generally high and this is maintained across the six experimental sessions (blocks 1 to 6) of the task, demonstrating that there is no egocentric learning in the task (see Figure 4.3.2.1). The results suggest that PTSD impairs egocentric navigation performance, but that trauma exposure does not.

4.3.2.2 ALLOCENTRIC PERFORMANCE

The second analysis compares allocentric performance (mean % *different direction* trial correctness) between the experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) (*n* = 138) over each of the six experimental sessions (blocks) of the task.

Figure 4.3.2.2 below illustrates that final allocentric performance in block 6 of the task varies significantly between *Trauma Unexposed* group and the *Trauma Exposed No PTSD* group.

A repeated measures 6 x 3 ANOVA with the between factor *group* (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) and the within factor *block* revealed a significant main effect of block, F (4.14, 135) = 32.5, $p < .01$, $\eta_p^2 = 0.19$. Performance increased over the experimental sessions (block 1 to 6), demonstrating an effect of learning in the task. Mean performance increased from 11.6% (*SD* ± 1.9%) in block 1 to 37.6% (*SD* ± 2.8%) in block 6.

The only significance differences found in pairwise comparisons with Bonferroni correction applied were between the *PTSD* group and the *Trauma Unexposed* group with the *PTSD* group's mean performance lower than that of the *Trauma Unexposed* group.

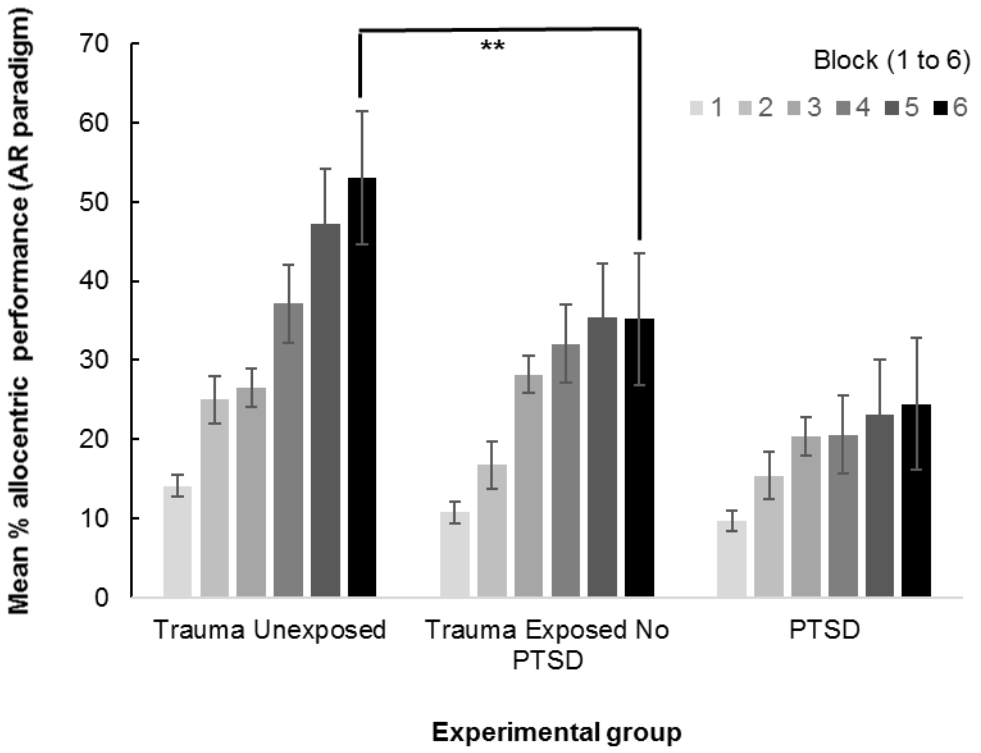


Figure 4.3.2.2: Mean (%) allocentric performance in the AR paradigm by experimental group (Trauma Unexposed, Trauma Exposed No PTSD, PTSD) for different direction trials by block (1 to 6) (n = 138) with standard error bars. The significant difference in allocentric performance between healthy trauma exposed participants and trauma unexposed participants in final performance at block 6, at $p = 0.01$ ** is highlighted.

There was a significant main effect of group, F (2, 135) = 4.23, p = 0.02, η_p^2 = 0.06. Pairwise comparisons (with Bonferroni correction) showed that the *PTSD* group performed significantly differently (M = 0.19, SD ± 0.03) to the *Trauma Unexposed* group (M = 0.34, SD ± 0.04) (*PTSD* vs *Trauma Unexposed*, p = 0.01). The *Trauma Exposed No PTSD* group (M = 0.27 ± 0.01) did not perform significantly differently to the *PTSD* group (*PTSD* vs *Trauma Exposed No PTSD* group, p = 0.29). The *Trauma Exposed No PTSD* group did not perform significantly differently to the *Trauma Unexposed* group (*Trauma Unexposed* vs *Trauma Exposed No PTSD*, p = 0.40).

There was a significant interaction between group and block, F (8.29, 135) = 2.84, p = 0.01, η_p^2 = 0.04. Performance by block gives an indication of an effect of learning and therefore this demonstrates that experimental group significantly affected allocentric learning in the navigation task. To explore the nature of this interaction between group and allocentric performance on route learning, post hoc t- tests were conducted. Allocentric performance (% mean correct different direction trials) in the first block of the task and allocentric performance (% mean correct different direction trials) in the last block of the task were calculated to assess differences in learning trajectories between the experimental groups.

There was no significant difference in performance in block 1 between the *Trauma Exposed No PTSD* and the *Trauma Unexposed* group. However, in block 6 there was a significant difference

with the former group scoring worse than the latter. In the first experimental block (Block 1), the *Trauma Exposed No PTSD* group (*M* = 0.11, *SD* ± 0.21) did not perform significantly differently from the *Trauma Unexposed* group (*M* = 0.14, *SD* ± 0.24, mean difference 0.03, *p* = 0.47). However, in the last experimental block (Block 6), the *Trauma Exposed No PTSD* group (*M* = 0.35, *SD* ± 0.30) performed significantly differently to the *Trauma Unexposed* group (*M* = 0.53, *SD* ± 0.33) with a mean difference of – 0.18, *p* = 0.01. A full list of the t-test results by block are available in the supplementary data at Appendix H.

There were no significant differences in performance between the *Trauma Exposed No PTSD* group and the *PTSD* group on either block 1 (*p* = 0.80) or block 6 (*p* = 0.08). In the first experimental block (block 1), the *PTSD* group (*M* = 0.10, *SD* ± 0.20) did not score significantly differently to the *Trauma Unexposed* group (*M* = 0.14, *SD* ± 0.24) mean difference -0.04, *p* = 0.37). In the last experimental block (block 6), the *PTSD* group scored significantly worse (*M* = 0.24, *SD* ± 0.31) than the *Trauma Unexposed* group (*M* = 0.53, *SD* ± 0.34, mean difference -0.29, *p* < 0.01)

4.2.3.3 CLINICAL AND DEMOGRAPHIC COVARIATES AND ALLOCENTRIC PROCESSING.

Observed impairments in allocentric learning described above were further analysed to see if they were independent of other clinical and demographic covariates identified as relevant in the literature (see Methodology Chapter 2, Section 2.5 and Chapter 3, Section 3.1.5). These clinical and demographic covariates included: age, gender, the taking of anti-depressants (Selective Serotonin Reuptake Inhibitors or SSRIs) and benzodiazepines or opiates, pain and sleep disturbance.

The first analysis entered each clinical and demographic covariate in to the repeated measures 6 x 3 ANOVA between experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) with the within factor *different direction score at each block*. Detailed results of each of these analyses can be found in Appendix H. Of all of the covariates entered, only one had a significant main effect, and this was pain (measured using the Numeric Rating Scale), *F* (1, 135) = 8.36, *p* < 0.01, $\eta_p^2 = 0.06$. Pain interfered with the main effect of group (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*), rendering it insignificant, *F* (2, 134) = 1.51, *p* = 0.22, $\eta_p^2 =$ 0.02. Pain did not significantly interact with block, *F* (4.14, 135) = 2.38, *p* = 0.13, $\eta_p^2 = 0.01$.

Significant differences in allocentric performance between groups (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) in the last block (block 6) of the route learning task were examined more closely using linear regression. A similar form of regression analysis of potentially confounding variables in the relationship between PTSD and allocentric processing was implemented in the similar study by Smith et al. (2015). All clinical and demographic variables were entered at step 1. By way of a reminder, these included: age, gender, the taking of anti-depressants (Selective Serotonin Reuptake Inhibitors or SSRI's) and benzodiazepines or opiates, pain and sleep disturbance. Experimental group (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) was entered at step 2. At step 1, the variables explained a significant amount of variance in allocentric processing score in the final block, *F* (6, 130) =

3.34, p <0.01, r^2 = 0.14, adjusted r^2 = 0.10. At step 2, group also explained a significant amount of variance, F (7, 120) = 5.86, p < 0.01, r^2 = 0.23, adjusted r^2 = 0.18. In the final equation, group provided a unique contribution, b (-1.65) = -3.65, p <.01, as did gender, b (-1.67) = -2.80, p = 0.01, and pain, b (-.027) = -2.07, p = 0.04.

A post hoc t-test was undertaken comparing performance as a function of gender (males, n = 76; females, n = 62) with the dependent variable *allocentric processing score by block*. It revealed no significant differences between males and females in any of the six blocks of the task. A full list of the t-test results is available in the supplementary data at Appendix H. A series of post hoc t-tests was then undertaken between those with any self- reported pain (n = 36 scoring above zero on the NRS) and those without any self-reported pain (n = 102 scoring zero on the NRS) with the dependent variable *allocentric processing score by block.* It revealed significant differences in five of the six blocks of the AR paradigm, suggesting that pain had a consistently significant negative effect on allocentric performance. To ascertain if this influence of pain was common to both allocentric and egocentric spatial processing, the same t-test was undertaken with the dependent variable *egocentric processing score by block* (measured using accuracy on same direction trials). It revealed no significant differences in egocentric processing between those in pain and not in pain in any experimental session (blocks 1 to 6). A full list of the t-test results is available in the supplementary data at Appendix H. These analyses suggest that whilst trauma affects allocentric processing and route learning in the AR paradigm, pain also contributes 2.7% to the variance in allocentric processing.

4.3.3 Strategy use

As well as performance levels, the Alternative Route (AR) paradigm also permits an assessment of the navigation strategies that individuals use which is indicative of spatial information processing bias. The strategies assessed were either: *allocentric* (knowledge based) or *egocentric* (response based). The allocentric strategy in the AR is referred to as the *configural strategy.* The two egocentric strategies are *associative cue strategy* (which involves acting on implicitly encoded directional turns previously associated with a landmark in the learned route) *beacon strategy* (which involves 'heading towards' in the direction of a landmark in the present environment, Wiener et al., 2013). A participants' use of each strategy is measurable by calculating the mean percentage usage of the strategy at type 3 trials in the Alternative Route. Mean percentage use is calculable at each of the six blocks and as an overall average for the whole task (by averaging the total strategy use at each block and converting the total to a percentage). Analyses was undertaken across each of the six experimental sessions (blocks 1 to 6) of the AR paradigm to differentiate strategy use between groups (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*). This approach was common to other studies of hippocampal dependent and *in*dependent strategy use in navigation (Wiener et al., 2013; Banner et al., 2011; Furnman et al., 2014). Overall strategy use was used in Furnman et al.'s (2014) navigation study and 'strategy by block' measures were used in studies by both Wiener et al. (2013) and Banner et al. (2011) to examine group differences in performance.

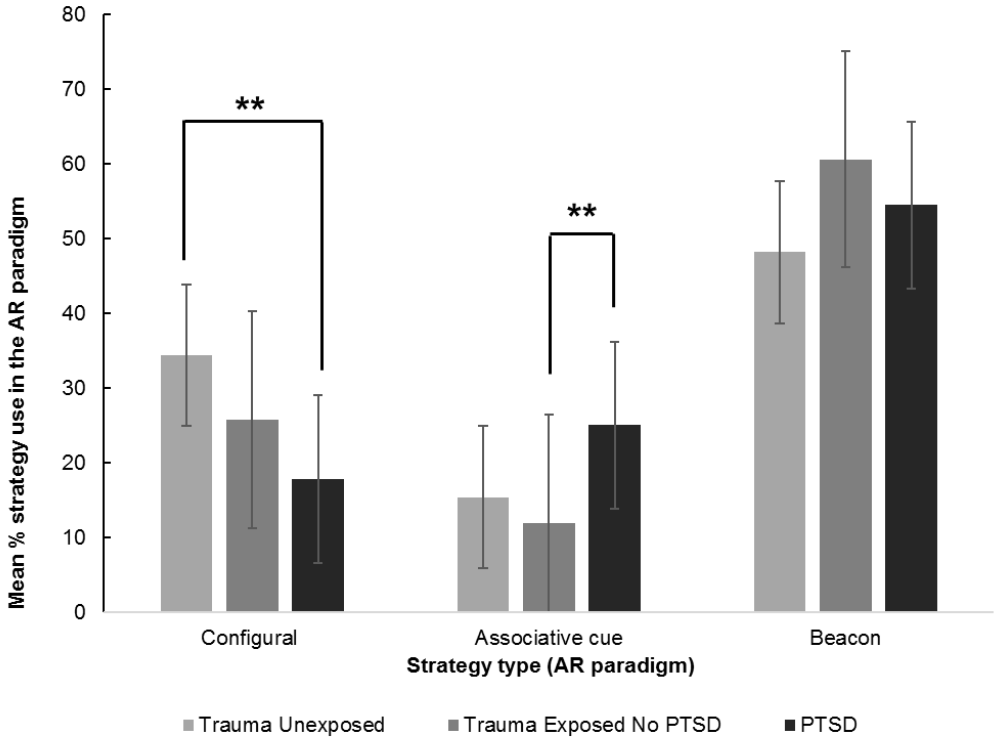


Figure 4.3.3: Mean strategy use (configural, associative cue and beacon) overall in the AR paradigm between experimental group (Trauma Unexposed, Trauma Exposed No PTSD, PTSD) (*n* = 138) with standard error bars.

By way of introduction to the strategy use data, Figure 4.3.3 above illustrates overall use of each of the navigation strategies (configural, associative cue and beacon strategy) in the AR paradigm by group (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*). Figure 4.3.3 shows highest use of the associative cue strategy amongst those with PTSD, highest use of configural strategy amongst those unexposed to trauma, and highest use of beacon strategy in those who have been trauma exposed but who have not developed clinical (or probable) levels of PTSD. Beacon strategy was the most commonly used strategy in all groups.

Independent t-tests were used to check for significant differences in the above figure. Configural strategy use overall was significantly higher in the *Trauma Unexposed* group ($M = 0.34$, $SD \pm 0.23$) than the *PTSD* group ($M = 0.18$, $SD \pm 0.22$), $t\ (78) = 3.24$, $p < 0.01$. Associative cue strategy use overall was significantly higher in the *PTSD* group ($M = 0.25$, $SD \pm 0.25$) than the *Trauma Exposed No PTSD* group ($M = 0.12$, $SD \pm 0.15$), $t\ (103) = 3.23$, $p < 0.01$.

To explore how strategies are used in the route learning paradigm in more detail, block by block analysis was undertaken. Figure 4.4.3.1 provides a visual overview of strategy use over the six blocks of the Alternative Route paradigm, in each of the trauma groups (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*). One can see in those without PTSD (the *Trauma Unexposed* and the *Trauma Exposed No PTSD* groups), beacon strategy use diminishes as the configural (allocentric) strategy is taken up. In the *PTSD* group, however, beacon strategy is not so consistently dropped, configural strategy is not taken up to the extent at which it is in the non-PTSD groups, and the associative cue strategy is maintained throughout, and to a higher degree than in the non-PTSD groups.

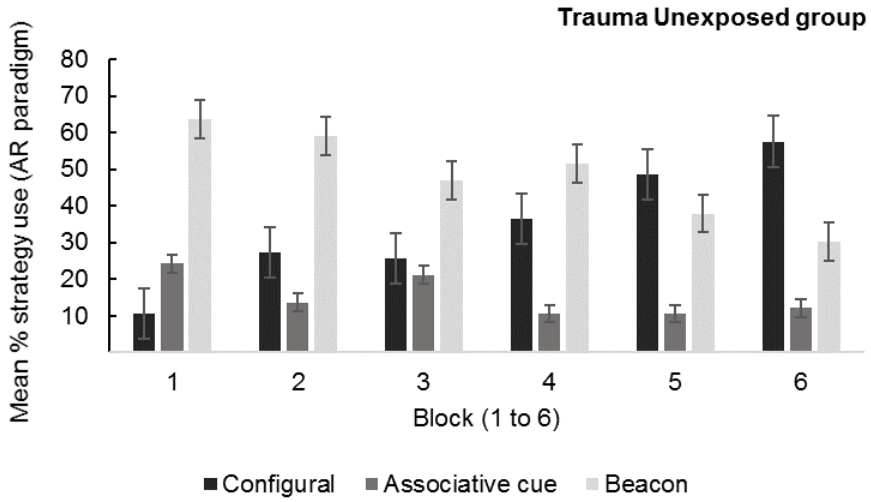


Figure 4.3.3.1: Mean AR strategy use by block in the AR in the Trauma Unexposed group (*n* = 33) with standard error bars.

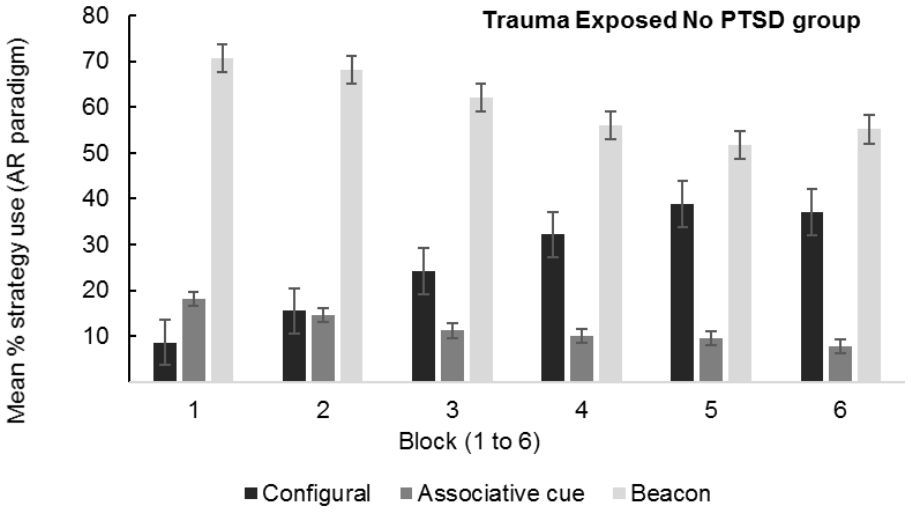


Figure 4.3.3.2: Mean strategy use by block in the AR in the *Trauma Exposed No PTSD* group (*n* = 58) with standard error bars.

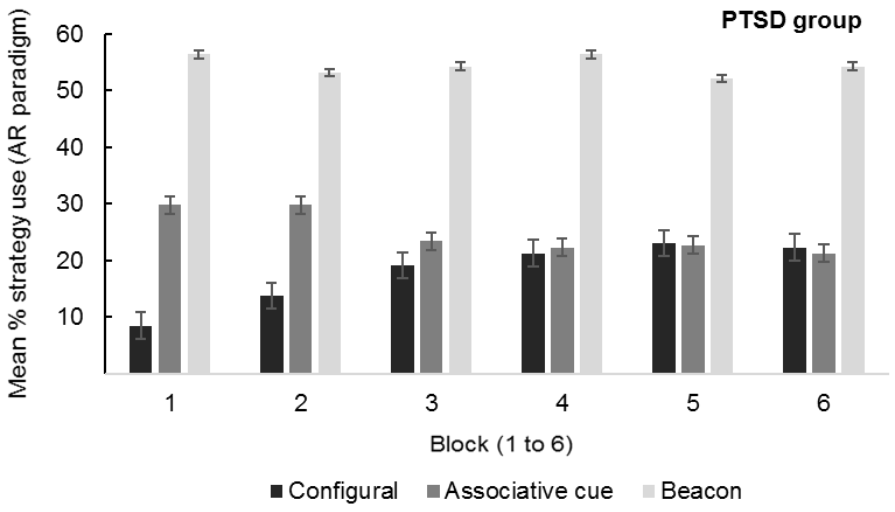


Figure 4.3.3.3: Mean strategy use by block in the AR in the *PTSD* group (*n* = 47) with standard error bars.

To investigate this statistically, repeated measures ANOVAs were undertaken for each strategy use (configural, associative cue and beacon) over the six experimental sessions (blocks 1 to 6) between groups (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*). This method of analysis was undertaken by Wiener et al. (2013) and similarly by Banner et al. (2011).

4.3.3.1 CONFIGURAL STRATEGY

Configural strategy use in each experimental session (blocks 1 to 6) over the AR paradigm was compared across groups. A repeated measures 6 x 3 ANOVA with the within factor *block* (1 to 6) and the between factor *group* (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) was undertaken. It revealed significant main effects of block, F (4.32, 135) = 22.3, $p < 0.01$, $\eta_p^2 = 0.14$. Configural strategy use was 9.2% (*SD* ± 2 %) in block 1 and this increased to 39% (*SD* ± 3.3%) in block 6. There was a significant main effect of group, F (2, 135) = 4.85, $p < 0.01$, $\eta_p^2 = 0.07$.

The *Trauma Unexposed* group had the highest use of configural strategy (*M* = 0.34, *SD* ± 0.04), followed by the *Trauma Exposed No PTSD* group (*M* = 0.26, *SD* ± 0.03) and the group with the lowest use of configural strategy was the *PTSD* group (*M* = 0.19, *SD* ± 0.03). There was a significant block x group interaction, F (8.63, 135) = 2.19, $p = 0.02$, $\eta_p^2 = 0.03$, showing use of configural strategy differs between groups during route learning.

Table 4.3.3.1: Pairwise comparisons of experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) for configural strategy uptake throughout the 6 blocks of the Alternative Route paradigm (*n* = 137).

Experimental group		**Mean Difference**	**Std. Error**	**Sig**	**95% Confidence**	
					Lower	**Upper**
Trauma Unexposed	Trauma Exposed No PTSD	.083	.051	.310	-.040	.205
	PTSD	.163	.053	.007*	.036	.291
Trauma Exposed No PTSD	Trauma Unexposed	-.083	.051	.310	-.205	.040
	PTSD	.080	.046	.240	-.030	.191
PTSD	Trauma Unexposed	-.163	.053	.007*	-.291	-.036
	Trauma Exposed No PTSD	-.080	.046	.240	-.191	.030

Pairwise comparisons (with Bonferroni corrections) between groups for configural strategy uptake revealed a significant difference between the *Trauma Unexposed* and those with *PTSD* (mean difference = 0.16, $p = 0.01$). The *Trauma Exposed No PTSD* group did not use configural strategy significantly more than the *Trauma Unexposed* group, nor significantly less than the *PTSD* group. These results reflect overall allocentric performance levels demonstrated in the earlier analysis, likely due to the inextricable link between configural strategy use and success in route learning (Wiener et al., 2013).

To investigate trauma exposure group differences in configural strategy use, post hoc t-tests were conducted for use of the configural strategy in the first block (block 1) and the last block

(block 6). This was undertaken between the *Trauma Exposed No PTSD* group and the *Trauma Unexposed* group, and latterly between the *Trauma Exposed No PTSD* and the *PTSD* group.

The first post hoc t-test revealed no significant difference between the *Trauma Exposed No PTSD* (M = 0.09, SD ± 0.25) and the *Trauma Unexposed* group (M = 0.11, SD ± 0.24, mean difference 0.02, p = 0.71) in the first experimental block (block 1). There were significant differences in configural strategy use between the *Trauma Exposed No PTSD* and the *Trauma Unexposed* groups in the last experimental block (block 6). The *Trauma Unexposed* group used configural strategy significantly more in the last block (M = 0.58, SD ± 0.44) than the *Trauma Exposed No PTSD* group (M = 0.37, SD ± 0.38, mean difference 0.21, p = 0.02). Again, this is likely to reflect allocentric performance. A full list of the t-test results are available in the supplementary data in Appendix H.

The second post hoc t-test revealed no significant differences in configural strategy use in the first block (block 1) between the *Trauma Exposed No PTSD* (M = 0.09, SD = 0.25) and the *PTSD* group (M = 0.09, SD ± 0.19, mean difference – 0.00, p = 0.98). In block 6, the *Trauma Exposed No PTSD* group (M = 0.37, SD ± 0.38) used configural strategy significantly more than the *PTSD* group (M = 0.22, SD ± 0.34, mean difference – 0.15, p = 0.04). A full list of the t-test results are available in the supplementary data at Appendix H.

4.3.3.2 ASSOCIATIVE CUE STRATEGY

Associative cue strategy use in each block (1 to 6) over the AR paradigm was compared across experimental groups. A repeated measures 6 x 3 ANOVA with the within factor *block* (1 to 6) and the between factor *trauma group* (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) revealed a significant main effect of block, F (4.67, 135) = 3.39, p = 0.01, η_p^2 = 0.02, and of trauma group, F (2, 135) = 5.56, p < 0.01, η_p^2 = 0.08. The *PTSD* group had the highest use of associative cue strategy (M = 0.25, SD ± 0.03), followed by the *Trauma Unexposed* group (M = 0.16, SD ± 0.04) and the group with the least use of associative cue strategy was the *Trauma Exposed No PTSD* group (M = 0.12, SD ±0.03). There was no significant interaction between block and group, F (9.33, 135) = 0.42, p = 0.93, η_p^2 = 0.01, suggesting no learning effect of associative cue.

Pairwise comparisons (with Bonferroni correction) revealed only significant differences amongst the trauma exposed, that is, between the *Trauma Exposed No PTSD* group and the *PTSD* group (p < 0.01).

Table 4.3.3.2: Pairwise comparisons of experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) for associative cue strategy uptake throughout the 6 blocks of the Alternative Route paradigm (*n* = 137).

Experimental group		Mean Difference	Std. Error	Sig	95% Confidence Interval	
					Lower	Upper
Trauma Unexposed	Trauma Exposed No PTSD	.035	.044	1.00	-.071	.142
	PTSD	-.095	.046	.121	-.206	.016
Trauma Exposed No PTSD	Trauma Unexposed	-.035	.044	1.00	-.142	.071
	PTSD	-.130	.040	.004*	-.226	-.034
PTSD	Trauma Unexposed	.095	.046	.121	-.016	.206
	Trauma Exposed No PTSD	.130*	.040	.004	.034	.226

To investigate trauma exposure group differences in associative cue strategy use, post hoc t-tests were conducted for use of the associative cue strategy in the block 1 and block 6: firstly between the *Trauma Exposed No PTSD* group and the *Trauma Unexposed* group, and secondly between the *Trauma Exposed No PTSD* and the *PTSD* group.

The first post hoc t-test revealed no significant differences in associative strategy use between the *Trauma Exposed No PTSD* and the *Trauma Unexposed* groups in any of the experimental sessions (blocks 1 and 6). A full list of the t-test results are available in the supplementary data at Appendix H.

The second post hoc t-test revealed that the *PTSD* group (M = 0.30, SD ± 0.37) did not use the associative cue strategy significantly more than the *Trauma Exposed No PTSD* group (M = 0.18, SD ± 0.37) in block 1. In block 6, the *PTSD* group (M = 0.22, SD ± 0.36) used the associative cue strategy significantly more than the *Trauma Exposed No PTSD* group (M = 0.08, SD ± 0.08, mean difference 0.12, p = 0.02). A full list of the t-test results are available in the supplementary data at Appendix H. It is worth noting that the *PTSD* group used the associative cue strategy significantly more than the *Trauma Exposed No PTSD* group in all blocks bar block 1. This suggests that those with PTSD use the associative cue strategy significantly more than those who have not developed PTSD following trauma exposure.

4.3.3.4 BEACON STRATEGY

Beacon strategy use in each block (1 to 6) over the AR paradigm was compared across groups. A repeated measures 6 x 3 ANOVA with the within factor *block* (1 to 6) and the between factor *groups* (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) was undertaken. It revealed a significant main effect of block, F (4.34, 135) = 5.92, p < 0.01, η_p^2 = 0.42, no main effect of group, F (2, 135) = 2.10, p = 0.13, η_p^2 = 0.30 and no significant block x group interaction, F (1.68, 135) = 1.66, p = 0.10, η_p^2 = 0.24. This suggests a learning effect of beacon strategy but also that trauma exposure did not affect beacon strategy use.

This confirms that participants' use of the egocentric beacon strategy (as opposed to the egocentric associative cue strategy) is not affected by trauma exposure or PTSD.

4.3.4 Clinical and demographic covariates and strategy use

To ascertain if the impact of trauma exposure and PTSD on configural and associative cue strategy use was independent of other clinical and demographic covariates, potentially confounding variables for allocentric processing which were identified in the literature (see Methodology) were analysed. These included: age, gender, the taking of anti-depressants (Selective Serotonin Reuptake Inhibitors or SSRIs) and benzodiazepines or opiates, pain and sleep disturbance.

A linear regression was conducted with 'overall configural strategy use' (the mean % use of configural strategy as an average over the six experimental sessions, blocks 1 to 6) as the dependent variable. Clinical and demographic covariates were entered at step 1 of the regression and experimental group (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) was entered at step 2. At step 1, clinical and demographic covariates did not explain a significant amount of variance in mean configural strategy use, F (6, 121) = 2.12, p = 0.06, r^2 = 0.10, adjusted r^2 = 0.05. At step 2, experimental group did explain a significant amount of variance, F (7, 120) = 2.74, p = 0.01, r^2 = 0.14, adjusted r^2 = 0.09, and in the final equation only experimental group (that is, trauma exposure and PTSD) provided a unique contribution to mean configural strategy use, b (-0.08) =-2.44, p = 0.02.

Linear regression was then conducted with overall associative cue strategy use (the mean of the six experimental sessions, blocks 1 to 6) as the dependent variable. Clinical and demographic covariates were entered at step 1 of the regression and experimental group (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) was entered at step 2. At step 1, clinical and demographic covariates did explain a significant amount of variance in mean associative cue strategy use, F (6, 121) = 2.19, p = 0.05, r^2 = 0.10, adjusted r^2 = 0.05. At step 2, experimental group also explained a significant amount of variance, F (7, 120) = 2.14, p = 0.05, r^2 = 0.11, adjusted r^2 = 0.06. However, in the final equation only gender provided a unique contribution to mean associative strategy use, b (-0.08) =-2.03, p = 0.05. A post hoc t-test with the dependent variable of overall associative cue strategy use between males and females revealed that is was males (M = 0.22, SD ± 0.24) who used associative cue strategy overall significantly more than females (M = 0.12, SD ± 0.16, mean difference – 0.10, p < 0.01). This may have been heavily influenced by the gender bias of the *PTSD* group (males n = 37, females n = 10, χ^2= 17.0, p <.01).

These results suggest that the contribution of trauma exposure and PTSD (experimental group) is mainly independent of clinical and demographic covariates, although gender may play a role in uptake of associative cue strategy overall, but that this may be due to the gender bias of the PTSD population.

4.4 DISCUSSION

Summary of findings

PTSD impaired both egocentric and allocentric spatial processing in the active navigation task (the Alternative Route paradigm) and, more specifically, PTSD impaired allocentric *learning*. This is different from Smith et al.'s (2015) findings that only showed impairments in allocentric spatial processing in the static spatial tasks (the Four Mountains and the Town Square tasks) and not in egocentric spatial processing.

The most revealing aspect of these Chapter 4 results was that allocentric learning on the AR task was not only impaired in those with PTSD but also in those who had been exposed to trauma but had not developed clinical levels of PTSD. The additional control group of the *Trauma Unexposed* group has provided new evidence that it may not just be the 'stress response' in PTSD which impairs hippocampal dependent processing, but instead, processing trauma even if levels of PTSD are subclinical may deplete hippocampal resources for active navigation. This provides further evidence for the concept of there being a 'competition for resources' within the hippocampus in cases of trauma exposure (Vasterling & Brewin, 2005).

The other key finding is that PTSD brings with it an associative bias which is transposed onto navigation behaviour: those with clinical or probable levels of PTSD disproportionately use the egocentric 'associative' cue strategy, compared to those who have had trauma exposure but who have not developed PTSD as a result (the *Trauma Exposed No PTSD* group). This builds on a long standing link between PTSD and associative thinking described in the trauma literature (Erwin, 2003 with reference to Freud; Eich et al., 2012; Lang, 1977, 1984). This new evidence could indicate that associative bias is a characteristic information processing style in cases of PTSD; a bias which has implications for other areas of an individual's cognition and behaviour in everyday life.

The discussion now evaluates the findings in relation to the original hypotheses presented in the introduction of this chapter.

4.4.1 "PTSD negatively impacts allocentric navigation performance".

The results supported this hypothesis and the predictions based on it. Chapter 3 demonstrated allocentric perspective-taking impairments in those with PTSD (the *PTSD* group) using the Four Mountains task. On this basis, it was predicted that the *PTSD* group would also demonstrate significantly lower scores in allocentric performance in more 'active' navigation (using the AR paradigm) than the *Trauma Unexposed* group. These forms of spatial processing involve movement and take place in an environmental frame of reference, rather than in vista or configural space (Wolbers & Wiener, 2014) as in previous 'static' paradigms (such as the Four Mountains task employed in the first stage of this study, and by Smith et al., 2015). The results showed that the *PTSD* group performed significantly worse than those not exposed to trauma (the *Trauma Unexposed* group) in both egocentric and allocentric 'active' navigation in the AR paradigm. Both the *PTSD* group and the *Trauma Exposed No PTSD* group showed significantly less improvement in allocentric learning during the task than the *Trauma Unexposed* group.

Clinical and demographic factors had little effect on the impact of PTSD on navigation. The effect of experimental group (*Trauma Unexposed, Trauma Exposed No PTSD,* PTSD) on allocentric learning was independent of age, which had previously been shown to impair allocentric performance in the same task (Wiener et al., 2013). Pain was a contributory factor in the impact of PTSD and trauma on allocentric processing (with 2.7% of the variance explained) but this was not the case with egocentric processing. This was an unexpected finding given that the only reference in the literature to pain was in relation to spatial memory in general, and was not specific to allocentric processing (Cardoso-Cruz et al., 2013). Further research would need to be undertaken to explore this finding further.

Overall, these results are supported by a substantial literature demonstrating the detrimental effects of the stress response on the hippocampus, which is said to evolve because the hippocampus is well supplied with receptors that are mobilised by stress hormones (Acheson et al., 2012; Schwabe et al., 2008; Conrad, 2006; Bisby et al., 2010; Pitman et al., 2012; Smith et al., 2015; Brewin in Vasterling & Brewin, 2005). The *PTSD* group all scored above 20 on the PDS scale (Foa et al., 1995) which indicates clinical or probable levels of post-traumatic stress. Up until now apart from Smith et al.'s study (2015) and this current study, only individual PTSD-related symptoms (such as visual intrusions or sleep disturbance, see Bisby et al. 2010; Tempesta et al.,2011) had been considered rather than a standardised measure of PTSD with a recognised threshold that encompasses multiple symptoms.

However, the role of stress in the relationship between trauma and navigation is more complex than PTSD simply *equating to a stress response*, and it is important to note certain limitations of the findings at this stage. Vasterling & Brewin (2005) acknowledge that there is little clarity in the literature as to whether 'high levels of stress hormones impair the consolidation of memories, their retrieval or both'. The AR paradigm (Wiener et al., 2013) was not designed to differentiate between 'consolidations' and 'retrieval' in the hippocampus and so no further explanation can be offered for this. Vasterling & Brewin (2005) also question 'whether reduced hippocampal function in PTSD is primarily related to the effects of stress, to pre-existing vulnerabilities or both' (Vasterling & Brewin, 2005). Whilst one can be confident that this study does demonstrate reduced hippocampal functionality in spatial processing as a result of post-traumatic stress, it is not possible to control for existing vulnerabilities to PTSD such as childhood trauma (Teicher et al., 2012; Bremner et al., 1997; Andersen et al., 2008; Kirmayer et al., 2007; Frodl et al., 2010; Carrion et al., 2001; Gee et al., 2013; Brewin et al., 2000; Vasterling & Brewin, 2005; McGowan & Szyf, 2010; Carballedo et al., 2013; Doidge, 2007). Other pre-existing vulnerabilities to hippocampal processing impairment were captured in the clinical and demographical data collected (including age, gender, sleep disturbance, pain or the taking of certain medications). What should also be acknowledged is that the study by Smith et al. (2015) found that education also contributed to variance in allocentric processing.

4.4.2 "Subclinical levels of unprocessed trauma will impair navigation performance."

The results supported this hypothesis and the predictions based on it. The inclusion of a *Trauma Exposed No PTSD* and a *Trauma Unexposed* group enabled us to investigate the nature of the post-traumatic stress response by comparing it to participants who did not self-report a stressful response to previous trauma exposure.

The *Trauma Exposed No PTSD* group had significantly lower allocentric (not egocentric) performance by the end of the AR task than the *Trauma Unexposed* group, demonstrating impairments in allocentric navigation as a result of trauma exposure, independent of their reporting current traumatic stress.

Again, clinical and demographic covariates had little effect on the impact of trauma exposure on navigation. In regression analyses, gender and self-reported pain provided a unique contribution to allocentric learning (i.e. allocentric performance in the last block of the AR) as well as trauma exposure. However, in post hoc tests for gender and pain, significant differences in allocentric learning were only found for pain. As with the previous analysis, this was also only for allocentric (not egocentric) performance measures. These findings were not expected, given that there was evidence in the literature reviewed that allocentric processing should be so adversely affected by self-reported pain.

The explanation for the observed impairment in navigation performance in those with trauma exposure requires a consideration of the broader trauma processing literature and hippocampal functionality. The findings showing navigation impairment as a consequence of PTSD were explicable on the basis that traumatic stress impairs hippocampal functionality. This was not necessarily the case for the *Trauma Exposed No PTSD* group, as they self-reported subclinical levels of post-traumatic stress (i.e. they score lower than the threshold of 20 on the PDS scale by Foa et al., 1995). However, even though they reported lower levels of stress, it would be too simplistic to completely rule out that they were affected by any stress response as a result of their previous exposure. Alternatively, the findings could suggest that there may be some continuum of experience of PTSD, similar to current thinking in relation to other diagnoses such as personality disorders and psychotic experiences (e.g. see Markon & Krueger, 2005; Krueger et al., 2007). That is to say, that symptomology and experiences of trauma impact may extend beyond categorised boundaries and the severity of impact may be also be more transient, depending on other conditions and comorbidities.

This impairment in active navigation from mere trauma exposure (not post-traumatic stress) also reminds us of the theory postulated by Brewin (in Vasterling & Brewin, 2005) that there is a 'competition for resources' in the hippocampus. One might speculate that a 'competition' for these limited hippocampal resources may be likely to arise when an individual has to manage trauma exposure at the same time as having to navigate. The hypothesis here was that in the *Trauma Exposed No PTSD* group, even though the impact of participants' trauma may not have been sufficient to yield clinical or probable levels of PTSD symptomatology (or 'traumatic stress

response') at test, the trauma experience was still sufficient to deplete their capacity to apply sufficient hippocampal dependent processing to active navigation tasks (i.e. route learning in the AR paradigm). To expand on this, Brewin (in Vasterling & Brewin, 2005) refers back to the work of Pierre Janet (1904) who distinguished between' trauma memory' and 'ordinary, normative memories', and explains that traumatic events demand more involved encoding than non-traumatic events. High demand for encoding trauma memory features strongly in PTSD theories. Dual Representation Theory (Dalgleish, 2004; Bisby et al., 2010; Brewin & Burgess, 2014), for example, describes how the sensory demands of highly evocative trauma memories require more hippocampal resources of allocentric processing to contextualise and consolidate them sufficiently than other memories. The DSM-IV criteria also remind us that traumatic incidents (which lead to PTSD) are *characteristically extreme* in nature: they involve 'intense horror and helplessness', compounded by 'perceived threat to life, serious injury or sexual violation' (APA, 2013). From this decryption alone, it is reasonable to infer that these experiences are, fundamentally, not easy to 'forget'.

The findings in this Chapter may be explained more comprehensively using the Dual Representation Theory (DRT) model (Dalgleish, 2004; Bisby et al., 2010) and Brewin's concept of 'competition for resources' (Vasterling & Brewin, 2005). In the *Trauma Exposed No PTSD* group, there is a 'competition' for hippocampal resources. The competition is between using hippocampal resources to a) contextualise implicit trauma memories, and b) to apply allocentric knowledge-based processing to the navigation task in hand (i.e. route learning in the AR paradigm). In the *Trauma Exposed No PTSD* group, successfully managing previous trauma exposure (this experimental group have no clinical symptoms of PTSD) depletes the allocentric resources required in the AR task; by block 6, route learning performance drops significantly below the level of that achieved by the *Trauma Unexposed* group. In the *PTSD* group, the competition for sufficient hippocampal resources has already been 'lost' for trauma processing, as stress symptoms are at clinical or probable levels of PTSD. Applying hippocampal resources to navigate in this stressful state is unsuccessful for those with PTSD and this disadvantage may be further compounded by their significantly low egocentric (as well as allocentric) performance. The implications of the 'competition for hippocampal resources' dynamic for PTSD and trauma exposure are further explored in this chapter (Section 4.4.5) and these are also summarised in the Discussion Chapter 8 (Section 8.2.3).

4.4.3 "Associative bias in PTSD will present in navigation behaviour".

This hypothesis and prediction was supported by the current findings. Primarily, this hypothesis was based on the link made in the trauma literature between trauma exposure and associative thinking styles (Erwin, 2003 with reference to Freud; Eich et al., 2012; Lang, 1977, 1984). An additional hypothesis was that competition for hippocampal resources may explain differences in navigation behaviour between those who are effected by trauma exposure and those who are not.

The *PTSD* group demonstrated the highest overall use of associative strategy compared to the other groups (*Trauma Unexposed* and *Trauma Exposed No PTSD*), and the lowest use of configural strategy (which is known to be the most effective strategy for the task). Even though the other egocentric strategy (beacon strategy) was the most commonly used strategy amongst all participants in the AR task, this did not differ between experimental groups and, unlike uptake of associative cue strategies, beacon strategy was not associated with trauma exposure status). Use of associative cue strategy differed significantly between the respective experimental groups. Across the task, associative cue strategy was maintained to a higher degree in the *PTSD* group and yet steadily decreased in those who had been trauma exposed but who had not subsequently developed PTSD (the *Trauma Exposed No PTSD* group). By the end of the route learning task (block 6), the only significant differences in associative cue strategy use were those between the *PTSD* group and the *Trauma Exposed No PTSD* group.

Demographic and clinical variables did not explain group differences in associative cue strategy use. In regression analysis, associative cue strategy was shown to be independent of age (although being female may have contributed to the use of associative cue strategy in spatial processing due to the gender bias in the *PTSD* group).

4.4.4 Applying the notion of associative bias in PTSD to navigation

The relationship between associative thinking in PTSD and in associative thinking in navigation is well grounded, but warrants further scrutiny. Maladaptive biases towards associative thinking have long been associated with PTSD, (Erwin, 2003 with reference to Freud; Eich et al., 2012; Lang, 1977, 1984). These associations date back to references to Pavlovian-type trauma associations in the traditional trauma literature and are integral to modern day theories of PTSD such as Dual Representation theory (Maren, 2008; Krystal et al. in Horowitz, 1999; Rudy et al., 2004; Acheson et al., 2012; Dalgleish, 2004; Bisby et al., 2010). There may be a good reason for there being a significant difference in associative information processing between those who develop PTSD after trauma and those who do not. According to Vasterling and Brewin (2005),

> "…information processing biases are not merely by-products of a negative mood state, but rather are important factors in the causation and maintenance of PTSD" (Vasterling & Brewin, 2005).

The onus on this discussion is now to understand *what it is about the associative bias* in PTSD that is translatable to the context of spatial processing and why this differentiates those with and without PTSD after trauma exposure. To fully appreciate that associative bias in PTSD is likely translatable to the context of spatial processing, one has to rule out that the processing bias is not simply a 'by-product' of performance differences between the experimental groups.

Extending Vasterling and Brewin's (2005) analogy of information processing biases being a by-product of mood state, one might speculate that information processing biases may be a by-product of poor *navigation performance*. However, this possibility can be discounted for three reasons. Firstly, if the associative cue use was purely about allocentric performance deficit, then one would expect that both non-egocentric strategies (associative cue and beacon) would be adopted similarly at the expense of the configural strategy across all groups. This is not the

case: the two egocentric strategies were adopted in different ways over the task (the beacon strategy was adopted the most out of all strategies across all groups, but associative cue strategy was taken up more in those with PTSD than it was for the *Trauma Exposed No PTSD* group). Furthermore, associative cue strategy use was not directly or equally proportionate to configural performance: so associative cue was not used simply because participants did not use an allocentric strategy[16]. Secondly, Burgess et al. (2008) pointed out that the reason individuals employ configural strategies in complex route learning tasks (like the Alternative Route paradigm) may well be because it is *easier* (or at least more efficient) in general to do so (see also Dror et al., 2005). Burgess et al.'s (2008) explanation is that given 'egocentric representations over multiple locations or extended layouts can be hard to compute, sometimes it is more efficient to employ allocentric skills to maintain a cognitive map of the world and update our location' (Burgess et al., 2008; Wills et al., 2010). With this in mind, the bias towards associative cue in the PTSD group would not be due to it being easier or a more effective use of resources, but may be intrinsically about 'having PTSD'. Thirdly, in their study about learned predictiveness and landmark strategies (strategies which are typically associative; see Furnman et al., 2014, for example), Buckley et al. (2015) mention that "salient landmarks will suffer a loss of attention as they are established as irrelevant to navigation towards a goal" (Buckley et al., 2015). This theory may explain that in cases of PTSD, one can see that landmarks do not suffer this loss of attention as individuals struggle to navigate towards a goal. If anything, an associative strategy in PTSD ensures that landmarks maintain their 'relevance' to an individual - to the detriment of other information about the environment which could otherwise facilitate successful allocentric processing and help those with PTSD solve the task.

If one can ascertain from this, that the relationship between associative cue strategy use and configural strategy use is *not purely a matter of trauma-related performance impairment*, this begs the question, what *is* the relationship about? So far, the findings have presented a plausible explanation for navigation performance differences between those with different responses to trauma in terms of a 'competition for resources' (Vasterling & Brewin, 2005) in the hippocampus. The performance data supports this with the *Trauma Exposed No PTSD* group being unable to apply allocentric processing fully to navigation in the AR paradigm, compared to those with no trauma exposure.

4.4.5 Competing for hippocampal resources and correcting bias

Discussion now turns to how results from Chapter 4 may be explained by the notion of there being a competition for hippocampal resources which manifests itself in active navigation behaviour.

In the *Trauma Unexposed* group, where there is no residual trauma (and *ergo* no associative bias from trauma), full hippocampal resources (those which are applied in using allocentric

[16] To confirm this, a bivariate correlation between associative cue strategy use in the last block (block 6) and allocentric performance in the last block (block 6) in the PTSD group was undertaken and this was not significant, r (47) = - 0.23, p = 0.12.

configural strategy) are deployable to solve the task. Configural strategy is the predominant strategy used in the last block of the AR paradigm. The difference between the associative and configural strategy is wide in this last block.

The *Trauma Exposed No PTSD* group have had trauma experiences to process (which are likely to demand hippocampal resources to encode) and are not currently reporting a current stress response. These participants are less able to maintain configural strategy use at the end of the task (than the *Trauma Unexposed* group are) and configural strategy is not the predominant strategy (the egocentric beacon strategy is the predominant strategy). The *Trauma Exposed No PTSD* use the associative cue strategy less during the route learning and the difference between their associative and configural strategy is narrower in the last block compared to the same difference in the *Trauma Unexposed* group.

In those with *PTSD*, un-encoded traumatic memories (and the potential stress-responses resulting from them) seemingly deplete resources for configural strategy use (e.g. O' Keefe & Nadel, 1978; Andersen et al., 2007; Schwabe et al., 2008; Conrad et al., 2006; Smith et al., 2015; Bisby et al., 2010; Gilbertson et al., 2002; Apfel et al., 2011; Teicher et al., 2012; Acheson et al., 2012; Bisby et al., 2010; Tempesta et al., 2012, Meyer et al., 2012; Miller & Wiener, 2014). Associative cue strategy is applied more than any other group and is used throughout the task, with negligible differences between it and configural strategy (the strategy required to solve the task) use at the end of the AR paradigm. The beacon strategy dominates in the last block, and has been maintained throughout.

The dynamics of this strategy use in the AR paradigm not only seem to reflect a competition for resources, but they may also illustrate deliberate correction of strategies. Beacon strategy is maintained throughout the AR task in all groups, but the dynamic between configural strategy and associative strategy use is distinctive for each group. In those with PTSD, the difference between use of the configural strategy and associative strategy in the last block of the AR is less discernible than in both the *Trauma Exposed No PTSD* group and the *Trauma Unexposed* group. Returning to Brewin's concept of there being a competition for resources in the hippocampus (Vasterling & Brewin, 2005), one could infer from this that in the *PTSD* group, there is a competition between the bias of the associative demand (of unprocessed trauma), and the configural demand of the allocentric task (route learning in the AR). The steady decline in associative cue strategy use in the non-PTSD groups, in line with a seemingly proportional uptake of the configural strategy, suggests that the outcome of this competition is correction. That is to say, where navigation 'wins the competition' for hippocampal resources, allocentric processing corrects associative bias in navigation. Where unprocessed trauma wins the competition for hippocampal resources, allocentric processing cannot be spared to correct the bias.

The notion of *correction* in navigation strategy use is not uncommon to literature about how the hippocampus works and the notion may well prove relevant to the findings of this Chapter.

Neuropsychological literature has long asserted that the hippocampus is an integral part of the Behavioural Inhibition System (BIS) which has the capacity to “arrest ongoing behaviour which is environmentally inappropriate” (Teicher et al., 2003) and to “compare present and previous experience of the environment” (Barrash, 2000). In the AR paradigm, the configural strategy is increasingly adopted by participants who become aware that neither the beacon nor the associative strategy of using landmarks as cues for direction turns (based on the implicit experience of the route learning trials) are ‘environmentally appropriate’ when faced with test intersections which are approached from a different direction.

Barrash’s (2000) analogy is particularly useful when one considers associative direction turns (turns which are encoded from past associations) in more detail, compared to beacon strategy. Beacon strategy is less about encoding and more about responding to environmental cues (that is, heading toward a seen landmark, regardless of previous directional turns made at it). In associative cue strategy, test intersections are likely to be compared to those previously experienced (encoded) in the route learning trials. In Figure 4.3.31 of the Results section, the rate at which associative cue strategy declines and configural strategy is adopted visually differs between experimental groups. The difference between associative cue strategy and configural strategy use in the last block is smallest in those with *PTSD,* followed by the *Trauma Exposed No PTSD* group, and is largest in the *Trauma Unexposed* group. The relationship between beacon strategy and configural strategy over the three experimental groups is far less consistent. From this, one could conclude that the associative cue strategy is the bias which is most likely corrected by the configural (the allocentric) strategy, independent of how much an individual defaults to the common beacon strategy.

To conclude, this interpretation of this AR data as being evidence of a competition for resources between trauma and navigation is speculative. Nonetheless, applying theories of trauma processing (e.g. competition for resources) to the dynamics of hippocampal processing (behavioural inhibition) in navigation, like this, has been encouraged in recent and well-respected research (Brewin & Burgess, 2014; Smith et al., 2015). Fanselow & Dong (2010) explain that the sort of computations that the hippocampus undertakes in correcting emotionally associative behaviour is “exactly what is needed to occur for navigation”. They conclude that, “the linkage of the hippocampus with emotion and affect is as striking as its relationship with memory” (Fanselow & Dong, 2010).

The wider study now progresses to Chapter 5 which investigates the extent to which information processing biases can be identified by self-report. The viability of using navigation questionnaires to predict allocentric processing performance is scrutinised, with a view to applying these psychometrics to cases of PTSD.

5 SELF-REPORTED NAVIGATION

ABSTRACT

Understanding individual differences in navigation styles may offer insight into how healthy participants and how participants with PTSD respond to navigation challenges. Chapter 3 and Chapter 4 demonstrated the negative impact that Post-Traumatic Stress Disorder (PTSD) and trauma exposure have on navigation. Chapter 5 examines *healthy individuals* as opposed to those with PTSD. The extent to which self-reported confidence in navigation was correlated with individuals' navigation performance was examined, with a view to understanding more about how accurate individuals' perception of their competence at egocentric and allocentric navigation was, compared to their actual performance. Whether or not the nature of this relationship between confidence (or awareness) and performance was affected in any way by *reported trauma exposure* in these healthy individuals was also considered.

Self-reported confidence in navigation was measured using a combination of questions from three navigation questionnaires which pertained specifically to allocentric and egocentric processing. Participants' responses to these questions were then correlated with navigation performance scores from the Four Mountains task (by Hartley et al., 2007, as studied in Chapter 3) and the Alternative Route paradigm (by Wiener et al., 2013, as studied in Chapter 4). Correlations revealed that allocentric navigation performance *is* highly correlated with self-reported allocentric navigation questions. Regression analyses showed allocentric navigation questions provided a unique contribution to variance in allocentric navigation performance, compared to other influences such as age, gender and trauma exposure. In contrast, egocentric performance was not predicted by egocentric navigation questions, nor did regression models demonstrate any contribution by any variable (such as age, gender, trauma and self-reported confidence) to egocentric navigation performance.

Further disaggregation of this healthy population (n = 88) into those reporting previous trauma exposure (n = 56) and those who did not (n = 32) produced surprising results. The predictive capacity of navigation questions for allocentric navigation performance was *unique* to those who had been exposed to trauma. That is to say, only those with past experience of trauma who had shown resilience to PTSD were accurate in their perception of (or 'aware' of) their ability to apply allocentric processing to active navigation. These findings underpin the analyses later reported in Chapter 6 in which considers how accurate individuals with PTSD are about their capacity for navigation.

5.1 INTRODUCTION

"Understanding individual differences in navigational styles, as well as the degree to which individuals can flexibly engage different styles and strategies, will offer substantial insights into how humans accomplish the difficult task of learning about environments and responding to navigational challenges" (Furnman et al., 2014).

Most studies addressing navigation behaviour use performance measures as a means of differentiating between egocentric and allocentric behaviour (see Chapter 4; Van Gerven et al., 2016; Smith et al., 2015; Iaria et al., 2003; Banner et al., 2011; Furnman et al., 2014). In Chapters 3 and 4, navigation behaviour was assessed using the Four Mountains (Hartley et al., 2007) and the Alternative Route (Wiener et al., 2013) tasks and replicated Smith et al.'s (2015) earlier finding that PTSD impairs allocentric spatial processing in static perspective taking. The findings from Chapter 4 also demonstrated that egocentric and allocentric navigation performance and strategy use was affected differently by PTSD and revealed for the first time that 'active' navigation was impaired by trauma exposure in healthy populations.

Another approach to understanding egocentric and allocentric navigation behaviour is to decipher how individuals *describe* how they have just completed a navigation task (be it egocentrically or allocentrically). Many studies have retrospectively coded how participants describe their approach to navigation tasks as being egocentric or allocentric (e.g. Banner et al., 2011; Iaria et al., 2003; and Bohbot et al., 2007; Van Gerven et al., 2016). Some studies (such as that by Lövdén et al., 2011) strive for more objectivity by presenting participants with predetermined egocentric and allocentric multiple choice questions from which participants could choose to describe how they had just solved the task.

In contrast to previous research, in this research reported here participants were asked how they saw themselves navigating *in general*, rather than how they '*had just' navigated* on a specific task. Navigation questionnaires were used to assess participants' perceived confidence in their egocentric and allocentric navigation in everyday life, and to explore other influences on self-reported competence, such as aging or traumatic stress. This research assessed for the first time whether self-report in navigation correlated with actual performance on the static 'perspective taking' task (The Four Mountains task) and/ or the active navigation task (the AR paradigm). Self-reported navigation confidence and performance in these tasks was examined in the healthy population, between: those who did and did not self-report trauma exposure.

Finally, with regard to demographics, Chapter 4 (Section 4.3.4, with reference to an expansive literature base) demonstrated that age was an influence that needed to be considered when assessing allocentric navigation performance. However, navigation *questionnaire* literature did not cover the influence of age as consistently. Conversely, gender featured heavily in navigation questionnaire literature (albeit with inconclusive findings) and yet did not feature as much in analyses of performance. For these reasons, no specific hypotheses are made in Chapter 5 regarding age and gender but these demographic factors are covered in detail in Sections 5.2.6 and 5.4.3).

5.2 A REVIEW OF NAVIGATION QUESTIONNAIRES

A review of navigation questionnaires was undertaken as part of the literature review for Chapter 5. Four different navigation questionnaires were identified and on the basis of the review, three of these were deemed appropriate for use in this study: the Santa Barbara Sense of Direction (SBSOD; Hegarty et al., 2002); the Questionnaire of Spatial Representation (QSR; Pazzaglia & De Beni, 2001); and the Fragebogen Räumliche Strategien" (FRS, i.e., the 'questionnaire on spatial strategies'; Münzer & Hölscher, 2011). The questionnaires had not previously been used in the context of trauma but had been applied (and validated) in research investigating allocentric navigation performance (Schinazi et al., 2013; Epstein et al., 2005; Nilsson, 2012; Janzen et al., 2008; Halko et al., 2014; Pazzaglia et al., 2011; Furnman et al., 2014). A summary of the research examining the navigation questionnaires employed in Chapters 5 and 6 is provided in Table 5.2 below and full copies of the questionnaires are provided in Appendix C.

Table 5.2: Summary of literature resources for qualitative assessment of navigation behaviour (i.e. the use of navigation questionnaires, including: the SBSOD (Hegarty et al., 2002), the QSR (Pazzaglia & de Beni, 2011), the FRS (Münzer & Hölscher, 2011) and the SPQ (Lawton et al., 1994).

Author	Navigation Questionnaire	Summary
Hegarty et al. (2002)	Santa Barbara Sense of Direction (SBSOD)	Overall score positively correlated with egocentric spatial updating and acquisition of spatial knowledge in vista space.
Schinazi et al. (2013)	SBSOD by Hegarty et al. (2002)	Overall score positively correlated with off-site pointing after cognitive-map building.
Epstein et al. (2013)	SBSOD by Hegarty et al. (2002)	Overall score positively correlated with representational differences between new and old places and views.
Nilsson (2012) *(Thesis)*	SBSOD by Hegarty et al. (2002)	Overall score positively correlated with both egocentric and allocentric spatial processing conditions.
Wegman et al. (2013)	SBSOD by Hegarty et al. (2002)	SBSOD did not correlate with navigation test-retest performance differences. Gender differences in the SBSOD were reported.
Halko et al. (2014)	SBSOD by Hegarty et al. (2002).	Overall SBSOD score was taken to indicate levels of navigation 'independence' in blind people.
Pazzaglia & De Beni (2001, 2011).	Questionnaire of Spatial Repre-sentation (QSR)	Allocentric 'survey' based items from the QSR positively correlate with a test of mental rotation.
Meneghetti et al. (2010)	QSR by Pazzaglia & De Beni (2001)	Participants who used an allocentric frame of reference performed better in map-drawing and route learning tasks, regardless of self-reported preferences being route-based or survey-based.
Furman et al. (2014)	QSR by Pazzaglia & De Beni (2001) and the SBSOD by Hegarty et al., (2002).	Positive correlation between a survey-based preference score and a survey-based solution score for a navigation task. No significant correlation was found between SBSOD scores and allocentric navigation.
Münzer & Hölscher, (2011), Münzer & Stahl (2011)	Fragebogen Räumliche Strategien" (FRS).	A positive correlation was found between egocentric survey questions and an egocentric route visualisation task. Allocentric survey questions are identified in the study, but only egocentric questions are correlated with 'egocentric' route learning.
Lawton et al. (1994)	Spatial Anxiety Questionnaire (SPQ).	The SPQ produces a Spatial Anxiety score anxiety score for eight situations which require spatial/navigational skills.

5.2.1 The Santa Barbara Sense of Direction (SBSOD) questionnaire

5.2.1.1 ABOUT THE SBSOD

The most commonly used navigation questionnaire in navigation literature to date is the Santa Barbara Sense of Direction (SBSOD) devised by Hegarty et al., 2002. The SBSOD has 15 questions and is typically used in its entirety as a general measure of navigation confidence (Epstein et al., 2013; Schinazi et al., 2013; Wegman et al., 2013; Halko et al., 2014). Questions are often phrased in the context of 'being good at' or 'enjoying' navigation and are centred around having a good "*sense of direction*". Examples of questions are: "I like to travel"; "I do not worry much about getting lost"; and "I do not confuse right and left much". Hegarty et al. (2002) reported internal consistency and good test-retest reliability in the Santa-Barbara Sense of Direction (SBSOD) questionnaire in the publication of the questionnaire. The internal reliability (Cronbach's alpha) for this administration of the scale is .89. No differentiation is made between egocentric or allocentric questions in SBSOD literature (e.g. Hegarty et al., 2002; Epstein et al., 2013; Schinazi et al., 2013). Gender and age were not specifically investigated by Hegarty et al. (2002). Scoring on the SBSOD requires reversing the scores on the negatively phrased items (i.e. 1, 3, 4, 5, 7, 9, and 14) to ensure that a high number indicates more self-reported competence.

5.2.1.2 THE ORIGINAL SBSOD STUDY

In the original study, Hegarty et al. (2002) tested whether the SBSOD had predictive capacity for general performance on a virtual environment navigation task (albeit it there was no differentiation between egocentric or allocentric processing in the task). The tasks used included: a pointing task (pointing to landmarks in environments at different scales of space[17]); a blindfolded 'updating task'; and an 'environmental learning task from different media'. Hegarty and her colleagues demonstrated that the SBSOD questionnaire reflected participants' ability to carry out tasks characteristic of the *environmental scale* of space but not the vista scale. (In Chapter 4, 'vista space' is described as the space of pictures of scenes, which can be 'visually apprehended from a single location without movement', compared to 'environmental' space "such as buildings, neighbourhoods or towns cannot be experienced from a single place but require considerable movement" (Wolbers & Wiener, 2014). There was a moderate correlation between the SBSOD and participants' ability to update their location through movement in the environment. There was a significant correlation between the SBSOD and navigation learning through 'direct experience' of moving in an environment (r = -.43**)[18] (more so than viewing a videotape of a route through an environment, r = -.33** and more so than navigating a desktop virtual environment, r = -.24**). The SBSOD was not significantly correlated with a paper-based 'embedded figures' test or the Vandenberg's Mental Rotation Test (Vandenberg & Kuse, 1978). The conclusions drawn from this research was that the SBSOD was a relatively good predictor

[17] The pointing task required students to point to objects within a room on campus (i.e.vista space) and to landmarks outside the room (i.e. environmental space).
[18] Other literature supports the notion that self-motion plays an interactive role in forming hippocampal spatial representations (such as Stackman et al., 2002 in Lövdén et al., 2011).

of navigation in environmental space (such as in a Virtual Environment) but was a poor predictor of mental rotation in figural space.

5.2.1.3 OTHER STUDIES USING THE SBSOD

The SBSOD has been used several times since by other navigation researchers, either as a generic measure of spatial confidence (e.g. Halko et al., 2014), or more specifically for tests of allocentric spatial knowledge (Schinazi et al., 2013) and perspective taking (Epstein et al., 2013). Schinazi et al. (2013) showed that total SBSOD scores were negatively correlated with errors in one allocentric test (which involved pointing after learning a route in a novel environment) but not in another (a map-drawing test). Epstein et al. (2013) used the total SBSOD score to categorise participants as "good" and "bad" navigators (based on self-report on the SBSOD) and were able to show that higher scorers on the SBSOD performed better on a perspective-taking task using photographs. Wegman et al. (2013) showed that males to score significantly higher on the SBSOD questionnaire than females.

To date, the SBSOD has been widely used as a generic measure of spatial confidence and its positive correlation with performance in perspective taking and active, allocentric VE tasks makes it relevant to use with the Alternative Route paradigm and the Four Mountains task in this study (e.g. Halko et al., 2014 and others; Hegarty et al., 2002; Schinazi et al., 2013; Epstein et al., 2013).

5.2.2 The Questionnaire of Spatial Representation (QSR)

5.2.2.1 ABOUT THE QSR

Another popular navigation questionnaire is the Questionnaire of Spatial Representation (QSR) by Pazzaglia & De Beni (2001) which has been used in specific research into allocentric strategy use. The QSR comprises 20 separate questions (some of which are agrregated, resulting in there being effectively only 11 numbered questions). As with the SBSOD, the QSR includes generic questions about confidence and being 'good at' navigation, but it also includes other questions which are much more specific (for example, questions about using distal cues, mentally visualising maps and being able to re-trace a route).

Pazzaglia et al. (2000) examined the psychometric characteristics of the QSR based on a sample of 285 participants. Factor analysis revealed the existence of five factors, one of which grouped items on preference for allocentric (or map-like, 'survey') representation of space. What is particularly pertinent to this study is that Pazzaglia & De Beni (2001) categorised the QSR questions as being: route based (*egocentric*) questions); survey based (*allocentric* questions); or landmark based (i.e. those which focus on characteristics of salient landmarks and which do not require an individual to maintain spatial features of the environment). Typically, the QSR is used on the basis of correlating scores from *survey* and *route* based questions with spatial processing tasks rather than correlating its total score with spatial processing tasks. Pazzaglia & De Beni derive a "QSR_{survey}" score from two specific allocentric 'survey based' questions and

a "QSR_{route}" score from two egocentric 'route' based questions. Cronbach's alpha for survey based questions was calculated at .62.

In their original study, Pazzaglia & De Beni (2001) found that the group of higher scorers on QSR_{survey} questions performed better on a mental rotation task (devised by Vanderberg & Kuse, 1978) than higher scorers on landmark-centred questions, with there being a significant main effect of group, $F(1, 42) = 7.85$, MSE 10.78, $p < 0.01$). Later, Pazzaglia & De Beni (2006) determined that participants who were high scorers on the same mental rotation task (devised by Vanderberg & Kuse, 1978) not only scored higher on the QSR_{survey} allocentric questions but also on the QSR_{route} egocentric questions (but not the $QSR_{landmark}$ questions). This suggested that the performance on the mental rotation task used may not have been specifically related to self-reported confidence in either allocentric or egocentric processing.

Pazzaglia et al. (2000) found that the reliability of the questionnaire split-half method was 0.75 (Pazzaglia et al., 2000) and based their use of survey and route scoring on an evidence base which "widely accepted distinction between survey and route representations" (citing, for example, Taylor & Tversky, 1992; Tversky, 1991, 1996). The questionnaire can be found in full at Appendix C and the survey, route and landmark questions are provided in the materials section of this chapter, Section 5.3.3.

5.2.2.2 OTHER STUDIES USING THE QSR

The QSR has been referred to in many navigation studies (such as Schinazi et al., 2010), but its use which is most notable is in the study by Furnman et al. (2014). Furnman et al. (2014) employed the QSR in conjunction with tasks which tested participants' ability to build a 'cognitive map' of a virtual environment and then to navigate in that environment. If participants were able to take shortcuts during navigation, they were considered to be using their cognitive map, i.e. allocentric processes. If participants only used familiar paths, they were considered to be only using egocentric processing. Furnman et al. (2014) did not correlate QSR_{survey} questions directly with the use of shortcuts, but devised an allocentric QSR score by subtracting route-based question scores from survey-based question scores. They referred to this as a "$QSR_{survey-route}$ score". Furnman et al., (2014) then demonstrated positive correlations between the $QSR_{survey-route}$ (QSR_{s-r}) score and an allocentric performance measure on the VE task (a measure which subtracted familiar path use from shortcut use and was referred to as a 'Solution Index' (SI) - see Chapter 4 Section 4.1 for more information about this distinction). Furnman et al. (2014) reported that the correlation between the QSR_{s-r} and SI "was amongst the strongest correlations we observed in the [study], $r = .58$, $p = .003$. This study suggested that the QSR_{survey} questions may well reflect allocentric processing and therefore could correlate with allocentric performance on a virtual reality navigation task. No gender differences were found in either performance in the task or self-reported confidence using the QSR responses.

Meneghetti et al. (2010) grouped participants in their study by the participants' scores on three QSR questions pertaining to cardinal directions. High scorers on these questions were

considered to have high preference for using extrinsic (or allocentric) frames of reference to process spatial information and were referred to as the H-EFR group. The H-EFR group had higher overall QSR scores and performed significantly better than those with lower allocentric preferences on the mental rotation task (see Vandenberg & Kuse, 1978); a map-drawing task (which required participants to listen to descriptions of environments based either route or survey type representations, and then draw maps of the environments described); and a geographical pointing task. Only one variation of the map-drawing task was referred to as being explicitly allocentric in nature. Males were more likely to have higher preference for using allocentric reference frames in the questionnaire. These findings suggest that allocentric performance in spatial processing may be predictable by QSR scoring (albeit on a cardinal, compass-point basis in this example by Meneghetti et al., 2010).

Given that the QSR_{survey} questions predict allocentric processing in a virtual environment task that is similar to the Alternative Route paradigm employed in this study (see Furnman et al., 2014), the QSR is employed in this study to differentiate between egocentric route learning and allocentric spatial processing in active navigation. Meneghetti et al.'s (2010) study also showed that those with an allocentric (or extrinsic) approach to processing spatial information had higher QSR scores overall, and higher allocentric scores on other performance measures, suggesting that the QSR is a reliable predictor of allocentric processing.

5.2.3 Fragebogen Räumliche Strategien" (FRS)

5.2.3.1 ABOUT THE FRS

The "Fragebogen Räumliche Strategien" (FRS; see Münzer & Hölscher, 2011; Münzer & Stahl, 2011) is a relatively new questionnaire which comprises 19 questions. Factor analysis (Münzer & Stahl, 2011) distinguished between three types of questions as follows:

(i) Ten '*global egocentric'* questions (e.g. I don't have any trouble finding my desitnation; my sense of direciton is very good) related to global self-confidence in navigation

(ii) Seven '*survey scale*' questionsand are described as being 'allocentric' (e.g. picturing' floor plans, overhead views and route retracing.)

(iii) Two '*knowledge of cardinal directions'* questions, of which both refer to navigation using cardinal compass points, north, south, east and west.

It is worth noting at this stage that the ten 'global egocentric' scale of questions incorporate non-specific questions about self-reported competence (such as "I don't have any trouble finding my destination" and "my 'sense of direction' is very good") and in neither article about the FRS do the authors (Münzer & Hölscher, 2011 or Münzer & Stahl, 2011) identify which of these ten questions are considered to be egocentric and which questions are considred to be non-specific. This is addressed in more detail in the discusson in Section 5.5.1.3 of this chapter. As with the QSR, the FRS is not typically used in its entirety (i.e. as a total score) and sub-scores based on global egocentric or survey based questions are more often used (Münzer & Stahl, 2011). The FRS questionnaire can be found in full at Appendix C and the lists of global egocentric and allocentric survey questions are provided in the materials section of this chapter.

5.2.3.2 FRS STUDIES

In their study of 2011, Münzer & Stahl demonstrated that participants' scores on the global egocentric questions predicted performance on (a) an animated egocentric route learning task set in a virtual environment (b) a visual spatial working memory test (the 'Mental Pathway Test') and (c) a perspective taking test involving spatial configuration of images, although neither of these further tests were described as specifically requiring egocentric or allocentric processing. There was a near significant negative correlation between FRS global egocentric questions and wayfinding uncertainty (r = -.22, p <.06) and a significant negative correlation between FRS global egocentric questions and errors in perspective taking (r = -.34, p < .001). With regard to the seven FRS allocentric survey questions, the FRS author, Stefan Münzer, assures us that the survey scale "predicted spatial overview learning when learning with an interactive virtual model of a complex building in a desktop virtual environment" (taken from direct correspondence which can be found at Appendix E). Cronbach's alpha for the two survey based questions was .88 (Münzer & Hölscher, 2011). In terms of demographics, Münzer & Stahl (2011) report that males had higher confidence in both the survey allocentric and global egocentric scales but that gender differences in the actual navigation task was minimal.

To conclude, the fact that the FRS has been shown to predict egocentric route learning is relevant to our study, which also employs a VE route-learning task, and which has both egocentric and allocentric measures of performance (i.e. the AR paradigm).

5.2.4 The Spatial Anxiety Questionnaire (SPQ)

The Spatial Anxiety Questionnaire (SPQ) was developed by Lawton et al. (1994[19]). The SPQ asks individuals to rate their capacity to navigate in anxiety-triggering situations. Questions from the spatial anxiety questionnaire included, for example, how anxious one would feel trying to find a short cut in an unknown environment without a map, or how anxious one would feel locating one's car in a large car park.

The SPQ was discounted for use in our study precisely because of its reference to anxiety and the implications this would hold for our PTSD sample group (in Chapter 6) and that the current research was designed to assess allocentric spatial processing bias as *distinct* from the associative (and often fear-based, according to Maren et al., 2008) information processing biases. For these reasons, the anxiety-based SPQ (Lawton et al., 1994) was not deemed an appropriate questionnaire to use for our investigation into PTSD and navigation.

[19] For information, another unnamed survey was also developed by Lawton et al. (1994) at the same time as they produced the more commonly known SPQ: this additional questionnaire unfortunately only came to our attention after the fieldowrk for our study had been completed. References to the additional questionnaire describe it as a "wayfinding strategy scale..which generates one score characterizing the degree to which participants use a route strategy and one score for their use of a survey strategy" (Wegman et al., 2013).

5.2.5 A note on cardinal or 'compass' based questions

It is worth noting that there was uncertainty in many navigation studies as to whether 'cardinal' or 'compass' point based questions were relevant to allocentric performance assessments and these questions were excluded from our study. Spatial processing which used cardinal (or compass) points of reference is generally understood to be allocentric (Meneghetti et al., 2011; Pazzaglia et al., 2001; Wiener et al., 2009, 2013; Wolbers & Wiener, 2014; Hegarty et al., 2002). However, cardinal questions do not typically feature in analyses of navigation questionnaires' capacity to quantify or predict allocentric processing. In their analysis of the QSR, Furnman et al. (2014) did not extract cardinal based questions for the survey-based 'Solution Index' used in analysis. Münzer & Stahl (2007) justified their exclusion of cardinal questions in analysis of the FRS on the basis that their task did not involve external visual cues with which cardinal points could be integrated into spatial processing. The tests used in our study (i.e. the Alternative Route paradigm and the Four Mountains task) also do not involve distal cues or cardinal (compass) based information and so Furnman et al.'s (2014) and Münzer & Stahl's (2007) exclusion of cardinal point questions is also upheld in our study.

5.2.6 Demographic influences

The only variables identified in the literature as pertinent to Chapter 5 and the assessment of navigation questionnaires were age and gender.

Age has been shown to have a negative impact on spatial memory which relies on the hippocampus as well as navigation performance in virtual environments (e.g. Smith et al., 2015; Daugherty et al.,2015; Rosenweig & Barnes, 2003; Raz et al., 2009; Moffat et al., 2001, 2009; Wiener et al., 2012, 2013 Driscoll et al. 2005). Age has mainly been controlled for in studies regarding self-reported confidence in navigation (e.g. Furnman et al., 2014) but some studies have also found age to positively affect self-reported confidence in navigation, but not performance (e.g. De Beni et al., 2006; Borella et al., 2014)

In some studies, gender has not featured as being influential over self-reported navigation confidence (e.g. Furnman et al., 2014; Epstein et al., 2013; Münzer & Hölscher, 2011). Nonetheless, many studies investigating self-reported navigation confidence have reported gender differences, typically with females reporting lower confidence levels than males (Lawton et al., 1994; Schmitzer-Torbert, 2007; Meneghetti et al., 2011; Luders et al., 2015) even if this is without commensurate performance differences (e.g. Münzer & Stahl, 2011; Menghetti et al., 2010). Given these gender differences, gender will be analysed in Chapter 5.

Hypotheses and predictions

PREDICTING NAVIGATION PERFORMANCE IN HEALTHY POPULATIONS

The overall hypothesis is that the navigation questionnaires will capture participants' navigation performance and preferences. Specifically, predictions comprise:

(i) 'The SBSOD total score will correlate with general measures of performance on the AR and on the Four Mountains task'. It was expected that the total score of the SBSOD would correlate positively with overall spatial processing (a combination of egocentric and allocentric performance measures) on the Alternative Route paradigm (Wiener et al., 2013) and on the Four Mountains task (Hegarty et al., 2007). This was on the basis that in previous studies, the SBSOD had proven to be a useful general measure of navigation confidence and 'independence' (Hegarty et al., 2002; Wegman et al., 2013; Schinazi et al., 2013; Halko et al., 2014). The variables for this prediction were: total SBSOD score as a percentage, Four Mountain score out of 15, mean overall AR score (same direction trials and different direction trial scores combined), mean same direction and mean different direction AR scores.

(ii) 'The egocentric QSR_{route} questions will predict egocentric (same direction trial) performance on the AR, but not allocentric (different direction trial) performance'. This hypothesis was based on the original factor analysis of the QSR (Pazzaglia et al., 2000) which revealed QSR_{route} question scores to be distinct spatial factors, as well as on the article by Pazzaglia & De Beni (2006) which identified route-based questions as being 'egocentric' in nature. The variables for this prediction were: egocentric QSR_{route} question total score, and mean same direction score on the AR (with mean different direction score for comparison).

(iii) 'The global egocentric FRS questions will predict egocentric (same direction trial) route learning performance on the AR, but not allocentric (different direction trial) performance'. This hypothesis was based on Münzer & Stahl's (2011) finding that the global egocentric scale of the FRS predicted performance on a route-learning task that assessed egocentric spatial processing. The variables for this prediction were: egocentric FRS question total score, and mean same direction score on the AR (with mean different direction score for comparison).

(iv) 'The allocentric QSR_{survey} score will predict allocentric (different direction trial) performance on the AR and the Four Mountains task, but not egocentric (same direction) trial performance'. This was based on Furnman et al.'s (2014) finding that the QSR_{survey} score contributed to an allocentric question score which correlated with an allocentric measure of navigation performance (that is, taking 'shortcuts' on a route learning paradigm). The variables for this prediction were: total score out of 15 for the Four Mountain task, egocentric QSR_{survey} question total score, and mean different direction score on the AR (with mean same direction score for comparison).

(v) 'The allocentric FRS survey questions will predict allocentric processing (different direction trial) performance on the AR, but not egocentric (same direction) trial performance'. This was on the assumption that the survey questions can be distinguished from global egocentric and cardinal questions (see Münzer & Hölscher, 2011). The variables for this prediction were: allocentric FRS question total score, and mean different direction score on the AR (with mean same direction score for comparison).

TRAUMA EXPOSURE STATUS

Chapter 4 showed that those who had been exposed to trauma in the healthy population (*the Trauma Exposed No PTSD* group) were significantly more impaired in allocentric navigation performance than *the Trauma Unexposed* group. This study examined the extent to which the predictive relationships between subjective reporting of navigation ability and task performance were the same for both of these groups. To do this, the healthy population in its entirety (as is typical in navigation literature) was analysed first, before the healthy sample was separated into two groups, the *Trauma Unexposed* group and the *Trauma Exposed No PTSD* group.

5.3 METHODS

5.3.1 Participants

Participants were a subset of 90 (51 females) participants from the whole sample population (*n* = 150) who did not have a diagnosis of PTSD. They were recruited via:

(i) Bournemouth University; including staff, students, and members of the University participant pool (*n* = 63)
(ii) Cambridgeshire Police and Dorset Police (*n* = 20)
(iii) The Intensive Psychotherapy Treatment Service (IPTS) at Dorset NHS Trust. Participants included four members of staff and one former patient (without PTSD)
(iv) Combat Stress (Ex Services Mental Welfare Society Registered Charity No. 206002, Surrey) through whom three members of staff were recruited.

The age profile of the healthy sample population (*n* = 90) was 36.7 years, with the range being between 19 years old and 59 years old. This was older than the generic student profile of other navigation questionnaire studies which typically had a mean age around 20 years old (Hegarty et al., 2002, Furman et al. 2014, Münzer & Hölscher, 2011). Given that age appears to impair allocentric performance on the AR paradigm (see Chapter 4), and given that there are significant group differences in age, age will need to be controlled for in later statistical analyses. The higher representation of females (particularly in the *Trauma Unexposed* group) also called for gender to be considered in the analysis.

Table 5.3 overleaf shows the age and gender of those in the Trauma Exposed and Unexposed groups.

Table 5.3: Descriptive statistics for demographic data for healthy sample (*n* = 90) which comprises the *Trauma Unexposed* (*n* = 32) and *Trauma Exposed No PTSD* groups (*n* = 56).

Demographic factor	Descriptive statistics		Group comparison
Age (years)	36.7 years, *SD* ± 10.8		*t* (88) = -2.74, *p* = 0.01*
Trauma Unexposed group (n = 32)	32.7 years, *SD* ± 10.6		
Trauma Exposed No PTSD group (n = 56)	38.9 years, *SD* ± 10.3		
Gender	Male 43% (*n* = 39)	Female 57% (*n* =51)	$\chi 2$ (90) = 0.69, *p* = 0.41
Trauma Unexposed group (n = 32)	Male 38% (*n* = 12)	Female 62% (*n* = 20)	
Trauma Exposed No PTSD group (n = 58)	Male 47% (*n* = 27)	Female 53% (*n* = 31)	

Three participants were excluded because data was incomplete on either the Four Mountains task, the Alternative Route paradigm or the navigation questionnaires. This healthy sample population comprised the *Trauma Unexposed* group (*n* = 32) and the *Trauma Exposed No PTSD* (*n* = 56) from Chapters 3 and 4.

Participants were offered a £10 financial reimbursement for their time apart from Dorset Police who participated during working hours. The study was approved by: the BU Graduate School Ethics Board; the Combat Stress Research Ethics Committee; and the NHS South West (Cornwall and Plymouth) National Research Ethics Service (NRES).

5.3.2 Procedure

Informed consent was sought from all participants (*n* = 88).

Participants completed the Life Events Checklist (LEC, Blake et al., 1995). Those who self-reported not having been exposed to trauma were assigned to the *Trauma Unexposed* group (*n* = 32). Those who self-reported having been exposed to trauma were given the Post-Traumatic Stress Disorder Diagnostic Scale (PDS, Foa et al., 1995) to ascertain the present day impact of the prior trauma. Those who self-reported PDS scores below the threshold of 21 were allocated to the *Trauma Exposed No PTSD* group (*n* = 56). Those who self-reported PDS scores at or above the threshold of 21 (as typically used by Foa et al., 1995 as an indicator of probable PTSD) were not included in this part of the study.

Participants were offered the option of completing LEC and navigation questionnaires (i.e. the SBSOD, QSR and the FRS) via email or in person at the beginning of the experiment session. Those willing to complete them in advance were sent an email with a unique identification code and a confidential link to an online version of the research surveys hosted securely at Bournemouth University. Those who wished to complete them at the experimental session were asked to allow 45 minutes to complete them either on paper or on a laptop *in situ.*

The participants then undertook the Four Mountains task (Hartley et al., 2007) which took 10 minutes to complete. Participants were given a series of three practice trials to familiarise them with the layout of the test and to ensure that instructions were understood. The participants then

undertook the AR which took 24 minutes to complete. Prior to the task, participants were given written instructions for the Alternative Route paradigm (Wiener et al., 2013) which were summarised verbally after being read by the participants. They were also given a demonstration of the task showing them how to use the controls and to advise the participants on the timing of the paradigm.

5.3.3 Materials

5.3.3.1 NAVIGATION QUESTIONNAIRES

All participants were asked to complete the Santa Barbara Sense of Direction (SBSOD) questionnaire (Hegarty et al., 2002); the Questionnaire of Spatial Representation (QSR, Pazzaglia & De Beni, 2001); and the Fragebogen Räumliche Strategien (FRS, Münzer & Hölscher, 2011).

Scoring comprised: overall SBSOD score, the QSR_{route} (egocentric questions), the QSR_{survey} (allocentric questions), the FRS global egocentric and the FRS survey (allocentric) questions scores. The SBSOD questions were on a 5-point Likert scale, with a score totalling 105. The QSR questions were scored on a 5-point Likert scale, resulting in a total QSR_{route} score of 10 and a total QSR_{survey} score of 10. The FRS questions were scored on a 7-point Likert scale, resulting in a total global egocentric score of 70 and a total allocentric survey score of 49. It is important to note that this selection of questions has not been tested for internal validity as a stand-alone psychometric questionnaire, and each set of generic SBSOD questions and allocentric and egocentric QSR and FRS questions are analysed separately.

Questionnaire scores were correlated with performance measures on the Four Mountains task and the AR paradigm. This gave a score of self-reported confidence in navigation as well as an indication of the degree to which an individual is aware of their own navigation ability.

5.3.3.2 THE FOUR MOUNTAINS TASK

The Four Mountains task (Hartley et al., 2007) is a static topographical (allocentric) test of spatial memory (Hartley et al., 2002; Hartley & Harlow, 2012; Bird et al., 2010). The test is fully introduced in Chapter 3, Section 3.1.3.

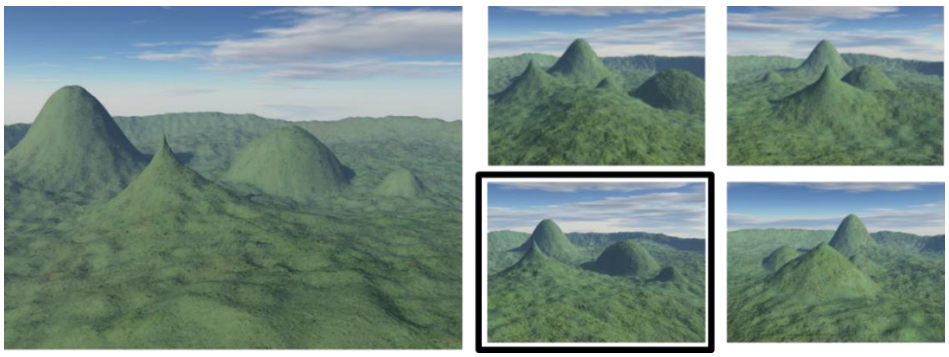


Figure 5.3.2.2: Image extracted from the Four Mountain task (Hartley et al., 2007). The highlighted box indicates the correct answer (the original scene but depicted from a different perspective).

5.3.3.3 THE ALTERNATIVE ROUTE PARADIGM

The Alternative Route (AR) paradigm was introduced by Wiener et al. (2013) as a novel route-learning paradigm to test allocentric and egocentric navigation performance. The paradigm is fully introduced in Chapter 4 in Section 4.1.8.

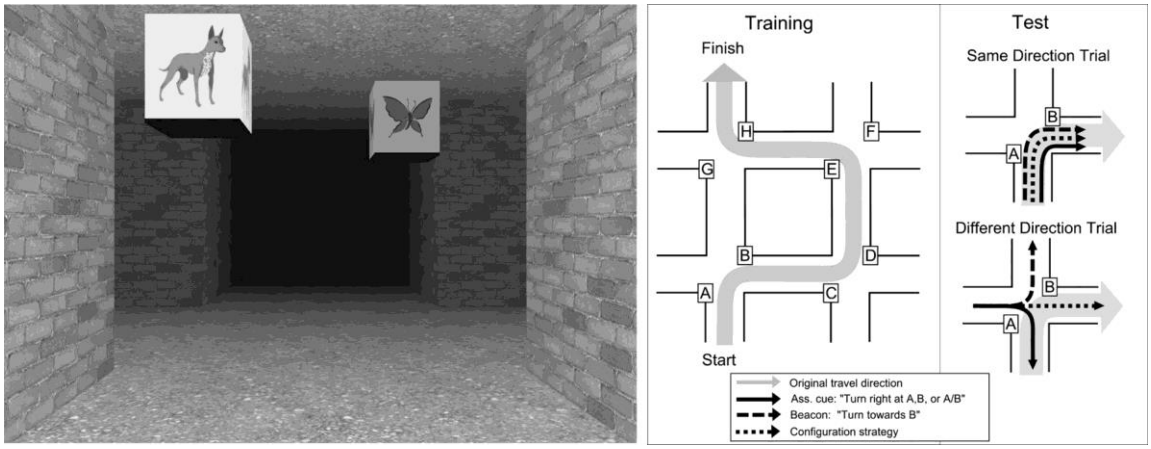


Figure 5.3.2.3: Screen shot from the Alternative Route Paradigm (Wiener et al., 2013) with diagrams of the training route and test intersections.

5.4 RESULTS

5.4.1 Design

All statistical analyses were performed using SPSS version 22 (SPSS, IBM Corp. in Armonk, NY).

Pearson's test of correlation was used which is a parametric test for variables with normal distributions and this is of the analyses undertaken previously with all the navigation questionnaires in their respective literatures (e.g. Hegarty et al., 2002; Pazzaglia & De Beni, 2001; Münzer & Hölscher, 2011).

Performance measures included: the Four Mountains score out of 15; the overall performance score on the Alternative Route (AR) paradigm which comprised a mean same direction trial (egocentric) and different direction trial (allocentric) combined; and then separate mean same direction trial (egocentric) and different direction trial (allocentric) measures.

The pattern of correlations between self-reported navigation confidence (navigation questionnaire scores) and navigation performance (on the Four Mountains and Alternative Route tasks) are reported below: firstly across the whole sample and then separately for those either exposed or not exposed to trauma.

With regard to missing values, three participants did not complete any of the navigation questionnaires; two missed one question from one questionnaire; and one participant missed two questions from one questionnaire. The three instances of *entire navigation questionnaires* not being completed were treated as missing cases. In the three instances of missing data for *single questions* on the SBSOD questionnaire, an average score of 4 from the questionnaire's

Likert-type scale was used as a mean substitution (Field, 2000, 2013). There were also two instances of missing data for two specifically allocentric QSR_{survey} questions. This was managed in a slightly different way using hot check imputation (Andridge et al., 2010). Hot check imputation was possible for these instances because there were very similar survey-based questions asked in another questionnaire (the FRS) from which an average score could be imputed. Hot check imputation in this instance therefore involved calculating an average QSR_{survey} score for this participant using the mean QSR_{survey} scores of all the other participants who scored the same on the similar FRS survey questions as the participant scored on the FRS survey questions.

5.4.2 All healthy participants

The table 5.4.2 below shows the correlations between the navigation questionnaires and the navigation tasks across the whole healthy population sample (n = 90). The allocentric questions (comprising the QSR_{survey} and the FRS allocentric survey scale questions) and the general sense of direction questions (the SBSOD) significantly and positively correlated with allocentric navigation (different direction trial) performance on the Alternative Route paradigm. No other significant correlations were found between navigation questions or performance measures. This is a strong indication that allocentric navigation performance (certainly on the AR paradigm) can be predicted by allocentric based navigation questions as well as those who self-report high levels of overall confidence.

Table 5.4.2: Correlations (r) between navigation questionnaire scores, age, gender, and navigation performance in healthy participants (n = 88), $p < 0.01$**, $p = < 0.05$*.

Questionnaire/ performance	Four Mountains	Overall (AR)	Egocentric (AR)	Allocentric (AR)	Age (years)	Gender (M / F)
SBSOD	0.15	0.11	-0.04	0.23**	0.11	-0.32**
QSR_{route} (egocentric)	0.10	0.10	0.07	0.18	-0.09	-0.12
FRS global (egocentric)	0.18	0.18	0.02	0.18	-0.03	-0.24*
QSR_{survey} (allocentric)	0.18	0.15	0.07	0.26**	0.28**	-0.31**
FRS survey (allocentric)	0.26	0.08	-0.02	0.26**	0.07	-0.27**
Age (years)	-0.11	-0.30**	-0.09	-0.14	-	-
Gender (M / F)	-0.22	-0.03	-0.09	0.02	-	-

Age significantly and positively correlated with some measures of self-reported navigation confidence, but did not significantly correlate with performance. Gender correlated significantly with nearly all measures of self-reported navigation confidence (bar the egocentric QSR_{route} measure), but did not significantly correlate with performance. Post hoc t-tests revealed males to report higher levels of confidence than females on the SBSOD, t (86) = 3.16, $p < 0.01$, the FRS global egocentric questions, t (86) = 2.29, p = 0.02, the QSR survey allocentric questions, t (86) = 3.00, $p < 0.01$, and the FRS survey allocentric questions, t (86) = 2.64, p = 0.01.

Figure 5.4.2 illustrates the relationship between self-reported confidence in allocentric navigation and actual performance in allocentric navigation between genders.

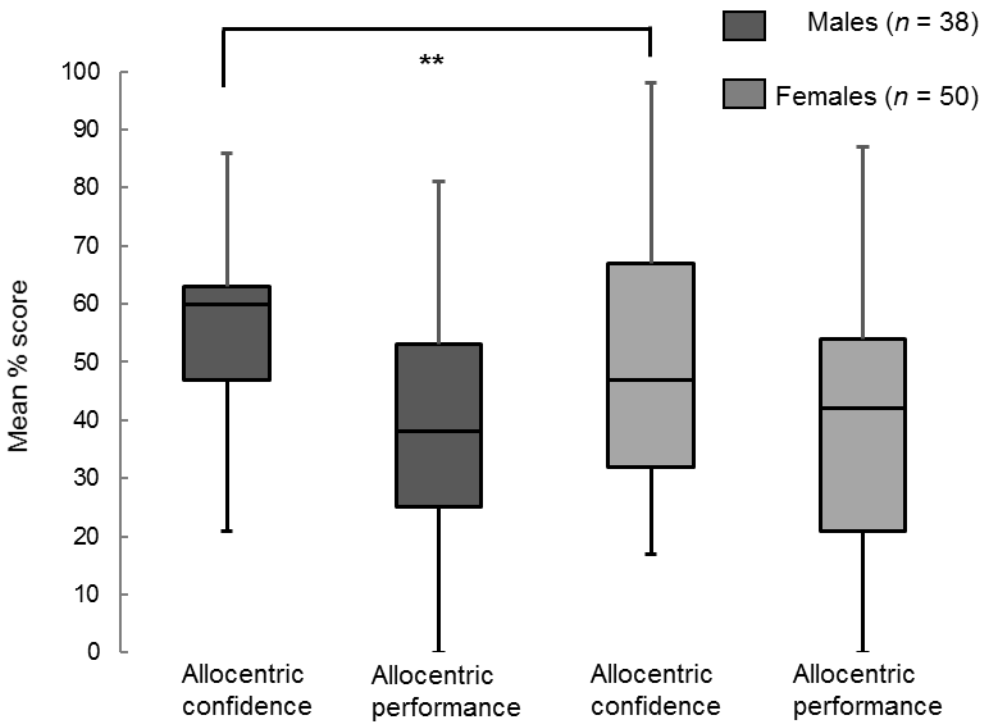


Figure 5.4.1: Gender differences in mean scores for QSR and FRS allocentric questions and mean allocentric performance (AR paradigm) in healthy populations (n = 90) with standard error bars. Males reported significantly higher confidence in allocentric navigation (p < 0.01**) despite having comparable allocentric performance levels.

5.4.3 Trauma exposure status

Chapter 4 showed that those who had been exposed to trauma in the healthy population (*the Trauma Exposed No PTSD* group) were significantly more impaired in allocentric navigation performance than those who have not been exposed to trauma (*the Trauma Unexposed* group). To investigate whether trauma exposure status interfered with the predictive capacity of the navigation questionnaires for navigation performance, the healthy sample was separated into two groups (i.e. the *Trauma Unexposed* group and the *Trauma Exposed No PTSD* group) and the analyses was repeated separately for both groups.

Independent samples t-tests between the *Trauma Unexposed* group and the *Trauma Exposed No PTSD* group revealed neither group differences in self-reported navigation confidence measures (the SBSOD, the QSR_{route}, the FRS 'global egocentric', the QSR_{survey} or the FRS survey scale questions) nor group differences in navigation performance measures (egocentric, allocentric and overall performance on the AR, or on the Four Mountains task) (all $p > 0.05$). However, when the correlations between questionnaires and performance in each subgroup were analysed, differences emerged between those who had processed trauma (the *Trauma Exposed No PTSD* group) and those who had not previously processed trauma (the *Trauma Unexposed* group).

5.4.3.1 THE *TRAUMA UNEXPOSED* GROUP

Table 5.4.3.1 below presents correlations between navigation questionnaires and navigation (and spatial processing) performance, age and gender in the *Trauma Unexposed* group (n = 32). This shows that the pattern of correlations with respect to the *allocentric* questions differed to that found in the whole healthy sample (n = 90), i.e. the correlations were not significant for those reporting no experience of trauma. In contrast, the FRS *global egocentric* scale seemed to predict overall performance and even Four Mountains performance (which is conventionally considered to be a measure of allocentric spatial processing, not egocentric processing).

Table 5.4.3.1: Correlations *(r)* between navigation questionnaire scores, age, gender, and performance in the Trauma Unexposed group (n = 32), $p < 0.05$*****, $p < 0.01$******

Questionnaire/ performance	Four Mountains	Overall (AR)	Egocentric (AR)	Allocentric (AR)	Age (years)	Gender (M / F)
SBSOD	0.31	0.05	-0.18	0.22	0.27	-0.44*
QSR_{route} (egocentric)	0.06	0.25	0.19	0.28	-0.22	-0.10
FRS global (egocentric)	0.41*	0.41*	0.16	0.29	-0.14	-0.33
QSR_{survey} (allocentric)	0.24	0.29	0.02	0.27	0.29	-0.39*
FRS survey (allocentric)	0.19	0.21	0.12	0.17	0.09	-0.41*
Age (years)	0.13	-0.39*	-0.37*	-0.14	-	-
Gender (M / F)	-0.23	-0.06	-0.03	-0.01	-	-

In those without trauma exposure, age was significantly and negatively correlated with egocentric and overall AR performance. Our findings from Chapter 4 were that age had a significant and negative influence over allocentric processing in the AR in the whole population. Gender was correlated with several sets of navigation questions. T-tests revealed that males were more confident than females in the SBSOD, t (30) = 2.71, p = 0.01, the QSR survey allocentric score, t (30) = 2.30, p = 0.03, and the FRS survey allocentric score, t (30) = 2.49, p = 0.02. Again, this heightened male confidence in navigation was to the exclusion of the egocentric QSR_{route} measure and this time also the FRS global egocentric measure.

5.4.3.2 THE TRAUMA EXPOSED NO PTSD GROUP

Table 5.4.3.2 presents correlations between navigation questionnaires and navigation (and spatial processing) performance, age and gender in the *Trauma Exposed No PTSD* group (n = 58).

Again, the pattern of correlations differed when compared to the sample as a whole. The correlation between allocentric questions (from the QSR_{survey} and FRS survey scores) for allocentric (different direction) performance on the AR that was reported for the all healthy participants persisted in –and was unique to- the *Trauma Exposed No PTSD* group.

The positive correlation between age and self-reported confidence in the questions (the allocentric QSR_{survey} questions) only approached significance in the *Trauma Exposed No PTSD*

group. The negative correlation between age and navigation performance was not statistically significant. The correlation between gender and self-reported confidence in allocentric navigation only approached significance and post hoc t-tests confirmed that males' heightened self-reported confidence in navigation was not significantly higher than females in the *Trauma Exposed No PTSD* group.

These patterns may suggest that allocentric navigation performance correlates more with allocentric navigation questions in those who have successfully processed trauma, than those who have not. Moreover, the influences of gender and age on self-reported confidence in navigation and in performance in this group is weaker in the *Trauma Exposed No PTSD* group than in those unexposed to trauma (the *Trauma Unexposed* group). In those with no trauma exposure (the *Trauma Unexposed* group) allocentric processing does not correlate as well as more 'general' measures of performance do with navigation questions. Possible explanations (other than sample size differences) for these surprising findings are provided in the discussion section of this Chapter.

Table 5.4.3.2: Correlations (*r)* between age, gender, navigation questionnaires and navigation performance in the Trauma Exposed No PTSD group (*n* = 56), *p* = < 0.05*****, *p* = < 0.01******, *p* = <0.09 +, *p* - <0.06++

Questionnaire/ performance	**Four Mountains**	**Overall (AR)**	**Egocentric (AR)**	**Allocentric (AR)**	**Age (years)**	**Gender (M / F)**
SBSOD	0.11	0.16	0.12	0.23+	0.01	-0.25
QSR_{route} (egocentric)	0.13	0.04	0.04	0.03	-0.08	-0.16
FRS global (egocentric)	0.07	0.06	-0.02	0.13	<0.01	-0.19
QSR_{survey} (allocentric)	0.15	0.11	0.08	0.27*	0.26++	-0.26++
FRS survey (allocentric)	0.19	-0.01	-0.07	0.31*	0.09	-0.02
Age (years)	-0.20	-0.24	-<0.01	-0.10	-	-
Gender (M / F)	-0.23+	-0.01	-0.10	0.02	-	-

5.4.4 Summary regression analyses

In order to summarise the influences of age, gender, trauma exposure status and self-reported navigation confidence on actual navigation performance, regression analyses was conducted for egocentric, allocentric and overall performance on the Alternative Route paradigm. It is important to note that the sample size limits the validity of the following analyses. G Power (Faul, et al., 2007) computed that a sample of *n* = 92 is required for a multiple regression using five predictors to produce an adequate level of power of 0.8 (according to Mayers, 2013). There were only 88 participants in this study, and this should be taken into consideration.

5.4.4.1 EGOCENTRIC NAVIGATION PERFORMANCE

To analyse the extent to which trauma exposure and self-reported confidence in navigation predicted egocentric performance as well as age and gender, fixed stepwise regression analysis was carried out with egocentric (same direction trial) performance on the AR as the dependent variable. Results are presented in Table 5.4.4.1. Age, gender and trauma group (*Trauma Unexposed* or *Trauma Exposed No PTSD*) were entered at step 1; and self-reported confidence in egocentric navigation (QSR_{route} and FRS 'global egocentric' scores separately) at step 2. At neither step did the demographic, trauma exposure status, or self-reported confidence explain any variance in egocentric performance and no variable provided a unique contribution to the model for egocentric navigation. At step 1, F (3, 84) = 0.49, p = 0.69, r^2 = 0.02, adjusted r^2 = -0.02 and at step 2, F (5, 82) = 0.34, p = 0.89, r^2 = 0.02, adjusted r^2 = -0.04.

Table 5.4.4.1: Regression table for egocentric performance in healthy populations (n = 88) with mean same direction trial performance on the Alternative Route paradigm) and at Step 1, age (in years), gender (male / female) and trauma group (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) and at Step 2, self-reported egocentric confidence (QSR and FRS questionnaire data).

Egocentric navigation	Predictor	ß	*t*	*p*
Step 1	Age	-0.001	-0.88	0.38
	Gender	-.028	-0.86	0.39
	Trauma Group	-.001	-0.04	0.97
Step 2	Age	0.00	-0.81	0.42
	Gender	-0.03	-0.82	0.41
	Trauma Group	0.00	-0.10	0.92
	QSR_{route} questions	0.00	0.52	0.61
	FRS egocentric questions	0.00	-0.23	0.82

5.4.3.2 ALLOCENTRIC NAVIGATION PERFORMANCE

To analyse the extent to which demographics, trauma exposure and self-reported confidence in navigation predicted allocentric performance, fixed stepwise regression analysis was carried out and is presented in Table 5.4.4.2 overleaf. The dependent variable was allocentric (different direction trial) performance on the AR; and age, gender and trauma group (*Trauma Unexposed* or *Trauma Exposed No PTSD*) was entered at step 1; and self-reported confidence in allocentric navigation (QSR_{survey} and FRS survey score) at step 2. In Step 1, no variables explained any variance in allocentric performance. In step 2, self-reported confidence explained a significant amount of variance in allocentric performance, F (5, 82) = 2.60, p = 0.03, r^2 = 0.14, adjusted r^2 = 0.08. In the final equation, the QSR_{survey} questions approached significance in their unique contribution to allocentric performance, b (<0.01) = 1.00, p = 0.06.

Table 5.4.4.2: Regression table for allocentric performance in healthy populations (n = 88) with mean different direction trial performance on the Alternative Route paradigm, and at Step 1, age (in years), gender (male / female) and trauma group (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) and at Step 2, self-reported allocentric confidence (QSR and FRS questionnaire data).

Allocentric navigation	**Predictor**	**ß**	***t***	***p***
Step 1	Age	< -0.01	-1.03	0.31
	Gender	< 0.01	0.03	0.98
	Trauma Group	-0.03	-0.50	0.62
Step 2	Age	< -0.01	-1.76	0.08
	Gender	0.05	1.09	0.28
	Trauma Group	-0.01	-0.30	0.77
	QSR_{survey} questions	< 0.01	1.91	0.06
	FRS allocentric questions	0.01	1.01	0.32

5.4.4.3 OVERALL NAVIGATION PERFORMANCE

To analyse the extent to which demographics, trauma exposure and self-reported confidence in navigation predicted overall performance, fixed stepwise regression analysis was carried out and is presented in Table 5.4.4.3. The dependent variable was overall (egocentric and allocentric) performance on the AR; and age, gender and trauma group (*Trauma Unexposed* or *Trauma Exposed No PTSD*) was entered at step 1; and self-reported confidence in general sense of direction (the SBSOD score) at step 2. In step 1, variables explained a significant amount of variance in overall performance in the AR, F (3, 84) = 2.82, p = 0.04, r^2 = 0.09, adjusted r^2 = 0.06. In step 2, variables also explained a significant amount of variance, F (4, 83) = 2.55, p = 0.05, r^2 = 0.09, adjusted r^2 = 0.07. In the final equation, only age made a unique contribution to overall performance on the AR which was negative, b (-0.03) = -2.95, p = 0.04.

Table 5.4.4.3: Regression table for overall performance in healthy populations (n = 88) with mean different direction trial performance on the Alternative Route paradigm, and at Step 1, age (in years), gender (male / female) and trauma group (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) and at Step 2, self-reported general confidence (SBSOD questionnaire data).

Overall navigation	**Predictor**	**ß**	***t***	***p***
Step 1	Age	-0.01	-2.84	<0.01
	Gender	<-0.01	-0.58	0.56
	Trauma Group	0.01	0.27	0.79
Step 2	Age	<-0.01	-2.95	<0.01
	Gender	<-0.01	-0.14	0.89
	Trauma Group	<-0.01	0.32	0.75
	SBSOD questions	0.01	1.30	0.20

In conclusion, from the regression analyses conducted, it is clear that egocentric processing in active navigation is not predicted by age, gender, trauma status or by egocentric navigation questions. Allocentric processing is, however, predicted by allocentric navigation questions, particularly the QSR_{survey} questions. Finally, age provides a unique and negative contribution to overall navigation performance.

5.5 DISCUSSION

Summary

The main aim of Chapter 5 was to understand individual differences in navigation styles to provide further insight into how our participants (with and without PTSD) respond to navigation challenges. Self-reported navigation confidence in navigation was measured using three validated questionnaires. Egocentric and allocentric questions from the QSR and the FRS were employed to examine the relationship between self-reported navigation ability and participants' performance on egocentric and allocentric measures on the Alternative Route paradigm (Wiener et al., 2013) and the Four Mountains task (Hartley et al., 2007). The SBSOD was a general measure of performance which was correlated with overall performance on the AR and Four Mountains task.

As expected, the analysis showed that the allocentric subscales of the QSR and the FRS questionnaires and the general sense of direction questionnaire (the SBSOD) correlated well with allocentric spatial processing performance on the AR. However, in contrast to the original hypotheses, egocentric performance was not correlated with any questionnaire or subset of questions.

Models of neural processing (e.g. Reber et al., 1996; Morris in Andersen et al., 2007) may provide some explanation as to why *allocentric* navigation performance correlates so well with self-report using navigation questionnaires and why *egocentric* navigation performance does not. Models of hippocampal dependent (allocentric) memory systems present allocentric processing as being essentially declarative, verbally accessed, and knowledge-based (e.g. Vermetten et al., 2003; Morris in Andersen et al., 2007; Bisby et al., 2010; Brewin & Burgess, 2014; Poldrack et al., 2001; Packard & Knowlton, 2002 in Furnman et al., 2014). These models present hippocampal *in*dependent (egocentric) processing as being more implicit, associative and response-based. The difference between these two types of neural processing might help explain the difference between the predictive qualities of each in navigation (Buckley et al., 2015[20], and see Buckley et al., 2016). Allocentric processing in navigation may be predictive because it is more describable: that is, individuals know how to talk about how they navigate using allocentric processing (such as creating mental maps or using overhead views, for example). On the other hand, egocentric processing is based more on an individuals' implicit associations and responses and does not use a form of knowledge about the environment which individuals may be able to so easily describe.

In addition, results from Chapter 5 show that there are differences within the healthy population between those who have successfully processed trauma in the past (the *Trauma Exposed No* PTSD group) and those who have not (the *Trauma Unexposed* group). When navigation questionnaires and performance data were analysed separately for the *Trauma Exposed No* PTSD group and the *Trauma Unexposed* group, the predictive capacity of the allocentric

[20] *"…the same associative processes as those that explained learning in non-spatial literature may also explain spatial learning phenomenon"* (Buckley et al., 2015).

navigation questions for allocentric navigation performance was unique to the *Trauma Exposed No* PTSD group. That is to say, self-reported confidence in allocentric navigation only correlated with allocentric navigation performance in those who had previous experience of trauma and had not developed PTSD.

These unexpected findings may also be explained with reference to the same models of neural processing as for the main findings. The interpretation of these results is such that those who have successfully processed trauma in the past are likely to have done so using hippocampal dependent (allocentric) processing -which is considered to be declarative and verbally accessible (Brewin & Burgess, 2014; Bisby et al., 2010). Results from Chapter 4 showed that allocentric performance in the *Trauma Exposed No PTSD* group was significantly poorer than that for the *Trauma Unexposed* group. Findings from Chapter 5 suggest that those with trauma exposure may have been experiencing an ongoing demand for hippocampal resources to contextualise and manage the trauma (Vasterling & Brewin, 2005), depleting the resources available to them for allocentric processing for navigation. Taking this argument forward, one could speculate that because of their trauma experiences, these individuals may well be more familiar with what it is like to employ hippocampal dependent processing (such as seeing things from an observer perspective, locating experiences correctly in memory) and are therefore more likely to know when they are applying this form of information processing to other areas of their life, such as navigation.

5.5.1 Navigation questionnaires

5.5.1.1 THE SANTA BARBARA SENSE OF DIRECTION (SBSOD).

The prediction was that the SBSOD questionnaire, typically used as a general measure of 'sense of direction' would correlate with general performance measures, such as overall performance on the AR and/ or the Four Mountains task. In healthy populations (n = 88), the SBSOD only correlated significantly with allocentric (different direction) performance. The SBSOD did not correlate with any other measure and there were no differences in the SBSOD's predictive capacity for spatial processing and navigation between the *Trauma Exposed No PTSD* and *Trauma Unexposed* groups.

The SBSOD has had a diverse history of sometimes correlating with some generic, VE route learning and perspective taking tests (Hegarty et al., 2002; Epstein et al., 2013; Schinazi et al., 2013) but not always correlating with other figural space mental rotation tests (Hegarty et al., 2002; Schinazi et al., 2013). Findings in this chapter included a significant correlation between the SBSOD score and allocentric (but not egocentric) performance in the VE route learning paradigm (the AR by Wiener et al., 2013). No significant correlation was found between the SBSOD and the perspective taking test of the Four Mountains task (by Hartley et al., 2007). In this current study, allocentric performance on the AR is perhaps the most robust active navigation performance measure (solving the AR paradigm allocentrically is notably more challenging than either using egocentric processing on the AR or perspective taking in the Four Mountains task). This general level of difficulty may explain the correlation with generic self-reported confidence on the SBSOD.

5.5.1.2 THE QUESTIONNAIRE OF SPATIAL REPRESENTATION (QSR)

Egocentric questions

In healthy populations (*n* = 88), contrary to the predictions, the QSR_{route} egocentric questions did not correlate significantly with *any* measure of performance, and trauma exposure status made no difference to the predictive capacity of QSR_{route} egocentric questions. The QSR_{route} based questions had not been tested in isolation[21] for their correlation with measures of egocentric spatial processing in the literature; either in Pazzaglia & De Beni's study (2006) or in that by Furnman et al. (2014).

Allocentric questions

In the healthy populations and in line with the prediction, the QSR_{survey} allocentric questions did significantly and positively correlate with allocentric performance (different direction trials) in the AR paradigm. They did not significantly correlate with any of the other tasks in healthy populations. The fact that the QSR_{survey} score correlated with allocentric performance on the AR supports findings by Furnman et al. (2014) that showed the QSR_{survey} score to contribute to a prediction of an allocentric solution to a route learning paradigm.

When looking at trauma exposure status, the significant and positive correlation between QSR_{survey} allocentric questions and allocentric performance (different direction trials) in the AR paradigm was unique to the *Trauma Exposed No PTSD* group. The QSR_{survey} questions were also highly sensitive to age (in so far as confidence in the questions increased with age) and to gender (in so far as males were more confident than females). Again, this effect was more visible in the *Trauma Exposed No PTSD* group than the *Trauma Unexposed* group.

5.5.1.3 THE FRAGEBOGENS ZU RÄUMLICHEN STRATEGIEN (FRS)

Egocentric questions

Contrary to the predictions (and as with the QSR egocentric questions), the FRS global egocentric scale questions did not significantly correlate with any egocentric navigation performance measure. These findings do not corroborate those by Münzer & Stahl (2011) which showed the global egocentric scale to be predictive of an egocentric VE route learning task (Münzer & Stahl, 2011).

When looking at trauma exposure status, in the *Trauma Unexposed* group that this 'global egocentric' scale correlated with the Four Mountains task performance and of overall performance on the AR. The correlation between this 'global egocentric' scale and the Four Mountains task also indicates that the questions may be indicative of allocentric spatial processing as well as egocentric and 'unspecific' spatial processing.

[21] The QSR_{route} score was subtracted from the QSR_{survey} score as an index to predict a performance measure which was structured in a similar way (familiar paths subtracted from shortcuts in a VE navigation paradigm).

These findings reflect nuances in the literature by Münzer & Stahl (2011) that the global egocentric scale may not be a measure of uniquely egocentric spatial processing. Münzer & Stahl clearly state that the scale

"...comprises egocentric strategies because the strategies are based on a particular position and orientation within an environment…. these strategies are related to items that indicate global (i.e., unspecific) confidence in wayfinding" (Münzer & Stahl 2011).

In neither article about the FRS (Münzer & Hölscher, 2011 or Münzer & Stahl, 2011) do the authors identify if any of these ten global egocentric questions are actually considered to be egocentric or if *all* are considred to be non-specific. What is more, some of the questions come across as being somewhat allocentric. A closer look at these questions (provided in Appendix C) reveals that some questions involve pointing to unseen landmarks, an example of such a question is "in a big building I can spontaneously point towards the entrance". There are similar questions to this question in the QSR which also involve pointing to unseen landmarks (one of which again involves pointing to the entrance in complex building). These 'pointing' type questions have been specifically identified (for example, by Meneghetti et al., 2010) as indicating participants' use of an extrinsic (allocentric) frame of reference. This may explain why the FRS global egocentric scale is in fact predcitive of overall perfromance on the AR (which includes both egocentric and allocentric performance as a measure) and the Four Mountains task score, and not purely egocentric performance on the AR.

The FRS global egocentric scale was not sensitive to age and was only sensitive to gender (with males reporting higher confidence than females) in the larger sample of healthy participants (n = 90), irrespective of trauma exposure status.

Allocentric questions

As predicted (and as with the QSR_{survey} questions), the FRS allocentric survey scale questions significantly correlated with allocentric (different direction trial) performance on the AR in the healthy population. The FRS allocentric survey questions did not significantly correlate with any other spatial processing or navigation performance measure. When looking at trauma exposure status, this correlation was unique the *Trauma Exposed No PTSD* group. The FRS allocentric survey was not sensitive to age, but was sensitive to gender (with males reporting higher confidence than females). The correlation between FRS survey questions and allocentric navigation performance in the AR is supported by Münzer & Hölscher's (2011) factor analysis of which showed allocentric survey questions as distinct from other cardinal and global egocentric questions. This also substantiates the previous findings to which Münzer refers in person in Appendix E.

5.5.2 Demographics

In summary, demographic data suggests that age has a positive influence on self-reported allocentric navigation confidence, despite having a negative influence on overall performance (demonstrated in Chapter 4, Section 4.1.9 and by others, such as Wiener et al., 2013). In terms of gender, males reported higher confidence in allocentric navigation, which was not commensurate with either their performance. Regression analysis demonstrated the relevance of age, gender and general self-reported confidence in navigation (SBSOD score) for overall navigation performance on the AR, with age making a unique contribution (of 3%).

5.5.2.1 AGE

With regard to age in particular, the findings show age have a moderating effect in the relationship between self-reported navigation confidence and navigation performance. The negative influence of age over allocentric navigation performance is well documented in navigation literature (Raz et al., 2009; Wiener et al., 2013; Daugherty et al., 2015; Driscoll et al., 2005; Erickson et al., 2010; Moffat et al., 2011; Nicole et al., 2003, Rogers et al., 2012) and was substantiated by our findings in Chapter 4 that age impaired allocentric performance on the AR paradigm.

The influence of age features less, however, in literature about self-reported confidence in navigation. This may be because age is often controlled for in questionnaire studies, typically at around a mean age of 20 years (e.g. Hegarty et al., 2002; Furman et al., 2014; Münzer & Hölscher, 2011). What is more, where studies have assessed age, findings have been contradictory. De Beni et al. (2006) found that self-reported QSR scores improved with age, but that performance in a mental rotation task did not and Borella et al. (2014) found that the influence of age on spatial skills across the adult life span was ‘considerable’ but that the effect of age on self-assessment ‘was more marginal’ in comparison (2014).

The results from this experiment show that age does provide a unique and positive contribution to self-reported confidence in allocentric navigation, despite its negative influence over navigation performance. The findings suggest that further research into the confounding factor of age be considered to maximise the validity of self-report questionnaires in navigation performance assessments.

5.5.2.2 GENDER

Gender also seems to have a confounding influence on the relationship between self-reported confidence in navigation and navigation performance. Many navigation studies which have found a gender bias of lower self-reported navigation confidence in females (Lawton et al., 1994; Hegarty et al., 2002; Schmitzer-Torbert, 2007; Meneghetti et al., 2011; Wegman et al., 2013; Pazzaglia et al., 2011). However, there are also other studies where gender is less remarkable an influence; Furnman et al. (2014), Epstein et al. (2013) and Münzer & Hölscher (2011) all reported finding found no gender differences in self-reported navigation.

The findings from this experiment show that gender does provide a unique contribution to self-reported confidence in allocentric navigation and that males have higher self-reported confidence in navigation than females overall. Moreover, this was not commensurate with their

performance, either in spatial processing on their Four Mountains score, or their active navigation on their AR paradigm performance. While there is a need for caution in interpreting a 'null result' here (that is, a lack of higher allocentric performance in males) as being conclusive of gender differences in navigation, these findings do substantiate those of others. Münzer & Stahl (2011) stated that females self-reported generally lower confidence in navigation but that actual navigation performance differences were mostly negligible, concluding that "gender differences in real-world route learning tasks have not reliably been found" (Münzer & Stahl, 2011). Together, previous literature and this study's findings suggest that navigation questionnaires may not provide any indication of likely gender differences in allocentric navigation performance.

5.5.3 Conclusion

To conclude, in Chapter 5, individual differences in navigation styles were investigated in a healthy population using navigation questionnaires (the SBSOD, QSR and FRS) to measure self-reported confidence in navigation, and navigation tasks (the Alternative Route paradigm and the Four Mountains task) to measure navigation performance. While researching how individuals recognise their own competence is understood to be complex (e.g. see Kruger & Dunning, 1999), Chapter 5 does provide some insight into recognition of navigation competence. Allocentric navigation performance was found to correlate with allocentric navigation questions, particularly in those who had successfully processed traumatic experiences in their lives. Our understanding of why allocentric navigation (particularly in those with a personal history of trauma) was more correlated with questionnaire data than egocentric processing was benefitted from neural models of hippocampal dependent memory systems (such as that presented by Morris in Andersen et al., 2007). This study argues that using the hippocampus in navigation is something which individuals can more easily articulate (compared to more implicit navigation behaviour) – and that this articulation is more accurate in individuals who have had to use this same type of neural processing in other areas of their personal lives (such as for encoding traumatic experiences).

In Chapter 6 the correlation between self-reported allocentric competence and actual navigation competence is assessed in a non-healthy population of individuals who have been trauma exposed and who have gone on to develop PTSD. Comparisons are then made between those who have military navigation training and those who have not.

6 NAVIGATION BEHAVIOUR IN COMBAT-RELATED PTSD (CR-PTSD)

ABSTRACT

The aim of this chapter is to assess whether people with Post-Traumatic Stress Disorder (PTSD) are accurate in their perceptions of their own performance in navigation (or indeed their impairment). The sample population comprised participants with combat-related PTSD (CR-PTSD) and non-combat related (civilian) PTSD. The military presents a useful example of where the pressure of chronic traumatic stress could well interact with pressure to perform well in navigation. Because of the military profile of this particular sample, it was also possible to consider the influence that military training (which involves navigation training) might have on perceptions of navigation performance in cases of PTSD.

The generic Santa Barbara Sense of Direction (SBSOD) questionnaire and the egocentric and allocentric questions extracted from the Questionnaire of Spatial Representation (QSR) and the Fragebogen Räumliche Strategien (FRS) were all correlated with Four Mountains task performance and overall, egocentric and allocentric performance on the Alternative Route (AR) paradigm. Correlation analysis was undertaken for the PTSD group as a whole and then separately for those with a military background (the *CR-PTSD* group) and those without a military background (the *Non-Combat PTSD* group).

Results showed that in PTSD populations, neither allocentric performance, nor egocentric performance, nor overall performance could be predicted by any of the navigation questionnaires (the SBSOD, the QSR or the FRS). Moreover, those with a military background (the *CR-PTSD* group) self-reported higher navigation confidence compared to those without (the *Non-Combat PTSD* group), which was not reflected in higher navigation performance levels.

The conclusion drawn from Chapter 6 is that conventional navigation self-assessment measures do not accurately predict navigation performance levels in those with PTSD and are unreliable measures of self-reported competence in those who have PTSD (including those who have experience of military training in navigation).

6.1 INTRODUCTION

6.1.1 Overview

Results from Chapter 5 showed that participants who were exposed to traumatic experiences but did not develop PTSD were accurate in their perception of their own allocentric navigation performance. Here, in Chapter 6, the focus is on those participants who were exposed to traumatic experiences who went on to develop PTSD, a group whose navigation performance was impaired (see Chapter 3 Section 3.3.1 and Chapter 4 Section 4.4.1). The main question was whether participants with PTSD were also able to assess their allocentric navigation performance (and impairment in it) accurately. The sample population comprised 27 participants with combat-related PTSD (CR-PTSD) and 19 participants with non-combat related (civilian) PTSD. The profile of the sample meant that it was also possible to ask if there were any differences in navigation confidence and/ or performance between those who had a military background (which included access to navigation training) and those who did not.

6.1.2 Navigation training in the military

From a military perspective, navigation and knowing where one is in space is vital to maximise performance in theatre. 'Situational Awareness'[22] is highly prized as a personal and strategic advantage in the UK military and improving navigation and situational awareness features as a funding priority for research under the Defence Science and Technology Laboratory Corporate Plan (2014 – 2019). Online resources revealed that navigation training has a high profile in military life; navigation training begins at recruitment in the British Army[23] and is assessed annually[24]. Training in more advanced navigation techniques features in many areas of the Armed Forces, including specialisms such as Royal Marine Commando training[25]. The *CR-PTSD* group were all former serving military personnel and all participants confirmed that they had received regular navigation training as part of their service. In contrast to this, the *Non-Combat PTSD* group all reported that they were not trained in military navigation techniques or skills.

The principle way in which military training could influence the accuracy of an individual's self-assessment is by raising confidence levels in those who have had navigation training[26]. One would therefore predict that self-reported confidence in navigation to be higher in those who were military trained (i.e. the *CR-PTSD* group) regardless of any impairment to their allocentric navigation performance as a result of having developed PTSD.

---

[23] Phase One Initial Training: https://www.army.mod.uk/training_education/24473.aspx http://www.army.mod.uk/documents/general/Navigation_jun11.pdf;

[24] Manual Annual Training Test (MAAT): http://www.army.mod.uk/training_education/24530.aspx

[25] http://www.royalnavy.mod.uk/careers/royal-marines/how-to-join-the-marines/rm-commando-training#week-05

[26] Another potential way in which military training could have influenced the predictability of an individual's navigation performance could have been by increasing the accuracy of self-assessment. However, there was no literature to support the development of this line of enquiry and it was beyond the scope of this research to explore this further.

Hypotheses and predictions

(i) 'Performance in allocentric navigation will correlate with navigation questionnaires in cases of PTSD, in contrast to egocentric performance which will not correlate'. This prediction was made on the basis of findings in Chapter 5 (summarised at Section 5.5) that allocentric navigation performance correlated with allocentric navigation questions in the healthy population while egocentric navigation performance did not correlate with egocentric navigation questions in the healthy population. Note that this prediction was also made on the assumption that PTSD would *not affect awareness* of one's own navigation competence and the lower levels of performance in cases of PTSD were expected to be reflected in lower levels of self-reported confidence.

(ii) 'Self-reported confidence levels in those with military training (i.e. the *CR-PTSD* group) will be higher than those without military training (the *Non-Combat PTSD* group)'. This prediction is made on the basis that military navigation training will have enhanced confidence in navigation in those who have had access to it (i.e. the *CR-PTSD* group).

Variables for analysis for these predictions include: the Four Mountain score out of 15, mean overall AR score (same direction trials and different direction trial scores combined), mean same direction and mean different direction AR scores, total SBSOD survey score as a percentage, total QSR_{route} (egocentric) and QSR_{survey} (allocentric) questions score as a percentage, total FRS global (egocentric) questions score as percentages, and total FRS survey (allocentric) questions score as a percentage.

6.2 METHODS

6.2.1 Participants

Participants were a subset of 46 (10 female) participants from the whole sample population (*n* = 150) who had with clinical or levels of probable PTSD. They were recruited via:

(i) Combat Stress (a military charity) PTSD Rehabilitation course (through Tyrwhitt House Treatment Centre, Leatherhead, Surrey) (*n* = 25)
(ii) Bournemouth University Psychology Research Volunteer Scheme (*n* = 1)
(iii) Cambridgeshire Constabulary (*n* = 1)
(iv) Dorset Constabulary (*n* = 1)
(v) The Intensive Psychotherapy Treatment Service (IPTS) at Dorset NHS (*n* = 4)

Table 6.2.1 below details the representation of age, gender and score on the PTSD Diagnostic Scale (PDS, by Foa et al., 1995) in the two PTSD groups (*n* = 46) and illustrates that gender was not controlled for as there were no females in the main CR-PTSD group. The significantly higher mean age in the *CR-PTSD* group required age to be considered in the analysis. PDS scores were comparable, negating the need to control for PTSD severity.

Table 6.2.1: Descriptive and inferential statistics for demographic and trauma impact data by combat-related PTSD (*CR- PTSD*) and *non-combat* related PTSD (*PTSD)* groups (*n* = 46).

Demographic or clinical factor		***CR- PTSD*** (*n* = 27)	***Non-Combat PTSD*** (*n* = 19)	**Group comparison**
Mean age (years)		41.5 *SD* ± 8.81	34.4 *SD* ± 9.13	*F* (1, 44) = -2.81, *p* = 0.01
Gender (%)	Male	100%	47%	χ^2= 18.7 *p* < 0.01
	Female	0 %	53%	
Mean PDS score		35.9 *SD* ± 9.29	34.4 *SD* ± 9.9	*F* (44) = -5.01, *p* = 0.62

Civilian participants were offered £10 financial reimbursement for their time (apart from Dorset Police participants who took part in the study during working hours). Participants from Combat Stress were offered £20 on advice from the Combat Stress Ethics Committee, given their travel and time commitment (their time commitment included receiving a lecture on PTSD and the Brain by the researcher for this study: more information about which is provided in the Methodology section).

The study was approved by: the BU Graduate School Ethics Board; the Combat Stress Research Ethics Committee; and the NHS South West (Cornwall and Plymouth) National Research Ethics Service (NRES).

One participant was excluded due to not having completed the questionnaire data. Two participants were excluded because of missing values in their data for either the Four Mountains task, the Alternative Route paradigm or the navigation questionnaires. There was one missing value which needed correcting: one participant missed the two allocentric QSR_{survey} questions but had completed the FRS survey questions. Hot-check imputation (Andridge et al., 2010) was conducted to replace the missing value and this was achieved by using the mean QSR_{survey} score from all the other participants who scored the same for the 'FRS survey' questions as the participant in that question. This was on the basis that the 'FRS survey' questions were closest in content to the QSR_{survey} scores (see the Methodology Chapter 2, Section 2.8.2.2).

All participants recruited through Bournemouth University in this study (*n* = 140) were asked if they had received navigation training or if they used navigation as part of their job role. The response rate was low and the data was not deemed reliable enough to use in statistical analysis (more information on this is provided in the Methodology Chapter 2, Section 2.5.4.3). With regard to the sample population for Chapter 6, five participants from the *Non-Combat PTSD* group reported having either received some form of navigation training or having used it as part of their work. Four of these individuals were Police officers. No participants in the *Non-Combat PTSD* group had received military navigation training. Military training was therefore considered a viable characteristic of *CR-PTSD* to consider in Chapter 6.

6.2.2 Procedure

Informed consent was sought from all participants (*n* = 46). Participants completed the Life Events Checklist (LEC, Blake et al. 1995). Those who self-reported having been exposed to trauma were given the Post-Traumatic Stress Disorder Diagnostic Scale (PDS, Foa 1995) to ascertain the present day impact of the prior trauma. Those who self-reported PDS scores below the threshold of 21 were allocated to the *Trauma Exposed No PTSD* group (*n* = 46). Those who self-reported PDS scores at or above the threshold of 21 (as typically used by Foa et al., 1995 as an indicator of probable PTSD) were not included in this part of the study. Those participants with PTSD who reported combat-related trauma exposure on their PDS were analysed as a subgroup (*Combat-Related PTSD*) and those who reported a civilian trauma exposure on their PDS were analysed as the civilian subgroup (*Non-Combat Related* PTSD)

The 21 Bournemouth University (BU) participants were offered the option of completing navigation questionnaires over email or in person at the beginning of the experiment session. Those willing to complete them in advance were sent an email with a unique identification code and a confidential link to an online version of the research surveys hosted securely at Bournemouth University. Those who wished to complete them at the experimental session were asked to allow 45 minutes to complete them either on paper or on a laptop *in situ.*

The participants then undertook the Four Mountains task (Hartley et al., 2007) which took 10 minutes to complete. Participants were given a series of three practice trials to familiarise them with the layout of the test and to ensure that instructions were understood. The participants then undertook the AR which took 24 minutes to complete. Prior to the task, participants were given written instructions for the AR paradigm (Wiener et al., 2013) which were summarised verbally after being read by the participants. They were also given a demonstration of the task showing them how to use the controls and to advise the participants on the timing of the paradigm.

The 25 Combat Stress participants were tested at the Combat Stress treatment centre with a clinical nurse on duty (in line with the ethics clearance authorised by Sir Prof. Simon Wessley and following the protocol of NHS site specific IRAS clearance). Dorset Police officers were also given extra information regarding the storage and destroying of DNA samples through the Dorset Police General Orders email system after an enquiry about DNA was made by a number of potential recruits who later declined to take part in the study. The researcher was advised by Dorset Police that there may be some unease in sharing DNA data and that further assurances about confidentiality would help to secure a good response rate to recruitment advertising.

6.2.3 Materials

6.2.3.1 NAVIGATION QUESTIONNAIRES

The three navigation questionnaires used in the experiment comprised: the Santa Barbara Sense of Direction (SBSOD: Hegarty et al., 2002); the Questionnaire of Spatial Representation (QSR; Pazzaglia & De Beni, 2001); and the Fragebogen Räumliche Strategien (FRS; Münzer & Hölscher, 2011). The SBSOD, the QSR and the FRS are fully introduced in Chapter 5, Section 5.5.1 and Appendix C provides a full list of questions in each survey.

N.B. It is worth pointing out at this stage that Chapter 4 demonstrated that individuals with PTSD were more likely to use associative cue strategies in navigation than those without (see Section 4.3.3). Navigation questionnaires were not assessed for their capacity to predict *associative cue strategy uptake* in cases of PTSD in Chapter 6 is because it was not possible to differentiate between egocentric questions in the SBSOD, QSR or FRS which would be likely to reflect either 'associative cue' or 'beacon' style strategy use in the AR paradigm[27].

6.2.3.2 NAVIGATION TASKS

The Four Mountains task (Hartley et al., 2007) is a static topographical (allocentric) test of spatial memory (Hartley et al., 2002; Hartley & Harlow, 2012; Bird et al., 2010; see Chapter 3 for full details of this test). The Alternative Route (AR) paradigm was introduced by Wiener et al. (2013) as a novel route-learning paradigm to test allocentric and egocentric navigation performance and to identify preferences (biases) for different navigation (spatial processing) strategies; for full details see Chapter 4, Section 4.2.3). The paradigm is employed in the same way in this chapter as it was for Chapter 5 (see Section 5.5.5.3).

6.3 RESULTS

The pattern of correlations across the sample (n = 46) and then separately for those with CR-PTSD (n = 28) and with non-CR-PTSD (n = 19) are reported below. All statistical analyses were performed using SPSS version 22 (SPSS, IBM Corp. in Armonk, NY).

6.3.1 Correlating navigation performance with questionnaires in cases of PTSD

Table 6.3.1 presents correlations between navigation questionnaires and navigation (and spatial processing) performance and age in the PTSD group (n = 46). Across the PTSD population (n = 46), no allocentric or general Sense of Direction questions predicted allocentric performance as it had done in the healthy population in Chapter 5. There were no significant correlations between egocentric navigation questions and egocentric performance on the AR (as was found with the healthy population) either. Age was moderately correlated with general confidence in Sense of Direction (SBSOD score), r (46) = 0.29, p = 0.047 mirroring findings in the healthy population (Chapter 5). Performance did not significantly correlate with age.

[27] Another more technical reason that strategy use in the AR is not being analysed for correlation with navigation questions is that performance on the AR is inextricably linked to use of the configural strategy in the AR (thus confusing any relationship between self-reported confidence and *performance* rather than of strategy preference over either associative or beacon strategy).

Table 6.3.1: Correlation (r) between navigation questionnaire scores, age and performance in participants with PTSD (n = 46) p < .05*****.

Questionnaire/ performance	Four Mountains	Overall performance (AR)	Egocentric performance (AR)	Allocentric performance (AR)	Age (years)
SBSOD	0.04	0.12	0.05	0.11	0.29*
QSR_{route} (egocentric)	0.11	-0.04	-0.03	0.24	0.14
FRS global (egocentric)	0.05	0.16	0.20	0.04	0.11
QSR_{survey} (allocentric)	-0.07	-0.04	-0.02	0.06	0.18
FRS survey (allocentric)	0.07	0.17	0.12	0.05	0.21
Age (years)	0.04	0.03	-0.17	-0.05	-

6.3.2 Self-reported navigation confidence and navigation performance in the non-military trained and military trained participants with PTSD

The performance of those in the *CR-PTSD* group was compared with those *Non-Combat PTSD* group using a series of independent t-tests. Figure 6.3.2 below illustrates that the *CR-PTSD* group self-reported navigation competence ratings were numerically higher for all questionnaires and subsets and that significant differences were found for the SBSOD total score, with the *CR-PTSD* group scoring higher (M = 67.9, SD ± 17.7) than the *Non-combat PTSD* group, M = 58.0, SD ± 14.8, t (44) = -2.05, p = 0.046 and also for the QSR_{survey} score, with the *CR-PTSD* group scoring higher (M = 66.7, SD ± 18.6) than the *Non-combat PTSD* group, M = 55.8, SD ± 15.7, t (44) = -2.08, p = 0.04. All other comparisons p > 0.05).

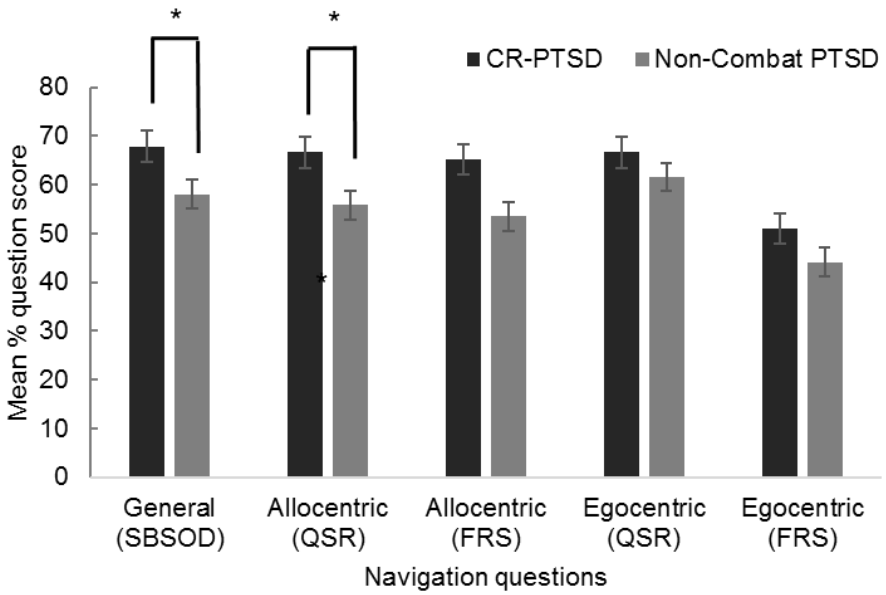


Figure 6.3.2: Differences in self-reported navigation confidence and performance between the combat-related PTSD group (CR-PTSD) (n = 28) and the non-combat related PTSD (PTSD) (n = 19) group with significant differences, p < 0.05* and standard error bars.

Figure 6.3.2.1 below shows performance in the navigation tasks. T-tests revealed no significant differences between the *Non-combat PTSD* and *CR-PTSD* groups on any performance measure ($p > 0.05$). It is important to note that these findings cannot be explained by differences in severity of PTSD (i.e. in the combat group in comparison to the non-combat group) because both groups were matched on PDS scores (see Section 6.2.1).

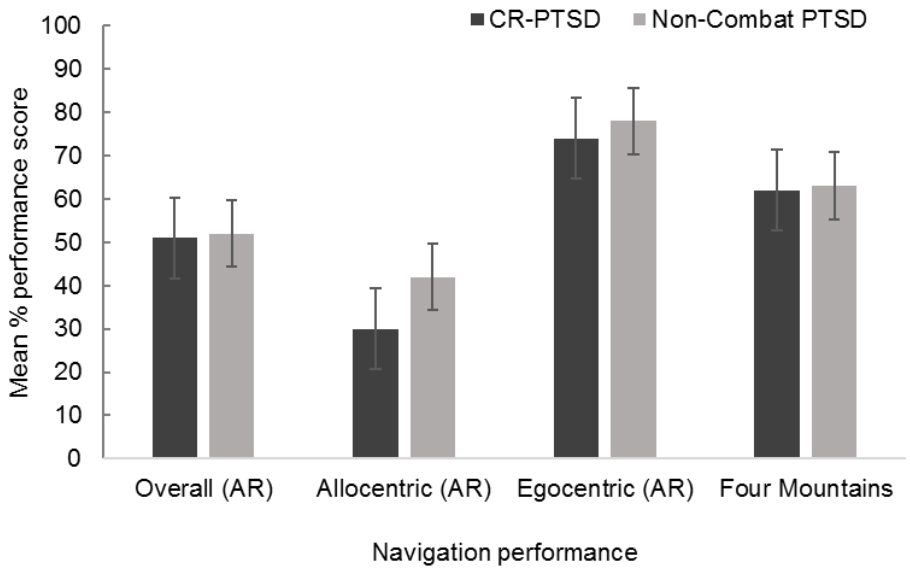


Figure 6.3.2.1: Differences in performance between the combat-related PTSD group (CR-PTSD) (*n* = 28) and the non-combat related PTSD (PTSD) (*n* = 19) group with standard error bars. Performance represents scores (%) on overall, allocentric and egocentric measures on the AR and the Four Mountains task.

6.3.3 Questionnaires and performance in military trained participants with PTSD

Given that there were higher levels of self-reported confidence in the *CR-PTSD* group, but *not* significantly higher performance levels, it was important to also compare how predictive the navigation questionnaires were of performance in the *CR-PTSD* group and the *Non-Combat PTSD* group.

Table 6.3.3 shows that, unlike in the healthy population, allocentric navigation performance in the *CR-PTSD* group did not correlate with allocentric navigation questions nor was there a correlation between egocentric navigation performance predictable and egocentric navigation questions. There were no general trends of correlation in the analysis. The positive influence of age on general sense of direction in the larger PTSD population (*n* = 46) did not persist in the *CR-PTSD* group.

There was an unexpected significant correlation between allocentric performance on the AR and preference for *egocentric* navigation in the QSR_{route} questions, r (27) = 0.40, p = 0.04. This finding may be attributable to the chance of false positives within the analysis, but another explanation for this finding could be that the combination of PTSD and military training distorts the relationship between self-reported confidence and performance. It is reasonable to consider that those with military training are trained to be confident in navigation, and that (given the research of the impact of PTSD on allocentric spatial processing (here in Chapter 4 but also in

Smith et al., 2015; Tempesta et al., 2012; etc) veterans with PTSD may have been used to relying on egocentric navigation strategies to get by in everyday way-finding. From this, one could speculate that over time, it is their confidence in egocentric navigation that predicts their navigation performance- and that it predicts *allocentric* navigation performance (not egocentric performance) because egocentric navigation performance is non-declarative.

Table 6.3.3: Correlation (r) between navigation questionnaire scores, age and performance in the CR-PTSD group (n = 28) $p < .05$*****.

Questionnaire/ performance	**Four Mountains**	**Overall performance (AR)**	**Egocentric performance (AR)**	**Allocentric performance (AR)**	**Age (years)**
SBSOD	0.01	0.13	0.03	0.25	0.22
QSR_{route} (egocentric)	0.08	0.02	-0.11	0.40*	0.13
FRS global (egocentric)	0.07	0.17	0.14	0.23	0.15
QSR_{survey} (allocentric)	-0.16	-0.01	-0.06	0.16	0.14
FRS survey (allocentric)	-0.03	0.31	0.20	0.17	0.27
Age (years)	-0.15	0.18	-0.26	-0.01	-

6.3.4 Questionnaires and performance in non-military trained participants with PTSD

Table 6.3.4 overleaf shows that, as with the total PTSD population and the *CR-PTSD* population, allocentric navigation performance was not predictable by allocentric navigation questions in the *Non-Combat PTSD* group. No correlations were found between self-reported egocentric confidence and egocentric navigation performance either (as was the case with the healthy population and the total *PTSD* population). The positive correlation between age and confidence in general sense of direction (SBSOD) in the total PTSD population (n = 46) did not reach significance in this *Non-Combat PTSD* group. Age was, however, positively correlated with overall performance on the AR, r (19) = 0.51, p = 0.03 which has not been found in any other data in this study, nor in the literature reviewed.

Table 6.3.4: Correlation (r) between navigation questionnaire scores, age and performance in the Non-Combat PTSD group (n = 19) $p < .05$*****.

Questionnaire/ performance	Four Mountains	Overall performance (AR)	Egocentric Performance (AR)	Allocentric performance (AR)	Age (years)
SBSOD	0.13	0.18	0.19	0.11	0.18
QSR_{route} (egocentric)	0.17	-0.15	0.14	0.11	0.06
FRS global (egocentric)	0.07	0.22	0.39	-0.07	-0.13
QSR_{survey} (allocentric)	0.08	-0.05	0.17	0.14	0.04
FRS survey (allocentric)	0.25	-0.07	0.06	0.04	-0.10
Age (years)	0.31	0.57*	0.06	0.10	-

6.4 DISCUSSION

6.4.1 Summary

The main aim of Chapter 6 was to ascertain if people with PTSD were accurate in their perceptions of their own competence (or impairment) in navigation. The second aim was to compare those from a military background and those not from a military background within our PTSD sample to ascertain if military experience influenced self-reported confidence and / or performance in navigation.

To address these questions, navigation questionnaires were correlated with navigation performance measures in the same manner as had been done in Chapter 5. The prediction was that, as with Chapter 5, self-reported confidence in allocentric navigation would correlate with allocentric navigation performance but that self-reported confidence in egocentric navigation would not correlate with egocentric navigation performance. It was also anticipated that there would be group differences in self-reported navigation confidence and/ or performance between those from a military background (the *CR-PTSD* group) and those not (the civilian *PTSD* group).

The results first demonstrated that, contrary to the prediction (and unlike the healthy population in Chapter 5) individuals with PTSD were not accurate in their perceptions of their own allocentric performance. Consistent with the hypothesis (and as with the healthy population), egocentric navigation performance showed no correlation with egocentric navigation questions in those with PTSD. The results also showed that the *CR-PTSD* group had higher self-reported confidence than the *Non-Combat PTSD* group. This was despite the fact that there were no actual significant performance differences between the military (*CR-PTSD*) and non-military (*Non-Combat PTSD)* groups.

Finally, Chapter 6 replicated the positive correlation between age and self-reported confidence in navigation that was reported in Chapter 5 (see also Borella et al., 2014 and Furnman et al., 2014) and which has been found in other studies (e.g. De Beni et al., 2006; Borella et al., 2014).

In contrast, the negative correlation between age and performance that was reported in Chapter 5 (see also Wiener et al., 2013; Raz et al., 2009; Moffat et al., 2010, etc.) did not persist in cases of PTSD in Chapter 6.

The conclusion for this chapter is that PTSD affects the relationship between allocentric navigation questions and allocentric navigation performance; a relationship which was apparent in the healthy population in Chapter 5. The low correlation between navigation questions and allocentric navigation performance in those with PTSD suggests that individuals with PTSD are may be unaware of their impairment in navigation. What is more, amongst those with PTSD, military experience may increase self-reported confidence in navigation but this increase in confidence does not equate to higher navigation performance; military experience therefore does not 'protect' individuals from PTSD-related performance impairment, nor from inaccurate perceptions of their own competence.

6.4.2 Combat-Related PTSD (CR-PTSD)

Whilst navigation training (as part of the military experience) was likely sufficient to explain why those with CR-PTSD were more confident in navigation that those with non-combat related PTSD, other elements of the military experience and of CR-PTSD were also considered. Literature about military life and combat trauma was reviewed for information about unique characteristics of combat-related trauma which may have explained confidence differences better than navigation training could have explained confidence differences. No such characteristics were identified. CR-PTSD is not differentiated from PTSD in conventional diagnostics (DSM-V, APA, 2015) and the diverse and rapidly growing literature about combat trauma does make reference to any unique characteristics of it which may have been pertinent to navigation (Gee et al., 2013; MacManus & Wessely, 2013; MacManus et al., 2014; Palmer, 2012; KCMHR, 2010; Gilbertson et al., 2002; King's College London, 2010; Pitman et al., 2012; Poyner, 2010; Hoge, 2011)[28]. There may be other factors which may influence confidence levels in the military such as personality types or the "psychology of war" (Palmer, 2012; KCMHR, 2010) but without detailed clinical studies into how these factors interact with PTSD to effect navigation performance, no conclusions can be made. One logical interpretation as to why there are differences in self-reported navigation confidence between those with *CR*-PTSD and those with civilian *PTSD* is the access to navigation training that individuals with CR-PTSD have had in the military (compared to those with civilian PTSD).

It is important to note that the study did not have the capacity to assess how military experience and combat exposure affects the predictability of navigation performance (or the reliability of self-assessment in navigation) in *healthy serving personnel*. The sample of individuals in

[28] Key themes in CR-PTSD literature included: prevalence rates, pre-existing vulnerabilities to PTSD, trauma processing interventions, what makes treatment successful, the influence of demographics such as age, and even clinical factors such as DNA and psychomotor speed (KCMHR, 2010; Ahmed et al., 2007; Apfel et al., 2011; Gilbertson et al., 2002; Browne et al., 2007; Dandeker et al., 2010; MacManus & Wessely, 2013; Duax et al., 2013; Palmer, 2012; Yehuda et al, 2015; Nievergelta et al., 2015; Hart et al., 2008).

Chapter 6 were *either* healthy *or* no longer serving in the military. It is possible that there may be serving personnel who *do* have clinical levels of CR-PTSD (Gee, 2014) for whom the findings of Chapter 6 are particularly relevant. However the aim of this study was not to be representative of the serving military population, but to understand better the sample population available to us: caution should be taken before interpreting these results as being indicative of currently serving personnel.

One final potential influence over the how the hippocampus is used for either trauma processing or spatial processing (or both) is the *plasticity* of the hippocampus. A determining factor for hippocampal plasticity which is being increasingly researched is DNA. In this final chapter, Chapter 7 explores the role of the Brain-Derived Neurotrophic Factor (BDNF) gene in the relationship between trauma and navigation.

7 BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF), PTSD & NAVIGATION

ABSTRACT

This thesis has so far confirmed that factors of PTSD and trauma exposure impair active navigation, and that PTSD (not trauma exposure) impairs an individual's perception of their own navigation competence. The aim of Chapter 7 is to now consider how a *genetic* factor (i.e. the Brain-Derived Neurotrophic Factor gene, BDNF) might influence the relationship between trauma, spatial processing and navigation. In doing so, this explorative final chapter brings navigation, trauma and the BDNF gene together for the first time in a human model.

Due to its role in maintaining hippocampal integrity, the BDNF gene has been identified in separate literatures as a candidate gene to explain differences in PTSD symptomology and differences in various components of spatial processing and navigation behaviour. Here, the investigation addresses whether differences in PTSD status, spatial processing and navigation behaviour can be related to BDNF genotype. This exploratory analysis using BDNF genotype as a grouping factor follows the same format of analysis as that in previous chapters to assess group differences in: spatial processing (using the Four Mountain's task); egocentric and allocentric processing in active navigation (using the Alternative Route, AR, paradigm); and self-reported confidence in navigation (using navigation questionnaires), correlated with navigation performance.

The BDNF genotype of each of the 150 participants in the study sample was determined using saliva samples and participants were classified as being either *met carriers* (representing up to 30% of the Caucasian population), or *valval homozygotes (*representing the remaining 70% of the Caucasian population). While the modest sample size and the exploratory nature of this analysis limit the conclusions that can be drawn from it, there are a number of interesting findings which invite future research.

As with the majority of the research in this area, the current data did not show there to be a direct relationship between BDNF and PTSD prevalence or PTSD severity in this sample population. Also consistent with the literature, carrying the BDNF met allele did not impair navigation performance. There was, however, evidence that BDNF met carriers approached egocentric processing differently to valval homozygotes and self-reported higher navigation confidence. There was also evidence that met carriers were less accurate in their perception of applying allocentric processing to navigation than valval homozygotes and some visual indications that they were delayed in their application of allocentric processing in the AR task. Differences between BDNF genotypes in the application (and awareness of) allocentric processing are considered later in the context of their potential relevance to trauma processing and navigation training (see the Discussion Chapter 8, Sections 8.3.2 and 8.4.3).

7.1 INTRODUCTION

"The role of the BDNF gene within the human population may have an important impact upon the processes of long term memory induction as well as rehabilitation and treatment of neurological disorders" (Chaeib et al., 2014).

7.1.1 About the BDNF gene

"It's like a teacher in the brain saying, '*Now <u>this</u> is what you need to know for the exam of life*" (*Michael Merzenich* talking about the role of the Brain-Derived Neurotrophic Factor gene in attention and plasticity in hippocampal dependent tasks in Doidge, 2007).

The Brain-Derived Neurotrophic Factor (BDNF) gene is increasingly studied for its contribution to hippocampal function and integrity (Doidge, 2007; Dodds et al., 2013). The BDNF gene codes for the BDNF protein (Egan et al., 2003 in Notaras et al., 2015) which promotes the growth and survival of neurons in the hippocampus, helps regulate synaptic plasticity, and reinforces changes as a result of that plasticity (Szesko et al. 2005; Chaieb et al. 2014; Ninan et al. 2010; Lövdén et al., 2011; Doidge, 2007; Egan et al., 2003; Bastrikova et al., 2008; Mowla et al., 1999). BDNF protein release and plasticity in the hippocampus has also been associated with critical periods (Doidge, 2007) of development and aging (e.g. Huang et al., 1999; Sambataro et al., 2010) and traumatic stress (Gatt et al., 2009; Elzinga et al., 2011) as well as environmental conditions and longer phases of learning (Salehi et al., 2013; Sanchez et al., 2011; Lövdén et al., 2011).

Humans carry two copies of most genes (one from our mother, one from our father) and these copies might vary. The BDNF gene has two variants which differ in their functionality (Egan et al., 2003 in Notaras et al., 2015). Specifically, the variations of the BDNF gene are the 'met' and 'val' alleles. Valval homozygotes carry two 'val' alleles, valmet heterozygotes carry one 'val' and one 'met' allele, and metmet homozygotes carry two 'met' alleles. In the Caucasian population 70% are *valval* homozygotes*,* 26% are *valmet* heterozygotes, and 4% are *metmet* homozygotes*.*

According to Chaeib et al. (2014), BDNF can be released in the hippocampus in two different ways: after electrical stimulation and "more generally as an activity-dependent response" (Chaeib et al., 2014). The BDNF protein is also released differently according to genotype (Frielingsdorf et al., 2010; Notaras et al., 2015; Petryshen et al., 2010). Those who carry at least one met allele ('met carriers') secrete *less* BDNF in response to hippocampal dependent activity which decreases hippocampal plasticity and is therefore considered as detrimental to hippocampal dependent (and declarative) memory and function (Notaras et al., 2015; Kambeitz et al., 2012).

Recent studies suggest that BDNF is released in response to trauma (e.g. Van de Heuvel et al., 2016). The release of BDNF increases neurogenesis (the active production of new neurons) and neuroplasticity (e.g. Chen et al., 2006; Anomal et al., 2012; Wang, 2015, etc.). Neurogenesis is also said to influence the ability of the hippocampus to process trauma: Brewin et al. (2010) suggest that new excitable neurons (created in neurogenesis) in the hippocampus

help individuals to be able to differentiate between past and present trauma, thus assisting with the processing and consolidation of trauma to memory. There is now strong evidence to suggest that BDNF is released in response to hippocampal dependent activity and training: including activity which involves allocentric spatial processing, such as navigation (e.g. Lövdén et al., 2011; Banner et al., 2011; Deadwyler et al., 1996; Egan et al., 2003; Hariri et al., 2003; Hashimoto et al., 2008; Jia et al., 2008; Goodman et al., 1996)

A recent review concluded that:

"…**taken as a whole, the conventional view is that the val66met[29] polymorphism disrupts the activity-dependent release of BDNF… potentially having consequences for physiological functions modulated by BDNF***"* (Notaras et al., 2015).

7.1.2 BDNF and Post-Traumatic Stress Disorder (PTSD)

7.1.2.1 HOW THE RELATIONSHIP BETWEEN PTSD AND BDNF HAS BEEN RESEARCHED

The search for a genetic marker for the condition of Post-Traumatic Stress Disorder (PTSD) has been vigorous and unrelenting (see Notaras et al., 2015, Wang, 2015 and Miller & Wiener, 2014 for reviews; and: Kolassa et al., 2012; Morey et al., 2011; Skelton et al., 2012; Zoldadz & Diamond, 2013; Yehuda et al, 2006, 2011, 2015). Since research identified BDNF *val66met* as being a functional variant of the BDNF gene in 2003, numerous studies have been undertaken to investigate its role in PTSD (Notaras, et al. 2015)[30]. These studies vary greatly in design, ranging from genome wide association studies, to small candidate gene studies (Koenen et al., 2009) and more recently, epigenetic studies (Schmidt et al., 2011; Rakofsky et al., 2011 in Wang, 2015; Roth et al., 2011; Morinobu et al., 2013).

Findings from several studies have identified BDNF as a candidate gene for PTSD aetiology as well as other threats to psychological well-being, be it in overall development, in mood disorders, depression or attempted suicide (Casey et al., 2009; Duman & Monteggia, 2006; Aguilera et al., 2009; Gatt et al., 2009; Perroud et al., 2008; Pregelj et al., 2011; Hasler et al., 2004; Wang et al., 2011). The dominant premise in the BDNF and trauma literature is that the met allele of the gene is disadvantageous and is a potential risk factor for PTSD (Notaras et al., 2015). Conversely, research in other areas of medicine (not related to the stress response) has shown that the BDNF met allele may have protective effects, for example against traumatic brain injury and systemic lupus (see Krueger et al., 2011; Beste et al., 2010; Oroszi et al., 2006).

[29] The reason the number 66 is included in the description of the BDNF genotype is because the allelic variation occurs at codon 66.

[30] Research designs have included: simulated trauma in rodent models *vs* self-reported trauma in human models (Notaras et al., 2015); assessing retrospective childhood trauma (Andersen et al, 2008; Dalvie et al., 2014; Elzinga et al. 2011; Perroud et al., 2008) *vs* remote and recent adult trauma (Hauck et al., 2010); assessment of BDNF through serum, plasma, blood *vs* saliva (Koenan et al., 2009; Notoaras et al., 2015; Wang, 2015); studies combining 'met' variations of polymorphisms *vs* those keeping them separate (e.g. Notaras et al., 2015, Banner et al., 2012, and Hariri et al., 2003); and studies which examine BDNF gene expression vs BDNF protein (and related neurotrophins) release (e.g. Lövdén et al., 2011 *vs* Hauck et al., 2010).

7.1.2.2 FINDINGS FROM PREVIOUS STUDIES OF PTSD AND BDNF

BDNF has been related to psychological conditions which share a common feature: the stress response. The stress response dominates genetic literature about PTSD (e.g. Liu et al., 2004; Beste et al., 2010; Berton et al., 2006 and for reviews, see Notaras et al., 2015; Miller & Wiener, 2014; Koenan et al., 2009).

Research into the relationship between BDNF and PTSD encompasses studies which look at individual PTSD symptoms or traits (e.g. Montag et al., 2008; Frielingsdorf et al., 2010; Rattiner et al., 2004); studies which address PTSD prevalence and severity (e.g. Suliman et al., 2013; Valente et al., 2011; Pivac et al., 2012; Zhang et al 2006); and those studies which examine the mechanisms by which the BDNF gene comes to influence cognition, memory, behaviour and physical health (e.g. Calabrese et al., 2015; Murakami et al., 2005; Pizarro et al., 2004; Hauck et al., 2010; Heinonen et al., 2014; Hofer et al., 1990; Tan et al., 2005; Ward et al., 2014).

There are several studies which have addressed specific stress-related and fear-based behaviours and traits of PTSD and in these studies met carriers show stronger anxiety and fear responses (Peters et al., 2010; Montag et al., 2008; Soliman et al., 2010; Takei et al., 2011; Torrents-Roda et al., 2012; Frielingsdorf et al., 2010; Rattineret al., 2004; Norrholm et al., 2013; Rosas-Vidal et al., 2014). For example, Montag et al. (2008) demonstrated that BDNF metmet homozygotic mice scored significantly higher than BDNF valval homozygotic mice on anxiety related facets of harm avoidance. Frielingsdorf et al. (2010) showed that human and mice BDNF met carriers (i.e. valmet heterozygotes and metmet homozygotes) showed slower suppression of the learned fear response than valval homozygotes.

Despite Notaras et al.'s (2015) overview that there is likely a connection between BDNF and PTSD, findings from many studies designed to assess the relationship between the BDNF gene and PTSD diagnosis, prevalence or severity (rather than individual stress-related symptoms) have not demonstrated any systematic relationship. Meta-analyses undertaken by Wang (2015) and Suliman et al. (2013) revealed no consistent association between BDNF genotype and PTSD. Valente et al. (2011) found no relationship between BDNF genotype and PTSD symptomology after trauma exposure in a study of urban violence (n = 65). While Pivac et al., (2012) showed that veterans with psychotic symptoms *in conjunction with* PTSD were more likely to carry BDNF met alleles than non-psychotic veterans with PTSD or veterans without PTSD, they did not find a direct relationship between BDNF and PTSD. Hemmings et al. (2012) reported an *epistatic effect* (the effect of one gene being dependent on the presence of one or more 'modifier genes') between the BDNF gene and another gene on the severity of PTSD symptoms but no direct relationship between BDNF and PTSD.

Other, BDNF studies were more mechanistic in nature, in so far as they addressed the influence of acute and chronic stress on hippocampal BDNF synthesis, expression and plasma levels (Murakami et al., 2005; Pizarro et al., 2004; Perroud et al., 2008; Calabrese et al., 2015). These studies looked at the mechanisms by which BDNF is released in reaction to stress, rather than how stressed individuals behave in relation to their BDNF levels or genotype. What is more, these studies focused on more acute stress and did not refer to the longer term chronic stress

of PTSD directly. Those mechanistic studies focusing specifically on PTSD did not demonstrate a significant relationship between BDNF and PTSD. Van de Heuvel et al. (2016) examined the relationship between BDNF and PTSD prevalence in 123 survivors of road traffic collisions, only ten of whom had clinical levels of PTSD. In this small sample, no significant relationship between BDNF genotype and PTSD prevalence or severity was found but levels of the BDNF protein in plasma were associated with traumatic load. An earlier study by Bonne et al. (2011) found no statistically significant associations between BDNF plasma levels and PTSD in 16 participants before or after receiving treatment for PTSD. Finally, Notaras et al. (2015) undertook a study which revealed that pure met homozygote mice had significantly higher contextual fear memory (a PTSD symptom, Foa et al., 1986) than valval homozygote mice when they were re-exposed to shock tones in familiar and novel environments. Surprisingly, upon exposure to chronic corticosterone known to induce glucocorticoid signalling (which is damaging to hippocampal function, see Vasterling & Brewin, 2005) the metmet homozygote mice also showed significantly *more* exploratory spatial behaviour[31] on a short term memory of the Y maze test (Notaras et al., 2015). Notaras et al. (2015) noted that earlier studies into BDNF as a modifier of hippocampal function (and *ergo* a 'locus of risk' for anxiety disorders such as PTSD) had failed to replicate hippocampal deficits associated with the BDNF met allele because of lack of power, regression towards to the mean, biased sampling, or failure to control for complex gene-environment interactions. The conclusion of their review was that,

…"cumulatively, these studies suggest that met carriers show dysregulated activation of brain regions involved in fear processing and autonomic arousal, which may predispose or increase risk of fear-related disorders such as PTSD" (Notaras et al., 2015).

It is important to consider the reasons why a direct relationship between BDNF and PTSD had not been found in previous studies. One explanation for why no direct relationship has been established between BDNF and PTSD is that the relationship does not exist, or that is it is complicated and is perhaps mediated by other factors which have not yet been fully understood. Many studies such as Van de Heuvel et al. (2016) and Bonne et al. (2011) had inadequate sample sizes for reliable genetic profiling amongst PTSD populations: Van de Heuvel et al. (2016) had a PTSD sample population of $n = 10$, and Bonne et al. (2011) had a PTSD sample population of $n = 16$. These sample sizes are limited, especially given the relatively rare distribution of the BNDF metmet homozygote (estimated at 4% of the Caucasian population by Petreyshen et al., 2010). Because of the challenges associated with their relative rarity, metmet homozygotes have not typically been analysed as a separate experimental group from valmet heterozygotes (e.g. Pezawas et al., 2004; Dempster et al., 2005; Zhang et al., 2014). Moreover, most studies controlled for neither the source of the trauma nor the opportunities indiviiduals may have already had to process trauma. Even in the study by Valente et al. (2011) which sought to recruit participants with a common source of trauma ('urban violence') it is notable that the study did not control for the nature, timing, duration or severity of that violence.

[31] In other literature, exploratory navigation behaviour is indicative of hippocampal integrity (e.g. Schomaker et al., 2014).

7.1.2.3 ZHANG ET AL. (2014), THE BDNF GENE AND PTSD

A notable study is that by Zhang et al. (2014) which had a PTSD sample population of *n* = 42 and which controlled for gene-environment interactions using a very homogenous sample. In 2014, Zhang et al. were first to report a direct relationship between the BNDF gene and PTSD. Specifically, they revealed that the allelic frequency of BDNF 'met' was twofold higher in those with probable PTSD in a population of serving Special Operations military personnel, compared to a population without PTSD. Zhang et al. (2014) also investigated the PTSD symptom, 'exaggerated startle' (similar to the 'hyperarousal 'symptoms described with DSM-V PTSD diagnostic criteria) and reported that the BDNF metmet homozygote was significantly more prevalent amongst those with 'exaggerated startle' scores, compared to those without exaggerated startle scores. Moreover, valval homozygotes were significantly more prevalent in the *non-exaggerated startle* groups than in the startle groups.

To summarise, examining the role of the BDNF gene in PTSD has been a focus of many studies since 2003 (e.g. Chen et al., 2006 and see Notaras et al., 2015). The premise of much of the research has been that hippocampal integrity (integrity which is required to manage the stress response and to process trauma) is impaired in those who carry the met allele of the BDNF gene (e.g. Notaras et al., 2015). Literature has pointed to poor controlling for the gene-environment interaction in small sample sizes as an explanation for largely inconclusive findings so far (see Zhang et al., 2014). This study seeks to examine the relationship between BDNF and PTSD in the sample population (*n* = 150), but with regard to another indicator of hippocampal integrity; allocentric processing in navigation.

7.1.3 BDNF and navigation literature

As mentioned in the General Introduction, Chapter 7 is exploratory in nature, and very few studies have addressed the relationship between genetics and navigation in any depth (Tsien et al., 1996; Guzowski et al., 2001; Kong et al., 2016).

Even fewer studies have explored the BDNF polymorphism in relation to active navigation. Studies about BDNF and hippocampal dependent processing in the context of navigation are often mechanistic in nature, looking at how BDNF influences learning and memory through BDNF release, neurogenesis, neuronal survival, and synaptic plasticity (Lu & Gottschalk, 2000; Poo, 2001 in Egan et al., 2003; Karnik et al., 2010). BDNF and navigation studies have focussed on BDNF release (Egan et al., 2003; Chaieb et al, 2014), demonstrating that individuals who carry either one or two BDNF met alleles (met carriers) are thought to generate fewer neurotrophins in response to hippocampal dependent activity (e.g. Kleim et al., 2006; Notaras et al., 2015; Lövdén et al., 2011) and have lower hippocampal volumes as a result (Hajek et al., 2012; Joffe et al., 2009; Szeszko et al., 2005). Differences in activity-dependent BDNF secretion are typically assessed at a cellular level using fluorescent microscopy and neuroimaging techniques (Egan et al., 2003; Perroud et al., 2008).

Reported differences in cognition and behaviour *as a result of disparity in BDNF release* between BDNF genotypes feature in a small but growing literature base. BDNF met carriers have been shown: to have a reluctance to explore novel environments (Chen et al., 2006) and

to have lower rates of hippocampal episodic learning and poorer declarative memory (Hariri et al., 2009; Hashimoto et al., 2008; Sanchez et al., 2011; Hansell et al., 2007; Kambeitz et al., 2012). BDNF has also been shown to interact with another gene to amplify the negative influence of the aging process on spatial working memory and executive function (Nagel et al., 2008). Colzato et al. (2011) found that BDNF valval homozygotes benefitted more from training than BDNF met carriers by demonstrating improvements in their dynamic attention (using 'wider fields of view'). Ceresa et al. (2010) observed that in cases of multiple sclerosis, BDNF met carriers demonstrated altered disengagement of the hippocampus on a static figure-based test of spatial working memory. Raz et al. (2009) reported that met carriers performed worse in comparing patterns of letters than valval homozygotes. Dennis et al. (2011) reported that met carriers exhibited increased MTL activation during both encoding and retrieval stages of item and relational memory tests, compared to non-carriers (but that reductions in cognitive performance observed in prior studies were not a ubiquitous effect associated with variants of the *BDNF val66met* genotype). Finally, Richter-Schmidinger et al. (2011) noted that BDNF met carriers performed significantly worse than valval homozygotes on an inventory of working memory tests, despite there being no differences in hippocampal volume or other measures of cognitive performance. Despite demonstrating notable differences in various elements of cognition and behaviour, none of these studies have explicitly demonstrated that BDNF met carriers perform worse in hippocampal dependent spatial processing or active navigation than the 70% of the Caucasian population not carrying the met allele (valval homozygotes).

There have only been two studies which have directly addressed differences in navigation behaviour between BDNF genotypes. Lövdén et al. (2011) studied differences in the activity-dependent secretion of hippocampal neurotrophin in response to navigation training between BDNF genotypes (n = 107). Banner et al. (2011) addressed differences between BDNF genotypes (n = 106) in spontaneous use of hippocampal dependent and *in*dependent strategies (i.e. use of either strategy when both were immediately available to participants).

7.1.3.1 BDNF AND HIPPOCAMPAL DEPENDENT ACTIVITY IN NAVIGATION (LÖVDÉN ET AL., 2011)

To take Lövdén et al. (2011) first, the study was important because it showed BDNF genotypes differing in their release of neurotrophins in response to hippocampal dependent activity *without* there being any concurrent performance differences between the genotypes. The 'activity' used in the experiment comprised of a four-month hippocampal dependent spatial training programme which required participants to walk through and learn the layout of several zoos. Participants were tested on their environmental knowledge of the zoos and were asked to draw maps of the zoo environments. Participants were also asked what strategies they think that they had used to learn the layout of the zoos and their neurotrophin levels were then measured using Magnetic Resonance Spectroscopy. The results indicated training-induced changes in Nacetyl-aspartate (NAA) were absent in carriers of the met allele. In valval homozygotes, training-related performance improvements were related to increases in NAA levels. However, it is important to note that BDNF groups (valvals versus valmets and metmets) did not differ statistically in baseline navigation performance (i.e. navigation performance levels prior to

training); nor in post-training navigation performance; nor in post-training map drawing performance; nor in the (egocentric or allocentric) navigation strategies they reported having used. The authors put forward that with lower BDNF secretion (such as is the case with BDNF met carriers) responses to hippocampal dependent activity "may require larger or more persistent changes in experiential demand" in order for them to materialise (Lövdén et al., 2011). Lövdén et al. (2011) describe the findings using a 'strategy account' which postulates that individuals of different BDNF genotypes may use spatial strategies that vary in the extent to which they require hippocampal involvement. More specifically, Lövdén et al. (2011) surmise that that,

..."valval homozygotes may have used hippocampal-dependent cognitive-map strategies to a greater extent, whereas BDNF met carriers may have relied more on cue-response strategies, which draw on, for example, the caudate nucleus (Hartley et al. 2003; Iaria et al. 2003)" (Lövdén et al., 2011).

Lövdén et al. (2011) also stated that an "important take-home message" for the role of BDNF in navigation and spatial processing was that *cognitive demands* can alter the concentrations of neurotrophins in the hippocampus and that BDNF genotype moderates these effects (Lövdén et al., 2011). The 'strategy account' and the concept of cognitive demand are both revisited in the hypotheses section and the discussion of this chapter.

7.3.1.2 BDNF AND STRATEGY USE IN NAVIGATION (BANNER ET AL., 2011)

The study by Banner et al. (2011) is highly relevant for this research as demonstrated how the multi memory systems involved in parallel processing of spatial information during navigation manifest in individuals' strategy use, and how visible this is (using neuroimaging techniques). The study also differentiated between hippocampal independent, egocentric 'stimulus-response' strategies (such as beacon strategy and associative cue strategy in the Alternative Route paradigm used in this study) and hippocampal, allocentric, 'spatial' (or configural) strategies. What is more, the study by Banner et al. (2011) is the only other known study to consider the influence of the BDNF gene (or indeed any gene) on when an individual is predisposed to a given strategy in a navigation task and whether this preference is liable to change in response to the challenge of that task.

Banner et al. (2011) investigated hippocampal dependent and hippocampal *in*dependent navigation strategy use between all three BDNF genotypes (valvals, valmets and metmets) and revealed some behavioural differences between BDNF genotypes which, again, were independent of actual performance differences. The task used by Banner et al. (2011) assessed whether participants (n = 106) spontaneously used an allocentric (spatial based) strategy in navigation, or an egocentric (response-based) strategy, and whether they were able to verbally identify which strategies they thought they had used.

The paradigm (the 4 / 8 Virtual Maze, see Chapter 4 Section 4.1.7) was based on the radial arms maze (an established paradigm in the animal literature) and incorporated distal cues (which facilitated spatial learning and allocentric processing) and local landmarks (which

supported response-learning and egocentric processing). Distal cues were removed at a specific point during the task. If participants' performance changed when the landmarks were removed, this indicated that their navigation strategy had been reliant on those cues, i.e. the strategy which was spontaneously spatial and allocentric. Banner et al. (2011) observed a significantly higher frequency of BDNF metmet homozygotes using egocentric response strategies than BDNF valval homozygotes, and a significantly higher frequency of valval homozygotes using allocentric spatial learning strategies (χ^2 =3.45, $p < 0.05$).

However, there were no significant differences in response or spatial learning strategies between heterozygotes and homozygotes (i.e. between metmet homozygotes and valmet heterozygotes, nor between valval homozygotes and valmet heterozygotes). This was interpreted as supporting previous studies (e.g. Hashimoto et al., 2008; Egan et al., 2003), which showed the effect of the met allele on hippocampus dependent memory as being dose-dependent. Banner et al. (2011) suggest there was a distinct bias for associative egocentric response-based spatial strategies in BDNF metmet homozygote, at the expense of allocentric (and hippocampal dependent*)* processing. Note, however, that there was no difference in errors on the 4 / 8 Virtual Maze task between the respective genotypes. In their concluding remarks, Banner et al. (2011) postulated that it is possible that stress plays an "intermediate modulatory role" between genotype and behaviour. Banner et al. (2011) suggested that being a BDNF valval homozygote may increase the likelihood of participants using a spatial rather than response strategy, even following stress exposure (this is on the basis that valval homozygotes benefit from increased BDNF expression and long-term potentiation in the hippocampus).

Finally, one last study was reviewed which was pertinent to this research; a 2007 rodent study by Heldt et al. They observed that deleting the BDNF gene in rodents' hippocampi impaired spatial learning in the Morris Water Maze (MWM). The rodents were tested for their spatial learning ability using the MWM after five training sessions spaced over 5 separate days. There was a significant interaction between learning phase and group, and only a significant learning effect for non knock-out mice, F (4, 52) = 14.36, p <0.001. Animals with BDNF deletions (knock-out mice) also showed significantly reduced extinction of conditioned fear. Whilst based on deleting genes rather than genotyping populations, Heldt et al.'s (2007) mouse study is the only study to suggest that cognitive spatial processing deficits and impairment in managing trauma may be directly related to BDNF gene expression in the hippocampus.

To summarise, research examining the role of the BDNF gene in navigation has been very limited and produced mixed findings with only limited support for a role in navigation (e.g. Egan et al., 2003; Chen et al., 2006; Colzato et al., 2011). This study therefore seeks to examine this relationship further by examining the claims made in recent relevant research (Banner et al., 2011; Lövdén et al., 2011) that BDNF met carriers may differ in their application of allocentric spatial strategies to navigation tasks.

Hypotheses and predictions

(i) 'The allelic frequency of BDNF met will be higher in those with PTSD compared to those with no PTSD after trauma exposure.' This is based on the findings by Zhang et al. (2014). *Note that Zhang et al. attributed their findings to controlling for environmental conditions using a homogenous military sample and this was not replicated in the current study.* The DV for this prediction was allelic frequency of BDNF.

(ii) 'The valval homozygote genotype will be significantly more frequent amongst those without exaggerated startle (*n* = 62) compared to those without exaggerated startle (*n* = 29).' This is based on the study by Zhang et al. (2014).

(iii) 'Egocentric strategy will be used at the expense of allocentric ('configural') strategy in BDNF met carriers over the course of the AR paradigm'. This refers to Banner et al.'s (2011) findings that the respective BDNF genotypes differed in their spontaneous use of two parallel strategies (allocentric versus egocentric) which were immediately available to participants for navigation. The DVs for this prediction comprise mean use of associative cue over the AR paradigm (and/ or beacon strategy, and compared to configural strategy).

(iv) Valval homozygotes will show higher self-reported confidence in allocentric navigation measured via questionnaires than met carriers, and higher allocentric confidence in valval homozygotes will correlate with allocentric strategy use. This is based on Lövdén et al.'s (2011) 'strategy account' and the concept of cognitive demand, whereby valval homozygotes are more likely to apply hippocampal dependent strategies on demand than met carriers. The hypothesis is also based on findings from Chapter 5 which showed that self-reported allocentric confidence correlated more with allocentric navigation performance than egocentric confidence did with egocentric performance. The DVs for this prediction comprise total score on allocentric questions from the QSR (QSR_{survey} score) different direction trial performance over the 6 blocks of the AR paradigm.

7.2 METHODS

7.2.1 Participants

One hundred and fifty participants were recruited as follows:

(i) Bournemouth University (*n* = 81) including staff, students, and members of the public through the Psychology Research Volunteer Scheme.

(ii) The Intensive Psychotherapy Treatment Service (IPTS) at Dorset NHS (*n* = 9).

(iii) Dorset and Cambridgeshire Police (*n* = 26).

(iv) Combat Stress (a military charity) PTSD Rehabilitation course at Tyrwhitt House Treatment Centre, Leatherhead, Surrey (*n* = 25).

(v) British Military Fitness and Forces Fit military fitness programmes (*n* = 2).

(vi) University College London (*n* = 1) through the participant pool from a previous NHS study (NHS ref: 21YHJ0044, later to be published as Smith et al., 2015)

Participants were offered a £10 financial reimbursement for their time. Those recruited through Combat Stress received £20 reimbursement to cover their additional travel costs. The study was approved by: the BU Graduate School Ethics Board; the Combat Stress Research Ethics Committee; and the NHS South West (Cornwall and Plymouth) National Research Ethics Service (NRES).

The total sample population (*n* = 150) is comparable in size to similar 'gene x environment' studies in the field (Zhang et al., 2014; Hemmings et al., 2009; 2014; and Gatt et al., 2009)[32]. Table 7.2.1 demonstrates that the DNA profile of the sample population for this study is comparable to the expected profile of the wider population (Frielingsdorf et al., 2010; Petreyshen et al., 2010). These proportions are set at an estimated 70% for valval homozygotes, 26% for valmets heterozygotes and 4% for metmet homozygotes. A Chi-square test revealed that there was no significant difference between observed and expected populations, χ^2 (2, 150) = 0.37, *p* = 0 .83 (see Petryshen et al., 2010; Zhang et al., 2014; Hemmings et al., 2009; 2014; and Gatt et al., 2009; Van de Heuvel et al., 2016).

Table 7.2.1: Observed and expected BDNF populations in study (n = 150).

BDNF genotype	**Valval**	**Valmet**	Metmet
Observed sample population (n)	104	39	7
Expected population (n)	105	36	9

As explained in the Methodology chapter, the BDNF metmet homozygote is carried by less than 4% of the population and in this study the sample size of this group was n = 7. Studies of this sample size (where there are fewer than ten individuals of the metmet genotype) typically

[32] Zhang et al. (2014) tested 49 Special Operation veterans with PTSD, and 491 without. Hemmings et al (2014) used a sample of 134 OCD patients and 188 controls when looking at childhood trauma. Hemmings et al. (2009) studied 150 'at risk' (many trauma exposed) participants and found statistical differences in PTSD development on the basis of BDNF genotype and another candidate gene, DRD2 Taq1A. Gatt et al. (2009) analysed brain imaging data from only 89 participants and found statistical differences between BDNF genotypes.

combine valmet and metmet groups together (e.g. Egan et al., 2003; Hariri et al., 2003; Pezawas et al., 2004; Dempster et al., 2005; Van de Heuvel et al., 2016). This was the approach taken in this study. Essentially, the experimental groups therefore comprised valval homozygotes (*n* = 104) and met carriers (*n* = 46). The implications of this aggregation are covered in more detail in the Discussion section 7.4.

7.2.2 Demographic and clinical covariates

Demographic and clinical variables that were shown to be relevant to the assessment of group differences in navigation behaviour in previous chapters included: age, gender, pain, the taking of Selective Serotonin Reuptake Inhibitors (SSRIs), benzodiazepines or opiates, and sleep disturbance. These were all controlled for in the studies presented in Chapter 7 and their role considered when reviewing BDNF literature.

Table 7.2.2 presents the demographic and clinical characteristics of the sample population (*n* = 150) and demonstrates that there were no significant differences between BDNF genotypes apart from with gender, where males constituted 'met carriers' nearly two-fold over females. Thus gender needs to be considered further in analysis.

Table 7.2.2: Descriptive statistics for demographic and clinical data: means and standard deviations by BDNF demonstrating an over-representation of males in met carriers in Chapter 7. PSQI-A (The Pittsburgh Sleep Quality Index-Addendum for PSTD), NRS: Numerical Rating Scale.

Demographic or clinical factor		**Valval homozygotes (*n* = 104)**	**Met carriers (*n* = 46)**	**Group comparison**
Age in years *(M, SD)*		36.8 *SD* ± 10.6	39.0 *SD* ± 10.0	*t* (148) = -1.2, *p* = 0.23
Gender	Male	*n* = 50	*n* = 31	$\chi 2$ (149) = 4.49 *p* = 0.03*
	Female	*n* = 54	*n* = 15	
Currently taking **SSRIs**		6.5% (*n* = 18)	17.3% (*n* = 3)	$\chi 2$ (147) = 2.98, *p* = 0.08
Currently taking **Benzodiazopines or opiates**		9.6% (*n* = 10)	<0.1% (*n* = 6)	$\chi 2$ (147) = 0.39, *p* = 0.53
Sleep Quality (PSQI-A score, *M, SD*)		3.52 *SD* ± 5.5	2.63 *SD* ± 4.59	*t* (133) = 0.92, *p* = 0.36
Pain (NRS score *M, SD*)		1.63 *SD* ± 2.95	1.15 *SD* ± 2.52	*t* (148) = 0.95, *p* = 0.35

Age has been shown to have a negative impact on hippocampal dependent spatial memory, (e.g. Smith et al., 2015; Daugherty et al., 2015; Rosenweig & Barnes, 2003; Raz et al., 2009; Moffat et al., 2001, 2009; Wiener et al., 2012, 2013; Driscoll et al., 2005; Rodgers et al., 2012). Findings from Chapter 4 of this study, however, did not show a unique contribution of age to either allocentric performance on the AR paradigm or configural (allocentric) strategy use. Chapter 5 showed that in healthy populations, while self-reported navigation confidence tends to increase with age, actual navigation performance worsens, which supported previous observations in the literature by De Beni et al. (2006) and Borella et al. (2014). Increasing age has also been associated with reduced hippocampal activation in PTSD (Carrion et al., 2010)

and in one case report, with the efficacy of trauma processing interventions (Duax et al., 2013). With regard to cases of PTSD in Chapter 6, age was not significantly associated with self-reported confidence and performance in navigation as it was in the healthy non-PTSD population in Chapter 5. Finally, age has also been studied in relation to BDNF and hippocampal volume (Erickson et al., 2010) and a study by Sanchez et al. (2011) showed that the BDNF met allele interacted with age to negatively affect performance on a navigation-related paradigm (a flight simulator). Given this complex interaction between age, navigation, trauma and BDNF in previous studies and earlier findings, age would need to be considered in analysis of any navigation performance related differences between BDNF genotypes.

In Chapter 4 of this study, gender featured as a contributing factor to one measure of allocentric performance in the AR paradigm but gender did not persist as a significant influence in post-hoc t-tests. Chapter 5 controlled for gender and demonstrated that being male positively influenced self-reported confidence in navigation, but not performance. These findings were supported by a literature which showed males tending to self-report higher confidence without demonstrating higher performance (e.g. Lawton et al., 1994; Schmitzer-Torbert, 2007; Münzer & Stahl, 2011; Menghetti et al., 2010). The only mention in the BDNF literature about the role of gender was in Notaras et al.'s (2015) review which reported on a Swedish study in which the BDNF met allele was overrepresented with depression among females, but selectively among those with a history of childhood adversity (Lavebratt et al., 2010). Whilst neither the navigation literature nor previous findings from Chapters 4 and 5 suggested gender needed to be controlled for in Chapter 7, the over-representation of males amongst BDNF met carriers in Chapter 7 was such that gender needed to be addressed in analysis.

In terms of clinical factors, Chapter 4 revealed that pain contributed 2.7% of the explained variance in performance in allocentric processing on the Alternative Route paradigm. In the animal literature, pain has shown to effect spatial memory in rats (Cardoso-Cruz et al., 2013) and to be related to low levels of BDNF (Duric & McCarson, 2005, 2006). Thus pain needs to be considered in analysis of any performance related differences between BDNF genotypes.

The taking of Selective Serotonin Reuptake Inhibitors (SSRIs) did not explain a significant amount of variance in performance in those studies reported in Chapter 4 but it has been linked to lower BDNF secretion in 'met' carrying BDNF genotypes (Anacker et al., 2011; Bath et al., 2012, Autry et al., 2012) and to hippocampal neurogenesis and plasticity (Anacker et al., 2011; Bath et al., 2012; Engel et al., 2013; Luo et al., 2005; Pu et al., 2005). Thus, taking of SSRIs would need to be considered in analysis of any performance-related differences between BDNF genotypes.

Sleep disturbance has been shown to affect hippocampal dependent processing in cases of PTSD (Tempesta et al., 2011) but did not explain a significant amount of variance in performance in Chapter 4 and therefore was not analysed further in relation to BDNF genotypes.

7.2.3 Procedure

Informed consent was sought from all participants (*n* = 150).

DNA was collected using self-administered saliva sample Orangene™ DNA kits (produced by DNA Genotek, Ottawa, Canada, ISO 13485:2003). Participants recruited by Bournemouth University (BU) through University College London (*n* = 13) were sent the saliva kits by mail. One hundred and thirty seven participants provided their sample during their visit to BU to undertake the lab-based navigation tasks. The process was simple and required participants to spit into a test tube which was sealed by the participant. The researcher then anonymously coded the samples and stored at Bournemouth University until the minimum batch size of samples (*n* = 50) was collated to be posted to DNA Genotek extraction services in the United States. Genomic DNA data was emailed back to Bournemouth University in the form of an Excel spreadsheet with the depersonalised codes and genotype results alongside (i.e. whether the participant was 'valval', 'valmet' or 'metmet').

Participants had completed a screen for trauma exposure using the Life Events Checklist (LEC, Blake et al., 1995). Those who had self-reported trauma exposure were given the Post-Traumatic Stress Disorder Diagnostic Scale (PDS, Foa et al., 1995) to ascertain the present day impact of the prior trauma. Those who self-reported PDS scores below the threshold of 21 were allocated to the *Trauma Exposed No PTSD* group.

Participants completed clinical measures of depression using the Beck Depression Inventory (BDI, Beck et al., 1996), pain using the standard Numerical Rating Scale (NRS Jensen et al., 1986) and sleep, using the Pittsburg Sleep Quality Index Addendum for PTSD (PSQI-A, Germain et al., 2005).

Participants then undertook the Four Mountains task (Hartley et al., 2007) which took 10 minutes to complete. Participants were given a series of three practice trials to familiarise them with the layout of the test and to ensure that instructions were understood.

The participants then undertook the AR which took 24 minutes to complete. Prior to the task, participants were given written instructions for the Alternative Route paradigm (Wiener et al., 2013) which were summarised verbally after being read by the participants. They were also given a demonstration of the task showing them how to use the controls and advise on details about timing.

7.2.4 Materials

7.2.3.1 NAVIGATION TASKS

The Four Mountains task (Hartley et al., 2007) is a static topographic (allocentric) test of spatial memory (Hartley et al., 2002; Hartley & Harlow, 2012; Bird et al., 2010; see Chapter 3 for full details of this test). The Alternative Route (AR) paradigm was introduced by Wiener et al. (2013) as a novel route-learning paradigm to test allocentric and egocentric navigation performance and to identify preferences (biases) for different navigation (spatial processing) strategies; for full details see Chapter 4, Section 4.1.8). The paradigm is employed in the same way in this chapter as it was for Chapter 4.

7.2.3.2 NAVIGATION QUESTIONNAIRES

As previously, three navigation questionnaires were used in the experiment: the Santa Barbara Sense of Direction (SBSOD) by Hegarty et al. (2002); the Questionnaire of Spatial Representation (QSR) by Pazzaglia & De Beni (2001); and the "Fragebogen Räumliche Strategien" (FRS) by Münzer & Hölscher (2011) and the same scores from the questionnaires were used to examine navigation behaviour (viz. the overall SBSOD score, the QSR_{route} (egocentric questions), the QSR_{survey} (allocentric questions), the FRS global egocentric and the FRS survey (allocentric) questions scores.

Pearson's correlation coefficients were calculated between questionnaire scores and measures of navigation performance on the Four Mountains task and the AR paradigm. This produced a score of self-reported confidence in navigation and provided an indication of the degree to which an individual's perception of their own navigation competence was accurate.

7.3 RESULTS

All statistical analyses were performed using SPSS version 22 (SPSS, IBM Corp. in Armonk, NY).

Analysis of navigation performance and strategy use in Chapter 7 between BDNF genotypes (valval homozygotes, met carriers) mirrors that of the analysis approach taken in Chapters 3 and 4 between the experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD,* PTSD). The influence of the BDNF gene on the relationship between trauma and navigation is investigated through between group analyses using BDNF genotypes (valval homozygotes vs met carriers).

PTSD is in effect controlled for in the analysis because there were no significant differences in PTSD prevalence or severity between BDNF groups (this will be explained further in the results, Section 7.3.3). Analysis of PTSD symptom severity and startle scores was undertaken using only those participants with clinical or probable levels of PTSD (n = 57), i.e. with a score of < 20 on the PDS (Foa et al., 1995).

7.3.1 BDNF and PTSD prevalence and severity

PTSD prevalence was investigated by comparing expected (Frielingsdorf et al., 2010; Petreyshen et al., 2010) and observed BDNF frequencies across trauma groups.
Table 7.3.1 illustrates that observed and expected prevalence BDNF populations (valval homozygotes and met carriers) were comparable to the respective experimental groups.

Table 7.3.1: Observed and expected (% and n) populations by BDNF genotype (valval homozygotes and met carriers) amongst Trauma Unexposed, Trauma Exposed No PTSD and PTSD groups.

Experimental group		***Trauma Unexposed***		***Trauma Exposed No PTSD***		***PTSD***	
Valvals	Observed	66%	*n* = 22	65%	*n* = 39	75%	*n* = 43
	Expected	70%	*n* = 23	70%	*n* = 42	70%	*n* = 40
Met carriers	Observed	27%	*n* = 11	29%	*n* = 21	28%	*n* = 14
	Expected	30%	*n* = 10	30%	*n* = 18	30%	*n* = 17

There were no significant differences between the observed BDNF genotypes frequencies and expected frequencies between the experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD,* and *PTSD*) for either the homozygous *valval* group, χ^2 = 0.24, *p* = 0 .88 or the combined 'met carrying' group, χ^2 = 0.04, *p* = 0.98. The observed frequencies in the sample therefore did not support findings by Zhang et al. (2014) that carrying the met allele (i.e. being BDNF genotype valmet or metmet) is more common in those with probable PTSD.
PTSD severity in those participants with probable or clinical PTSD (*n* = 56) was compared between BDNF *valval homozygotes* and *met carriers*. As explained in Section 7.1.2, where sample sizes of metmet homozygotes *n* <10, then metmet homozygotes are analysed with valmet heterozygotes to form one group of 'met carriers' (e.g. see Pezewas et al., 2004; Dempster et al., 2005; etc.). An Independent t-test revealed there were no significant differences in PDS scores between valval homozygotes and met carriers (Foa et al., 1995), *t* (54) = -1.23, *p* = 0.23.

7.3.2 BDNF and the startle symptom in PTSD

Startle scores were compared between *valval homozygotes* and *met carriers* in the same way as PTSD severity, only selecting a single item on the PDS (Foa et al., 1995) scale: question 17. Question 17 asks participants how often participants felt that they were "being jumpy or easily startled, for example, when someone walks up behind [them]", rated on a scale of 0 to 3 (where 0 = never, and 3 = more than five times in a week). A one-way ANOVA did not reveal significant between-group (BDNF *met carriers* versus *valval* homozygotes) differences in scores on this item in those participants with PTSD, *F* (1, 47) = 0.51, *p* = 0.48. *Met carriers* (n = 13) had a mean PTSD startle score of 2.38 (*SD* ± 0.77) and *valvals* (n = 36) had a mean PTSD startle score of 2.40 (*SD* ± 1.15).

Zhang et al. (2013) grouped participants by startle score being 'exaggerated' or 'not exaggerated' and then looked at BDNF populations within the two groups. They showed that the frequency of valvals was significantly higher in the non-exaggerated startle group compared to the exaggerated startle group. The publication by Zhang et al. (2014) did not state the threshold by which a startle response was considered to be 'exaggerated'. In this study, participants were

allocated to an 'exaggerated startle group' if they reported a PDS score of 3 (the highest level score on the PDS scale) on question 17. On this basis, this study does not replicate findings by Zhang et al. (2014). In the 'no exaggerated startle' group (*n* = 62) BDNF *valval homozygotes* represented 67.7 % of the population (*n* = 42) which is in line with the representation of the genotype expected in the wider population (i.e. 70%, Petreyshen et al., 2010). Chi- square analysis showed no significant association between BDNF genotype and startle status (exaggerated vs. non exaggerated), $\chi 2 = 0.62$, p = 0.43.

7.3.3 Controlling for PTSD

Prevalence and severity of PTSD did not differ between valval homozygotes and met carriers. This effectively controlled for trauma exposure in the analysis of the influence of BDNF over navigation behaviour (i.e. spatial processing, active egocentric and allocentric navigation performance and self-reported confidence). This is because across the sample those with the respective BDNF genotypes did not differ in their relative experiences of PTSD and therefore PTSD could not have an additional effect on the relationship between BDNF and spatial processing or active navigation. As a precautionary measure, all the analyses undertaken in Chapter 7 was repeated, entering experimental trauma group (*Trauma Unexposed, Trauma Exposed No PTSD* and *PTSD*) as a covariate in the analysis. This made no difference to the findings.

7.3.4 BDNF and spatial processing (The Four Mountains task)

An independent samples t-test between BDNF *valval homozygotes* (*n* = 101) and *met carriers* (*n* = 46) showed no significant differences in overall Four Mountains score (out of 15), with *valval homozygotes* scoring on average 10.9 (*SD* ± 2.44) and *met carriers* scoring on average 10.6 (*SD* ± 2.64), *t* (145) = 1.17, *p* = 0.25).

7.3.5 BDNF and navigation performance (The Alternative Route paradigm)

Differences between BDNF *valval homozygotes* (*n* = 94) and *met carriers* (*n* = 44) in egocentric AR performance (mean same direction trial score) and then allocentric performance (mean different direction score) was assessed by replicating the analysis undertaken in Chapter 4.

7.3.5.1 EGOCENTRIC PERFORMANCE

A repeated measures 2 x 6 ANOVA with the between factor *BDNF group* (valval homozygotes versus met carriers) and the within factor *block* (1 to 6) was used with Bonferonni to correct for multiplicity (or family wise error rates). The ANOVA did not reveal a significant main effects of block, F (4.49, 138) = 0.90, p = 0.48, $\eta_p^2 < 0.01$, or BDNF group, F (1, 138) = 0.99, p = 0.32, $\eta_p^2 < 0.01$, but there was a significant group x block interaction, F (4.49, 138) = 2.48, p = 0.03, $\eta_p^2 = 0.02$. To investigate the *BDNF group* (valval homozygotes and met carriers) x block interaction, independent t-tests were conducted for each block. Figure 7.3.5.1 below shows a different pattern of egocentric and allocentric performance between the BDNF genotypes across the 6 blocks and a significant difference in egocentric performance the final block as a function BDNF.

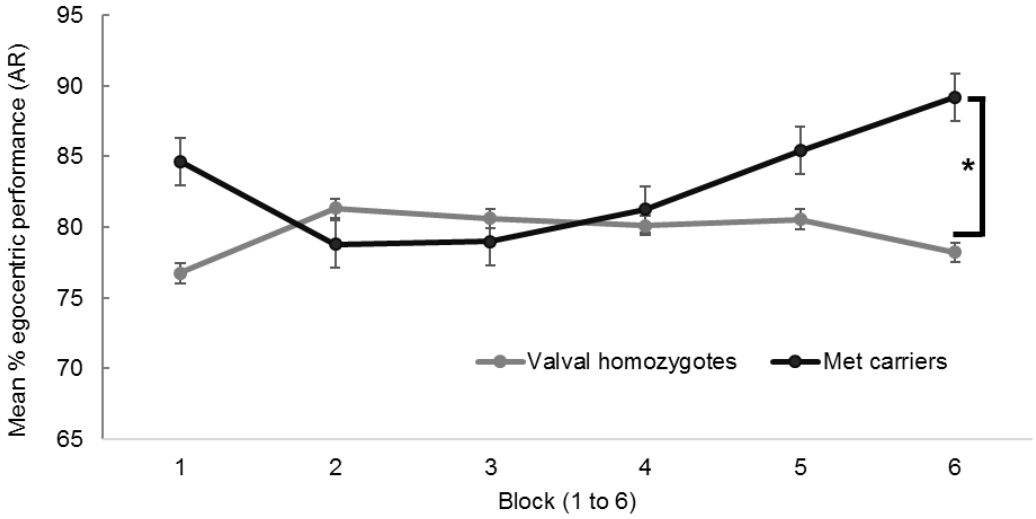


Figure 7.3.5.1: Mean egocentric performance (same direction trials) on the AR paradigm by block between BDNF valval homozygotes and met carriers (n = 146) with standard error bars and showing the significant difference in egocentric perfromance by block 6, $p < .05$.

Egocentric performance did not differ significantly as a function of BDNF group for blocks 1 to 5 (all $p > 0.05$). However, with Bonferroni corrections, BDNF *met carriers* performed better in block 6 as compared to *valval homozygotes* (78% SD ± 2.8% vs. 89% SD ± 17%), t (138) = 5.65, $p = 0.02$). These findings indicate that BDNF genotypes may differ in their application of spatial processing in active navigation and that carrying the met allele may be advantageous for egocentric processing performance. This may support Lövdén et al.'s (2011) 'strategy account' (explained in Section 7.1.3) which suggests that the BDNF met carriers may inherently rely on egocentric processing in preference to an allocentric processing.

7.5.3.2 ALLOCENTRIC PERFORMANCE

A repeated measures 2 x 6 ANOVA with the between factor *BDNF group* (valval homozygotes versus met carriers) and the within factor *block* (1 to 6) revealed a significant main effect of block, F (4.07, 138) = 27.2, $p < 0.01$, $\eta_p^2 = 0.17$, but no significant main effect of BDNF group, F (1, 138) = 2.20, $p = 0.14$, $\eta_p^2 = 0.02$, and no significant interaction F (4.07, 138) = 1.71, $p = 0.14$, $\eta_p^2 = 0.01$. Specifically, performance increased over the experimental sessions (block 1 to 6) from 13.5% ± 2.0% (*SD*) in block 1 to 37.8% ± 3.0% (*SD*) in block 6.

7.3.6 BDNF and navigation strategy (The Alternative Route paradigm)

In Chapter 4, strategy use over the six blocks of the AR paradigm was compared between trauma groups. Here this analysis was replicated but this time it used BDNF group as the between group factor (i.e. with valval homozygotes versus met carriers). As with Chapter 4, separate 6 x 3 repeated measures ANOVAs were undertaken for each strategy (configural, associative cue and beacon) with the within factor experimental sessions (blocks 1 to 6) and the between factor *BDNF group* (valval homozygotes versus met carrier genotypes).

For **configural strategy** use, there was a significant main effect of block, F (4.23, 136) = 18.5, p < 0.01, η_p^2 = 0.12. Configural strategy use increased from 10% ± 2.0% (*SD*) in block 1 to 38% ± 3.0% (*SD*) in block 6. There was no significant interaction between block and BDNF group, F (4.23, 136) = 1.26, p = 0.28, η_p^2 < 0.01 and no significant main effect of BDNF group, F (1, 136) = 1.05, p = 0.31, η_p^2 = 0.08.

There may be value in observing a visual difference in BDNF met carriers' configural strategy use mid-way through the AR paradigm (between blocks 3 and 4 in Figure 7.3.6b). Whilst there is no statistically significant interaction between BDNF group and block, there is a possibility that this (purely visual) change in strategy use may be reflective of a recent proposition in BDNF literature. The proposition is that, unprompted to use allocentric strategies, BDNF met carriers experience a delay in their application of allocentric processing in navigation due to differences in activity-dependent BDNF release between genotypes (Banner et al., 2011; Lövdén et al., 2011).

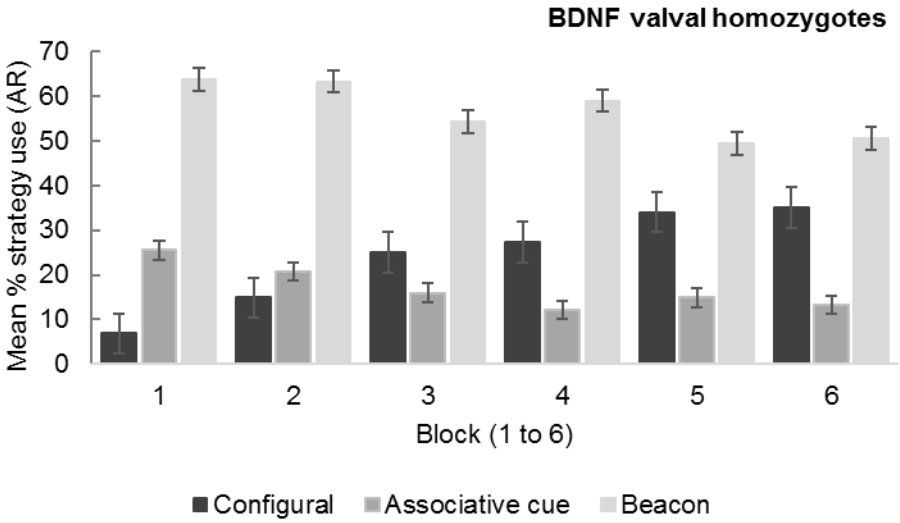


Figure 7.3.6a: Mean strategy use by block (1 to 6) in valval BDNF homozygotes (n = 102) with standard error bars

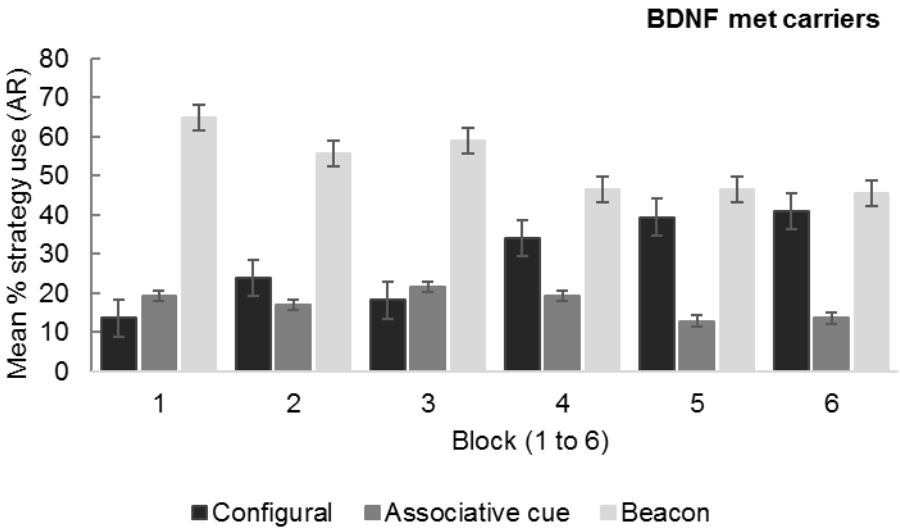


Figure 7.3.6b: Mean strategy use by block (1 to 6) in met carrying BDNF genotypes (n = 44) with stnadard error bars showing a visual increase in configural strategy midway through the AR task between block 3 and 4 (albeit there was no statistically significant interaction between BDNF group and block).

For **associative cue strategy** use, there was a near significant main effect of block, F (4.66, 136) = 2.22, p= 0.06, η_p^2 < 0.01. Associative cue strategy use decreased from 22% ± 3.0% (*SD*) in block 1 to 13.5% ± 3.0% (*SD*) in block 6. There was no significant interaction between block and group, F (4.66, 136) = 1.30, p = 0.26, η_p^2 = 0.09. There was no significant main effect of BDNF group, F (1, 136) <0.01, p = 0.95, η_p^2 <0.01. For **beacon strategy** use, there was a significant main effect of block, F (4.23, 136) = 4.96, p <0.01, η_p^2 = 0.35. Beacon strategy use decreased from 64% ± 3.0% (*SD*) in block 1 to 48% ± 4.0% (*SD*) in block 6. There was no significant interaction between block and group, F (4.28, 136) = 1.11, p = 0.35, η_p^2 = 0.08. There was no significant main effect of BDNF group, F (1, 136) = 0.51, p = 0.48, η_p^2 <0.01.

Taken together, these results showed no statistically significant influence of BDNF on strategy use across the AR paradigm.

7.3.7 BDNF and self-reported navigation confidence

To explore if there was any influence of BDNF genotype on self-reported navigation confidence, independent samples t-tests were undertaken between the BDNF valval homozygotes and BDNF met carriers (n = 140) for the different questionnaires. The results are summarised in Figure 7.3.7a and Table 7.3.7.b. Self-reported navigation confidence was numerically higher in BDNF met carriers than it was in valval homozygotes in *all questionnaires* and this was particularly notable in questions based on allocentric processing. Confidence in general 'Sense of Direction' (SBSOD score) was significantly higher in BDNF met carriers in a one-tailed t-test, t (140) = -1.76, p = 0.04. This is a new finding for BDNF and navigation literature. However, the differences were no longer significant once Bonferroni corrections for multiple comparisons were applied, F (1, 140) = 3.12, p = 0.08. Given that the statistical significance of these findings did not survive alpha level corrections for multiple comparisons, they should be treated with caution (Mayers, 2013; Lavrakas, 2008).

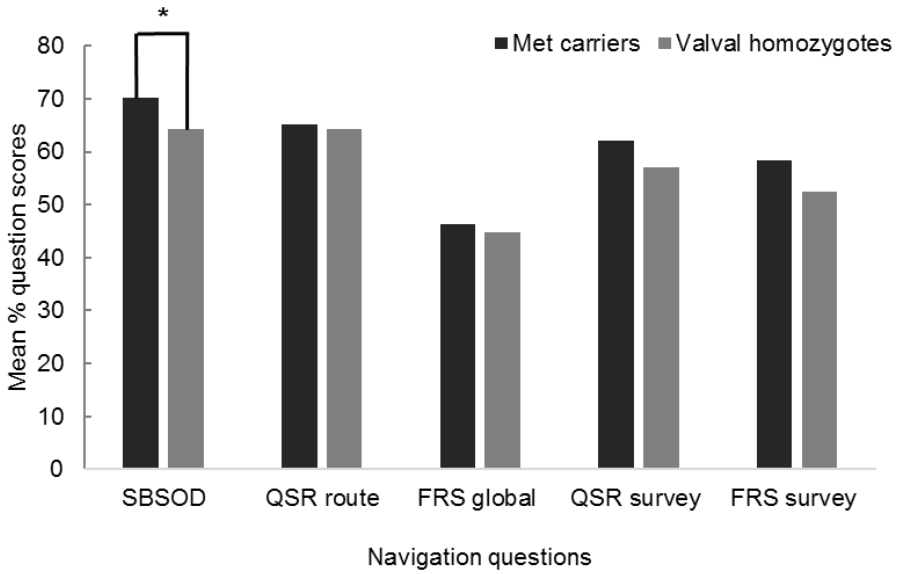


Figure 7.3.7a: % Scores of self-reported navigation confidence using the SBSOD, the QSR and the FRS in BDNF met carriers and valval homozygotes (n = 140).

Table 7.3.7b: Descriptive statistics for navigation questionnaire data (SBSOD, QSR and the FRS) between BDNF genotypes *valval homozygotes* and *met carriers* (*n* = 140).

Navigation questionnaire[33]	BNDF genotype	*n*	Mean total score (%)	*SD*
SBSOD	Valval homozygote	99	64.3	± 19.1
	Met carrier	43	70.1	± 15.0
QSRroute	Valval homozygote	102	64.3	± 20.1
	Met carrier	45	65.1	± 19.7
FRS egocentric	Valval homozygote	102	44.7	± 14.4
	Met carrier	45	46.3	± 12.7
QSRsurvey	Valval homozygote	101	57.1	± 21.0
	Met carrier	45	62.0	± 23.3
FRS allocentric	Valval homozygote	102	52.5	± 23.0
	Met carrier	45	58.4	± 21.5

To explore whether there were associations between BDNF genotype and self-reported navigation confidence and performance, correlational analyses (Pearson's Product Moment) were conducted separately for BDNF valval homozygotes (see Table 7.3.7c) and BDNF met carrying genotypes (see table 7.3.7d). Allocentric performance correlated with self-reported confidence *only* in *valval homozygotes*, but *not in met carriers*.

In both BDNF groups, gender affected self-reported confidence, but not performance (with males self-reporting higher confidence).

Table 7.3.7c: Pearson's correlations (r) between navigation questionnaires (SBSOD, QSR, FRS, gender and egocentric, allocentric and overall measures on the Alternative Route paradigm and Four Mountains score in valval BDNF genotypes (*n* = 102), $p < 0.01$**, $p < 0.05$*.

BDNF valval homozygotes (*n* = 102)	**Four Mountains**	**Overall (AR)**	**Egocentric (AR)**	**Allocentric (AR)**	**Gender**
SBSOD	0.12	0.12	<-0.01	0.26*	-0.32**
QSR_{route} (egocentric)	0.10	0.03	0.03	0.22*	-0.87
FRS global (egocentric)	0.09	0.15	<0.01	0.17	-0.25*
QSR_{survey} (allocentric)	0.18	0.05	0.02	0.28**	-0.29**
FRS survey (allocentric)	0.12	-0.02	-0.11	0.14	-0.30**
Gender	-0.05	0.12	0.10	0.11	-

[33] The questionnaires comprised: the Santa Barbara Sense of Direction (SBSOD; Hegarty et al., (2002); the Questionnaire of Spatial Representation (QSR; Pazzaglia & De Beni (2001); and the Fragebogen Räumliche Strategien" (FRS, i.e., the 'questionnaire on spatial strategies'; Münzer & Hölscher, (2011).

Table 7.3.7d Pearson's correlations (r) between navigation questionnaires (SBSOD, QSR, FRS, gender and egocentric, allocentric and overall measures on the Alternative Route paradigm and Four Mountains score in met carrying BDNF genotypes (n = 45), $p < 0.01$**, $p < 0.05$*.

BDNF met carriers *(n* = 45)	**Four Mountains**	**Overall (AR)**	**Egocentric (AR)**	**Allocentric (AR)**	**Gender**
SBSOD	0.20	0.12	0.20	0.05	-0.17
QSR_{route} (egocentric)	-0.12	0.09	0.14	-0.13	-0.28
FRS global (egocentric)	0.05	0.03	0.04	-0.11	-0.38**
QSR_{survey} (allocentric)	-0.14	0.08	0.02	0.03	-0.35*
FRS survey (allocentric)	<0.01	0.18	0.13	0.16	-0.37*
Gender	0.07	0.07	0.15	0.08	-

7.4 DISCUSSION

Summary

The study did not find higher prevalence or increased severity of (diagnosed or probable) PTSD (or of startle response with PTSD) in BDNF met carrying genotypes as compared to valval homozygotes in the sample population (which has not controlled for environmental conditions of trauma exposure and trauma processing opportunities). The proportion of BDNF genotypes with exaggerated startle and without exaggerated startle were also comparable.

BDNF genotypes (met carriers vs non-met carriers) did not differ in spatial processing in perspective taking (the Four Mountains task) or allocentric performance in active navigation (in the AR paradigm). BDNF met carriers showed a different pattern of egocentric performance over the six blocks of the AR paradigm and some advantage over valval homozygotes in final egocentric performance in the last block.

There was no statistically significant interaction between BDNF genotype (met carriers vs non-met carriers) and strategy use over the AR paradigm. However, a visual inspection of the data suggests that BDNF met carriers presented a marked increase in allocentric strategy use mid-way through the task, compared to valval homozygotes who appeared to apply allocentric strategy more incrementally over the course of the task.

Contrary to predictions, individuals who were BDNF valval homozygotes did not self-report higher allocentric navigation confidence than met carriers; and instead, BDNF *met carriers* consistently showed numerically higher levels of self-reported navigation confidence across a range of measures.

BDNF genotype predicted correlations between self-reported navigation confidence and navigation performance. Specifically, it was only in valval homozygous individuals that greater confidence manifested in better allocentric navigation performance.

7.4.1 BDNF and PTSD prevalence

In line with the majority of previous studies, there were no demonstrable differences in rates and severity of PTSD as a function of BDNF genotypes in this sample (*n* = 150). This could be simply be because, despite extensive research into the relationship between BDNF and PTSD that has been undertaken to date (e.g. Notaras et al., 2015; Wang, 2015; Miller & Wiener, 2014) there may be no such relationship. Another possibility, and that which is proposed in this thesis, is that the relationship between BDNF and PTSD is not direct, and is in fact influenced by another component: environmental conditions of trauma (in terms of the nature and timing of trauma exposure and the capacity that individuals have had to process it).

By way of explanation, there has only been one study that has established a direct relationship between the BDNF gene and PTSD: that by Zhang et al. (2014). Zhang et al. (2014) reflected that the reason that their latter 2014 study had produced findings which demonstrated that BDNF influenced PTSD prevalence and severity of a key symptom (exaggerated startle), compared to a former study undertaken in 2006 which did not produce such findings) was due to the trauma-controlled conditions of latter sample population.

In their former study in 2006, Zhang et al. (2006) recruited their PTSD sample population from a public health service. They did not report any attempt to control for whether the original trauma event had been acute or chronic (repeated) or whether participants had accessed or received any treatment. In the latter study reported in 2014, Zhang et al. (2014) used a different approach. They recruited participants with *CR*-PTSD from a sample population who were all active serving Special Operations forces personnel in the US military. This sample population were more homogenous in terms of both the source of their trauma exposure and the access they may have had to trauma processing interventions. That is to say, the environmental conditions of their trauma was more controlled within the sample. What is more, it may also be reasonable to speculate that the 2014 participants in active military service may been further *depleted* in the hippocampal resources (Vasterling & Brewin, 2005) available to them for trauma processing, given that hippocampus resources may well have been being used in their line of work, which is likely to have demanded a high degree of navigation aptitude (as explained in Chapter 6, see Section 6.1.2). Therefore, the more controlled environmental conditions of the military may have magnified the disadvantage to PTSD of carrying the met allele of the BDNF genotype. Zhang and colleagues do argue that the profile of the 2014 study sample population would have influenced the visibility of genetic influences in PTSD and would likely explain the difference in findings compared to those in 2006.

The implications of Zhang et al.'s (2014) observation for this thesis about PTSD, navigation and BDNF are considerable, given that the sample of the current study is comparable to Zhang et al.'s former, more diverse and less controlled, 2006 study sample. In this thesis, the PTSD population comprised: those receiving treatment from NHS psychotherapy treatment programmes, veterans beginning rehabilitation programs, and civilians and Police officers who may or may not have accessed any trauma processing interventions. Attempts to control for this by collecting data on previous treatment were unsuccessful in this study with 21% missing

values (Section 2.5.4.3). It is arguable that the reason that BDNF did not directly relate to PTSD prevalence or severity in this sample is because the effect of BDNF may be being masked by the fact that individuals differed greatly in how much trauma they had to process and whether they had started to do so or not. With the findings from Zhang et al. (in 2006 and in 2014) and findings from this study in mind, Chapter 8 speculates that the impact of the BDNF gene on PTSD may be particularly relevant to those in active military service and suggests that further research with military populations may be worth undertaking in the future (see Section 8.4.3).

7.4.2 BDNF and allocentric processing in navigation

Findings from Chapter 7 build on an increasing body of evidence suggesting that carrying the BDNF *met* allele may not be inherently disadvantageous to allocentric processing (e.g. Krueger et al., 2011). In line with the studies by Banner et al. (2011) and Lövdén et al. (2011), the results provide more evidence that BDNF met carrying genotypes did not perform any worse than valval homozygotes on tests that require allocentric processing. What is more, there was some evidence that met carriers actually performed better in non-allocentric (i.e. egocentric) navigation on the AR task.

Those with the respective BDNF genotypes did not statistically differ in strategy use in the AR paradigm. This may be due to the nature of the AR being about *maladaptive bias* in strategy use (rather than 'spontaneous' strategy use as with Banner et al., 2011). That is to say, in the context of the AR paradigm, Wiener et al. (2013) have previously demonstrated how readily participants relinquish egocentric strategies and take up allocentric strategies *over the course* of the AR task in order to be able to solve the task. The paradigm used in Banner et al.'s (2011) study was different and assessed participants' *spontaneous* decision to use either allocentric or egocentric strategies when both strategies were equally available to them. Another possible explanation as to why in this study there were no statistically significant differences in strategy use as a function of BDNF genotypes is that BDNF met carriers might not inherently rely on either allocentric or egocentric strategies more or less than valval homozygotes. This explanation contradicts Lövdén et al.'s (2011) 'strategy account' (explained in Section 7.1.3) which suggests that met carriers may inherently rely on response based, egocentric strategies (i.e. associative and beacon, in the case of this study) in preference to an allocentric (configural) strategy.

It may be interesting to note for further research that in this study's data there was some visual indication that BDNF met carriers were more delayed (and less steadily incremental) in their application of allocentric processing to the AR paradigm, compared to valval homozygotes (see Figures 7.3.6a and 7.3.6b). There was also a distinctly different pattern of egocentric performance between BDNF genotypes, with met carriers excelling in the final block (Figures 7.5.3.1 and 7.5.3.2). These observations are sympathetic to Banner et al.'s (2011) demonstration of met carriers' being less spontaneous in their application of allocentric processing in navigation. The observations are also sympathetic to Lövdén et al.'s (2011) suggestion that BDNF met carriers may need more obvious changes in experiential demand (or more obvious cues) to deploy sufficient hippocampal resources to complete a navigation task.

What should not be overlooked is the inherent limitation of only distinguishing between met carriers and non-met carriers, with regard to BDNF genotypes. The limitations of the sample size for the less common metmet genotype (i.e. less than 5% of the Caucasian population. Frielingsdorf et al., 2010) means that dose dependent analysis (e.g. Zhang et al. 2014) of carrying the met allele is not possible and nor is the comparison of homozygotes *(valval* and *metmet*, e.g. Banner et al., 2011). It is reasonable to speculate that a larger sample size of *metmet* genotypes in this study may have clarified whether differences in allocentric strategy use on the AR paradigm which were only visible graphically in this study (see Figure 7.3.6b), were statistically significant or not. Whether or not differentiating between met homozygotes and met heterozygotes would have affected the significance of BDNF differences in allocentric performance on the AR (at Section 7.3.3.2) can also only be speculated.

7.4.3 BDNF and self-reported navigation competence

The results indicate that BDNF met carriers' self-reported confidence in navigation may be higher than valval homozygotes, while their actual navigation performance did not differ. The results showed for the first time that the BDNF gene influenced how accurate an individual may be in their perception of their own navigation competence. Valval homozygotes were more accurate in their perceptions of being able to apply allocentric processing to the AR task than met carriers; their self-reported allocentric confidence correlated with their allocentric spatial processing performance. BDNF met carrying genotypes' self-reported confidence, in contrast, did not correlate with their navigation performance. These exploratory findings about the 'declarative nature' of individuals' wayfinding abilities do resonate with conclusions from a meta-analyses of BDNF studies (Kambeitz et al., 2012) that carrying the BDNF met allele has a negative impact on declarative memory. The relevance of this for professions that rely on individuals' accuracy in self-reported navigation competence is discussed in Section 8.4.3.

Together, the findings may raise questions for a long-standing dialogue in literature about hippocampal dependent memory systems being more declarative than hippocampal *in*dependent or associative memory systems (e.g. Bisby et al., 2010; Furnman et al., 2014; Morris in Andersen et al., 2007; Buckley et al., 2015, etc.). There have been calls for more research to be undertaken to better understand if there are qualitative differences between (hippocampal) spatial learning and (non-hippocampal) implicit learning (see Richard Morris in Andersen et al., 2007). One might speculate from this study's findings that spatial learning in navigation (which we take to be hippocampal dependent and allocentric) is more describable than implicit learning in navigation (which we take here to be hippocampal *in*dependent and associative). One might even speculate from the differences in the accuracy of self-reported competence in allocentric navigation found between BDNF genotypes that the declarative quality of allocentric spatial learning could prove to be genetically determined. In sum, these findings are exploratory in nature and may raise more questions for the debate than they do provide answers. Nonetheless, the ambiguity of whether BDNF influences individuals' ability to accurately self-assess their own navigation competence may be worth closer examination in further research.

7.4.4 BDNF, PTSD and navigation

Finally, Banner et al.'s (2011) proposition about the potential relationship between stress, BDNF and spatial behaviour is revisited:

"It is possible that stress plays an intermediate modulatory role between genotype and behaviour, whereby the impact of BDNF on learning and memory strategies may be influenced by exposure to stress. Having the valval genotype may increase the likelihood of participants using a spatial strategy, even following stress exposure, via increased BDNF expression and long-term potentiation in the hippocampus. On the other hand, participants with the Met allele would be more likely to use response strategies in their everyday lives, following stress exposure" (Banner et al., 2012).

This study's analyses exploring the influence of BDNF on navigation behaviour controlled for PTSD diagnosis and trauma exposure (proportions of BDNF genotypes amongst the *PTSD* group and the *Trauma Exposed No PTSD* group were comparable with the wider population and trauma groups was also entered into preliminary analysis as a covariant). Findings from the current study call Banner et al.'s (2011) premise (above) into question: BDNF valval homozygotes are not more likely to use a spatial strategy after having experienced traumatic stress, and BDNF met carriers are not more likely to use a response strategy after trauma exposure. However, it is imperative that in understanding the implications of this study for research into BDNF and PTSD that one acknowledges its limitations. As this study did not control for trauma exposure and trauma processing (as Zhang et al. did in their 2014 study by limiting their sample to serving US military), and as this study did not incorporate trauma exposure into the experiment itself, one cannot rule out the influence of BDNF on trauma processing and PTSD nor the confounding effect this may have on hippocampal dependent navigation behaviour.

8 DISCUSSION

Essentially, this thesis has contributed to our understanding of how traumatic experiences -and even the BDNF genotype- may affect how healthy individuals find their way in their environment, how they process spatial information and how they navigate. The research sheds new light on previous observations in the literature (and in clinical practice[34]) that those who develop PTSD after trauma exposure may also experience difficulties travelling, driving and exploring new places (e.g. Osofsky et al., 2010; Ehring et al., 2006; Kowitz, 2011; Ehlers et al., 1998; Lubit et al., 2003; Adler et al., 2009; Handley et al., 2009; Butler et al., 1999). The findings from this study (its review of the literature and its data) may have implications for: clinical treatment of PTSD; for trauma processing interventions in the military; and for all professions which rely on effective navigation training and reliable self-assessment.

8.1 Summary of key findings

Chapter 3 (Section 3.3.1) confirmed findings from a contemporary study (by Smith et al., 2015) that PTSD impaired allocentric processing in a static memory-based perspective taking task and that this influence was unique to PTSD and was independent of any other demographic or clinical factors that were considered (Section 3.3.2). The impairment was explained by the known detrimental effect of chronic stress on hippocampal functionality and the allocentric processing for which the hippocampus is crucial (e.g. O'Keefe & Nadel, 1978; Andersen et al., 2007; Smith et al., 2015). Trauma exposure alone (i.e. without PTSD) did not impair allocentric performance on the static memory-based perspective taking task.

Chapter 4 extended the investigation by assessing participants' performance on a longer and more complex wayfinding task which measured egocentric and allocentric performance and strategy use (the Alternative Route, AR paradigm by Weiner et al., 2013). Those with PTSD exhibited significant navigation impairments in situations that required both egocentric and allocentric processing, and specific impairment in allocentric learning in the task (Section 4.3.2). The AR paradigm was more sensitive to trauma exposure than the Four Mountains task and for the first time, trauma exposure without PTSD was shown to be detrimental to healthy individuals' allocentric navigation performance (Section 4.3.2.2). Chapter 4 also revealed that an associative information processing bias central to trauma theories of PTSD (e.g. Brewin & Holmes, 2003; Eich et al., 2012; Lang, 1977; Le Doux, 2000) also manifested itself in the active navigation behaviour of those with PTSD (Section 4.3.3). This was by virtue of the fact that those with PTSD maintained a significantly higher use of an associative strategy throughout the navigation task than those who were trauma exposed without PTSD (and this was not affected by any other clinical or demographic factors). The findings were explained using Brewin's notion

[34] Anecdotal evidence from the author's work in trauma support indicated that trauma exposure often results in an unwillingness to travel or be responsible for navigation. (The author worked for the Cambridgeshire Police Critical Incident Personal Support Team, CIPST 2004-2009). Exchanges with practising clinicians at the British Psychological Society (BPS) conferences on Military Psychiatry 2012-2015 also revealed that many had clients who expressed difficulties in and concerns over travel and navigation throughout their treatment.

that those who have had trauma to process experience a 'competition' for hippocampal resources (Vasterling & Brewin, 2005) when faced with a hippocampal-dependent navigation task. For those who had not been able to apply sufficient hippocampal resources to consolidate traumatic experiences in their memory (i.e. the *PTSD* group), their navigation was biased toward associative processing and was inherently limited. Those who had been able to apply sufficient resources to contextualise traumatic experiences (i.e. the *Trauma Exposed No PTSD* group) found the static perspective taking (the Four Mountains task) manageable, but their allocentric performance on the more demanding wayfinding paradigm (the AR) was specifically compromised.

Chapter 5 examined how well individuals perceived their own navigation abilities and behaviour. Findings revealed that the significant and positive correlations shown between self-report questions about allocentric navigation and actual allocentric navigation performance were *unique* to those healthy participants *who had been exposed to trauma* but who had not developed PTSD (Section 5.4.2). One could infer from this that individuals who may have been using hippocampal resources to contextualise and encode previous trauma might therefore be more perceptive of when they apply similar such resources to active navigation. This pattern of findings might be explained by spatial hippocampal memory processes being hypothesised in neuropsychological literature as forming part of declarative memory systems, and being more verbally accessible, compared to more implicit and associative memory systems (see Morris in Andersen et al., 2007; Buckley et al., 2016; Eichenbaum, et a., 1997; and Vermetten et al., 2003, with regard to PTSD). In terms of demographics, findings showed that while self-reported confidence in allocentric navigation increased with age actual allocentric *performance decreased* with age. Males self-reported higher navigation confidence than females but did not demonstrate higher performance (Section 5.4.3). Similar patterns of findings related to age, gender, self-reported navigation confidence and actual performance have been reported frequently in previous studies (such as De Beni et al., 2006; Borella et al., 2014; Münzer & Stahl, 2011; Menghetti et al., 2010).

Chapter 6 examined how perceptive individuals with PTSD were of their own navigation competence and compared combat (military trained) with non-combat (non-military trained) groups. The chapter contributes further to our understanding by showing that the allocentric processing which was describable in trauma exposed healthy populations (in Chapter 5, Section 5.4.2) was not so in PTSD populations (Section 6.3). What is more, those who had been military trained in applying allocentric navigation techniques (i.e. in the combat-related PTSD group) self-reported higher confidence in allocentric navigation than those with civilian PTSD, but did not demonstrate higher navigation performance (Section 6.3.3). This suggested that in cases of PTSD, previous military training did not contribute any accuracy to individual's perceptions of their own navigation competence.

Chapter 7 was exploratory in nature and brought together PTSD and trauma, spatial processing and navigation, and the BDNF gene for the first time in a human model. In Chapter 7 the

analysis of spatial processing and navigation undertaken in Chapters 3 and 4 was repeated, but looking at the effect of BDNF genotypes, controlling for trauma group status (i.e. whether individuals had been trauma exposed and if they had developed PTSD or not, Section 7.3). This was with a view to investigating previous assertions in the BDNF literature that the BDNF gene may influence PTSD (and trauma processing) and allocentric spatial learning, by virtue of its role in maintaining hippocampal integrity.

Contrary to findings from recent studies (e.g. Zhang et al., 2014), the BDNF genotype did not influence PTSD prevalence or symptom severity (Sections 7.3.1 and 7.3.2). One possible explanation for this failure to replicate the previous findings reported in the literature (Zhang et al., 2014) is that this study's sample population did not control for environmental conditions as well as Zhang et al. (2014)'s sample serving military Special Operations personnel had. The sample in the study by Zhang et al. (2014) was homogenous in terms of the type, extent and even timing of participants' trauma exposure and the likely opportunities they may have had to process trauma since the exposure. The profile of the sample in this thesis was more diverse in the nature and timing of trauma exposure, comprising civilian and veteran populations. Furthermore, some participants reported having had structured opportunities to process previous trauma exposure prior to testing and others did not, and data regarding access to treatment was not reliable (see Methodology Sections 2.5.4 and 2.8.2.2). The potential for variance in environmental conditions (i.e. type and extent of trauma exposure and trauma processing) to mask any genetic effect of BDNF should not be discounted (Zhang et al., 2014, 2006).

BDNF met carriers' pattern of egocentric navigation performance differed to that of valval homozygotes in the Alternative Route (AR) paradigm (Figure 7.3.5.1) with some evidence of a possible performance advantage for BDNF met carriers (Figure 7.3.5.2). There was no significant main effect of BDNF group on allocentric performance in either the Four Mountains task or the AR paradigm and this was consistent with earlier literature (e.g. Raz et al., 2009; Dennis et al., 2011; Sakata et al., 2013). There were some visual observations of a delay in BDNF met carriers' application of allocentric strategy use during the AR task, compared to the incremental application by valval homozygotes and this was similar to findings by Banner et al. (2011). Lövdén et al. (2011) speculated that met carriers may require more obvious 'cues' to apply allocentric processing to a given task than valval homozygotes may do and this may explain our visual observations and Banner et al's significant findings (2011).

In Chapter 7 (Table 7.3.7c) a significant positive correlation between self-reported measures of allocentric competence and actual allocentric performance was observed only for BDNF valval homozygotes. One could interpret from this that BDNF met carriers may be less perceptive of their ability to apply allocentric processing in navigation, thereby finding it harder to describe than valval homozygotes. Together, these findings suggest that BDNF genotypes may differ in the strategies they apply to navigation (and their perceptions of how they navigate) but that these differences may not be manifest in gross measures of performance.

8.2 The relationship between trauma, BDNF, allocentric processing and navigation

To provide some clarity to this discussion, the dynamics between allocentric (spatial) processing, egocentric (associative) processing, trauma exposure, BDNF genotypes and navigation are presented visually at Figure 8.2.

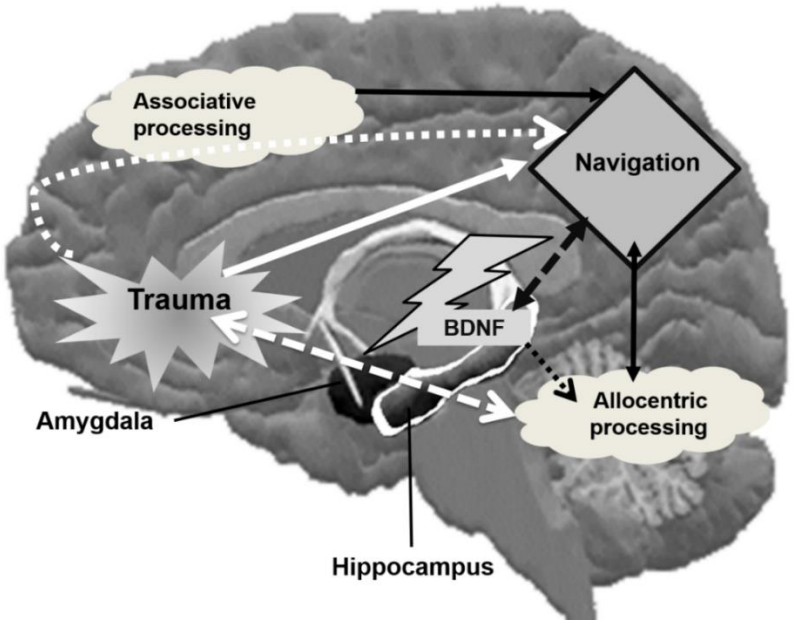


Figure 8.2: Trauma and spatial processing in BDNF genotypes. This model illustrates the functionality of allocentric processing navigation and BDNF. The solid white arrow represents the negative impact of trauma on navigation. The curved dotted white arrow represents the associative bias of PTSD which manifests in navigation behaviour. The dashed white arrow represents the relationship between trauma and allocentric processing. The horizontal solid black arrow represents the role of associative processing in navigation, and the vertical solid black arrow, allocentric processing. The dotted black arrow represents the impact of BDNF on allocentric processing and the dashed black arrow represents the relationship between BDNF and navigation. The lightning symbol represents BDNF release.

8.2.1 ALLOCENTRIC PROCESSING AND NAVIGATION

Since the discovery of place cells in the hippocampus of freely moving rats it has been long understood that the hippocampus facilitates allocentric processing (O'Keefe & Dostrovsky, 1971; Arnold et al., 2013; Andersen et al., 2007; De Araujo et al., 2001; Moser et al., 2008; Wolbers & Wiener, 2014). Allocentric spatial processing enables individuals to acquire and store environmental information, configure a mental representation of the environment, and to make decisions about when to use this map- that is, to *navigate* (Erkstrom et al., 2014; Wiener et al., 2009, 2013, and *represented by the vertical solid black arrow* in Figure 8.2). The relationship between navigation and allocentric (or hippocampal dependent) processing is bi-directional because it has been shown that navigation training (more specifically, that requiring allocentric processing, such as building and using mental maps) can improve hippocampal neuronal integrity and volume (e.g. Maguire et al., 2000; Lövdén et al., 2011).

This thesis showed that healthy individuals were accurate in their perception of their capacity to apply allocentric processing in active navigation: in those without PTSD, allocentric questions from navigation questionnaires positively correlated with their allocentric navigation

performance (Section 5.4.1). The fact that this is accuracy may be particular to those who have applied allocentric processing to manage previous trauma and to BDNF valval homozygotes is discussed in Sections 5.4.2 and 8.2.6.

8.2.2 PTSD, TRAUMA AND NAVIGATION

Recent research (Smith et al., 2015 building on work by Bisby et al., 2010) has demonstrated that clinical levels of PTSD impair allocentric spatial processing. This is represented in Figure 8.2 by *the solid white arrow.* Findings in Section 4.3.2 of this study demonstrated that in cases of PTSD *and* in cases of trauma exposure (without clinical symptoms of unprocessed trauma, or PTSD) allocentric processing and allocentric learning in active navigation was impaired. Egocentric navigation performance was also impaired in cases of PTSD (but on in trauma exposed healthy individuals).

Trauma literature describes how sustained glucocorticoid release in chronic stress damages the hippocampus (e.g. Andersen et al., 2007; Bremner & Elzinga, 2002, etc.). This may explain the findings in this thesis that PTSD impaired hippocampal dependent (allocentric) spatial processing and navigation. The fact that this study reveals impairment in hippocampal dependent (allocentric) spatial processing and navigation in those with trauma exposure who *are not exhibiting a stress response* (i.e. who have not developed PTSD) may be explained by a competition for hippocampal resources between long term trauma processing and immediate spatial processing (Vasterling & Brewin, 2005; and see Brewin & Burgess, 2014; Smith et al., 2015, *represented by the dashed white arrow* in Figure 8.2). It may be useful in further research to compare this thesis' findings about *chronic traumatic stress* interfering with allocentric performance with very recent research published by Van Gerven et al. (2016) which (surprisingly) suggested that *acute* stress can incur preferences for allocentric strategies.

8.2.3 ALLOCENTRIC PROCESSING AND TRAUMA

Theories about PTSD have been revised to include accounts of how deliberate application of hippocampal processing to contextualise traumatic memories might prevent individuals developing PTSD (Bisby et al., 2010, and also Eichenbaum, 2006; Bremner & Elzinga, 2002; Brewin & Burgess, 2014; Smith et al., 2015).

Hippocampal dependent contextualisation and allocentric processing of trauma is represented in Figure 8.2 by *the dashed white arrow.* This arrow is bi-directional because this thesis findings (at Section 4.3.2.2) and those by Smith et al. (2015) demonstrated that allocentric processing is negatively affected by PTSD and trauma exposure. Trauma literature also explains that allocentric processing is required to contextualise and encode traumatic experiences (Brewin & Burgess, 2014; Smith et al., 2105; Bisby et al., 2010, etc). As explained in Section 4.1.6, allocentric processing has long featured as a cognitive process which is necessary in effective trauma processing, albeit referred to using different terminology in trauma literature, such as the 'overhead view' or the 'observer perspective' (see McIsaac & Eich, 2004; Eich et al., 2011, 2012; Steel et al., 2005; Neuner et al., 2008; Siegal, 2012; and now Kaur et al., 2016).

This thesis demonstrated (Section 5.4.2) that participants who had been managing trauma exposure sufficiently not to develop PTSD (i.e. the *Trauma Exposed No PTSD* group) were unique in their accurate perceptions of how they apply allocentric processing in navigation: only their scores in self-reported competence at allocentric navigation positively correlated with their allocentric performance levels on the AR paradigm (in Section 5.4.2). In healthy individuals without that experience of trauma exposure (the *Trauma Unexposed* participants) there was no correlation between self-reported competence at allocentric navigation and allocentric performance levels. One could speculate that healthy trauma exposed participants are particularly accurate in their perceptions about using allocentric processing because they have already been applying similar resources to contextualise, encode and manage previous trauma exposure, and they therefore have the ability to recognise better when they are applying it in other everyday contexts.

8.2.4 ASSOCIATIVE BIAS IN PTSD AND ACTIVE NAVIGATION

Applying allocentric processing to trauma memories (again, *represented by the dashed white arrow* in Figure 8.2) is thought to counteract associative bias in PTSD (Brewin et al., 2010; Smith et al., 2015; Bisby et al., 2010, etc.). The *curved dotted white arrow* in Figure 8.2 represents the associated thinking of PTSD manifesting itself in participants' navigation behaviour. Those with clinical or probable levels of PTSD used associative cue strategies in the AR paradigm significantly more than those unexposed to trauma and those exposed to trauma but who reported no PTSD (Section 4.3.3.2). This therefore suggests that bias toward associative strategies was not an effect of trauma exposure, but likely the result of trauma exposure *not having been processed,* which had resulted in PTSD. These new findings are supported by a well-established literature about trauma which describes associative states and biases in information processing in cases of prolonged or extreme traumatic stress (e.g. Brewin & Holmes, 2003; Eich et al., 2012; Lang, 1977; Le Doux, 2000). One infers from this that those with PTSD have not been able to counteract their associative bias (e.g. Brewin et al., 2010, etc.) and this remaining bias is now visible in another area of cognition and behaviour: navigation.

Associative (egocentric) strategies used in navigation (*represented by the horizontal solid black arrow* in Figure 8.2) are hippocampal independent (e.g. Furnman et al., 2014; Van Kesteren et al., 2013; Janzen et al., 2008). In this study, egocentric strategies in the AR paradigm included associative cue and beacon strategies. In Sections 5.4 and 7.3.7, where subjective measures of navigation (the SBSOD, QSR and FRS questionnaires) and objective measures of navigation (AR and Four Mountains performance) were compared, it became apparent that there was no relationship between subjective responses to navigation questions concerning *egocentric* processing and egocentric navigation performance. This suggests that egocentric processing was not something which individuals consciously perceived or were able to accurately describe.

This observation may contribute to debates across neuroscience literature about how implicit learning (through associative, hippocampal *in*dependent networks) differs from explicit

knowledge-based learning (such as hippocampal dependent or spatial learning networks, e.g. Brewin & Burgess, 2014; Morris in Andersen et al., 2007; Buckley et al., 2015; Vermetten et al., 2003).

8.2.5 BDNF

The relationship between BDNF and navigation is represented by the *bi-directional dashed black arrow* in Figure 8.2. The BDNF literature has shown that hippocampal dependent navigation training results in higher neurotrophin concentration in BDNF valval homozygotes (70% of the Caucasian population) but not in BDNF met carriers (i.e. the remaining 30% of the Caucasian population, Lövdén et al., 2011). Banner et al. (2011) explain that BDNF met carriers adopt allocentric processing strategies in navigation tasks less spontaneously than valval homozygotes. This is despite there being no absolute performance differences between BDNF genotypes in Banner et al.'s (2011) study, nor in those similar to it (e.g. Raz et al., 2009; Dennis et al., 2011; Lövdén et al., 2011, etc.).

Consistent with the literature, there were no absolute performance differences in allocentric navigation between the BDNF genotypes in findings from Section 7.4.4.2. In Section 7.3.6, results showed that BDNF met carriers were less accurate in their perception of their own allocentric navigation competence than valval homozygotes, as only valval homozygotes' self-reported allocentric confidence in navigation positively correlated with their allocentric performance on the AR paradigm.

The relationship between BDNF and allocentric processing is represented by the *dotted black arrow* in Figure 8.2. Lövdén et al. (2011) developed a 'strategy account' of allocentric and egocentric processing differences between BDNF genotypes which proposed that met carriers may be more inclined toward egocentric strategy use than allocentric strategy use. This account may explain findings in this thesis that met carriers displayed a different pattern of (and slight advantage in) egocentric performance (in Section 7.4.3.1) compared to valval homozygotes (Figures 7.3.5.1 and 7.3.5.2).

BDNF *release* is not investigated in this study but the theory behind BDNF release is depicted in Figure 8.2 *by the flash symbol* for the purposes of discussion. How responsive BDNF met carriers are to demands for allocentric processing may be explained further by literature about BDNF protein release. From this more mechanistic BDNF literature, one understands that higher levels of BDNF are associated with greater responsiveness to hippocampal dependent activity (see Egan, 2003; Notaras et al., 2015, etc.). Other literature refers to there being a release of BDNF neurotrophins in response to trauma -but the mechanism by which BDNF is released in response to trauma is not clarified (Chaieb et al., 2013; Van der Heuval et al., 2016). The potential relevance for BDNF release for future research is addressed in Section 8.5.

Finally, data from Sections 7.3.1 and 7.3.2 did not demonstrate a relationship between the BDNF gene and PTSD. There is only one study in the BDNF literature (by Zhang et al., 2014)

which has demonstrated a direct relationship between the BDNF met allele and PTSD prevalence and this was done so in a sample population which controlled for key environmental conditions (i.e. trauma exposure and trauma processing). One could speculate that the relationship between BDNF and PTSD may be not be direct, but may be confounded by individuals' proficiency in (and awareness of) applying hippocampal dependent processing when circumstances demand it (be they circumstances of trauma exposure and of trauma processing or of finding one's way in the environment).

From the findings of this thesis summarised above, it seems that further research needs to be undertaken to systematically examine whether BDNF's relationship to the demands on the hippocampus and on allocentric processing for *navigation tasks* is the same as its relationship to the demands on the hippocampus and on allocentric processing for *trauma processing*. However, results of this research may already have important implications for how allocentric processing is applied and understood in both clinical and military settings.

8.3 Clinical implications

The success of PTSD treatment is attracting increasing levels of public attention.[35] This attention may well derive from: an increase in the number of people being diagnosed with PTSD (Combat Stress, 2015; Houston et al., 2015) after recent overseas military operations; cuts to emergency services in the UK; and also from recent scrutiny over the effectiveness of PTSD interventions (Combat Stress, 2012; BBC, 2013)[36].

8.3.1 ALLOCENTRIC PROCESSING IN TREATMENT

As explained in Section 4.1.6.2 and in Figure 8.2, allocentric processing is a cognitive process which is necessary in effective trauma processing. Recently updated theories of PTSD and an emerging literature about allocentric processing and trauma suggest that trauma processing interventions should actively encourage individuals to apply allocentric (hippocampal dependent) techniques to counteract the egocentric and associative thinking characteristic of PTSD (Bisby et al., 2010; Brewin & Burgess, 2014; Smith et al., 2015; Brewin et al, 2010; Brewin in Vasterling & Brewin, 2005). These techniques may include using existing (and well-established) methods such as adopting the 'overhead view' (e.g. viewing a scene as if from above) or visualising scenes from the perspective of an observer (e.g. McIsaac & Eich, 2004; Eich et al., 2011, 2012; etc.). At the time of submission of this thesis, an exploratory case study was published (Kaur et al., 2016) which reported that the deliberate application of allocentric spatial processing to trauma re-exposure techniques was effected in reducing PTSD symptomology in two combat veterans who were experiencing exaggerated disassociation.

[35] Time magazine: http://time.com/3982440/ptsd-veterans/

[36] http://www.bbc.co.uk/news/uk-england-27505518. 6,404 veterans were being supported by Combat Stress in 2015, up from 5,400 in 2014. Combat Stress reported that their PTSD rehabilitation was modelled on an Australian programme which accepted a 30% failure rate, and this was challenged by the BBC programme *Panorama* in 2013 ('Broken by Battle').

A practical example of these techniques is presented in Figure 8.3. In the first image at Figure 8.3, the scene is being recalled from an egocentric, personal perspective (the photograph was taken by a survivor of the M5 road traffic collision in 2011 on his mobile phone at the scene). The second image in Figure 8.3 is taken from news coverage and presents the scene more allocentrically, incorporating other people in the image (and therefore the possibility of others' perspectives). The final image is taken from a helicopter and presents an 'overhead' view of the traumatic scene, such as often encouraged in traditional trauma therapies and interventions (e.g. Steel et al., 2005; Neuner et al., 2008; etc).

a) Egocentric trauma recall b) Allocentric trauma processing

Figure 8.3 Differentiating between a) egocentric trauma recall and b) allocentric trauma processing. *Image courtesy of Prof Kozhevnikov*, Mental Imagery and Human-Computer Interaction Lab, Harvard Medical School. Images of the M5 crash taken by survivor Rob Emony (*The Independent*, 2011); and Sky News Skycopter. Copyright © Jessica K Miller for the British Red Cross trauma training module 2016.

While it is clear that applying allocentric processing techniques to contextualise and encode trauma is recognised as being useful to prevent and recover from PTSD, this thesis has raised questions as to whether this approach is as easy to achieve for some individuals as it may be for others.

The research presented in this thesis has demonstrated that individuals who have PTSD are not accurate about their own approach to applying allocentric processing in navigation. Furthermore, those who have successfully *avoided PTSD* after trauma exposure were *most* accurate about their own approach to applying allocentric processing in navigation. Together, these findings (presented at Sections 6.3 and 5.4.2) indicate that some individuals with PTSD may experience difficulty in adopting the allocentric approach and may benefit from deliberate instruction and practice in applying allocentric processing when it is required in therapy. Clinically, this might mean therapists could offer more deliberate verbal instructions to encourage patients to move from recalling trauma scenes from an egocentric perspective (image *a* in Figure 8.3) to a more allocentric, observer-based perspective (image *b* in Figure 8.3).

For those individuals who are less 'allocentrically minded' (i.e. those who may be inhibited or unclear in using an allocentric processing approach), it may be appropriate to offer alternative exercises and techniques to help with contextualisation and gaining an observer perspective. Mindfulness-Based Stress Reduction (MBSR) training (Hanson, 2011; Kabat-Zinn, 2013; Holzel

et al., 2010; Farb et al., 2007; Tang et al., 2015) and Acceptance and Commitment Therapy (ACT) (Clarke et al., 2015; Hayes, 2004) are two examples of interventions which involve developing mental agility in different aspects of cognitive functioning which, over time, are said to release individuals from associative, stimulus-response style information processing biases (this is increasingly referred to as '*self-directed neuroplasticity*', see Hanson, 2011)[37].

The priorities of MBSR and ACT diametrically oppose several trademark symptoms of PTSD. MBSR and ACT prioritise: control of sensory awareness; witnessing thoughts from a non-egocentric perspective; and attending to the present moment (Kabat-Zinn, 2013; Hayes, 2004). These could well counteract respective PTSD dynamics and symptoms of: experiencing unbidden sensory intrusions; egocentric associative recall; re-experiencing the past and a sense of foreboding about the future (Foa et al., 1995; Brewin et al., 2010). As such, this study suggests that MBSR and ACT therapies may well provide alternative means of dealing with PTSD and refocus perspective, without relying on individuals' aptitude in allocentric processing (thereby minimising any genetic disadvantage in treatment outcomes for BDNF met carriers). The increased mental agility that arises from the development of these practices comes from using several areas of the brain, many of which have been seen to undergo structural change as a result of long term practice (Davidson et al., 2013 and Farb et al., 2007 in Kabat-Zinn, 2013; Holzel et al., 2010; Luders et al., 2015). It is interesting to note that the density of the hippocampal formation is one such structural change (Holzel et al., 2010).

8.3.2 BDNF GENOTYPES AND ALLOCENTRIC PROCESSING

Previous research has already suggested that an individual's genetic make-up may influence the clinical outcome of trauma treatments and interventions (see: Kemp et al., 2008; Arnsten et al., 2015; Ahmed, 2007). With regards to BDNF, increased BDNF neurotrophin levels have been linked to positive clinical outcomes for patients being treated for anxiety-related disorders (Wang et al., 2011; Kurita et al., 2012; Schmidt & Duman, 2007). Furthermore, a review by Andero & Ressler (2012) suggests that BDNF signalling[38] could be an important and novel way to enhance the effectiveness of treatment.

The literature reviewed in Chapter 7 suggested that BDNF met carriers are at a disadvantage in some areas of cognitive function which are called upon in trauma processing therapies, including: consolidating new safety cues in treatment, extinguishing fear responses, or withstanding the incongruity of re-exposure to traumatic material (Soliman et al., 2010; Neuner et al., 2008; Andero & Ressler, 2012; Felmingham et al., 2013; Kurita et al., 2012). Crucially,

[37] Recent research has shown that applying MBSR techniques through extensive practice can result in structural changes in neural systems involved in trauma processing, e.g. decreased volume of the amygdala and increased hippocampal density (Davidson et al., 2013 and Farb et al., 2007 in Kabat-Zinn, 2013; Holzel et al., 2010).

[38] 'BDNF signalling' alludes to the chemical change produced by the BDNF neurotrophin within neurons which causes them to fire along neural pathways.

BDNF met carriers with PTSD were shown to respond significantly more poorly to exposure therapy than BDNF valval homozygotes with PTSD (Felmingham et al., 2013)[39].

This is particularly interesting, given the findings from this thesis reported in Section 7.4.3 which suggested that BDNF met carriers may be at a disadvantage when it comes to being accurate about their capacity for allocentric processing, despite their apparent confidence in it. This may have implications for BDNF met carriers' engagement in those trauma processing interventions which typically re-expose an individual to trauma and then rely on an allocentric therapeutic approach to manage the experience. Adjustments to clinical practice could be similar to those already advocated (in Section 8.3.1) i.e. providing BDNF carriers with either more deliberate prompts to apply allocentric processing in trauma therapy (as suggested by Lövdén et al. in 2011 but in relation to trauma processing rather than navigation training) or with alternative therapies such as MBSR or ACT.

8.4 Military implications

8.4.1 ALLOCENTRIC PROCESSING AND THE MILITARY: NAVIGATION

Navigation competence and situational awareness are highly prized in the UK military and to be able to assess performance accurately and to sustain high levels of performance in traumatic conditions may be of relevance to further military research (DSTL, 2015). Fundamentally, results in Section 4.3.2.2 demonstrated that in healthy individuals prior exposure to trauma had a detrimental effect on their capacity to navigate, rendering them less capable of applying allocentric processing when required. Much navigation literature reiterates how vital a component allocentric processing is to many types of navigation (e.g. Erkstrom et al., 2014; Wiener et al., 2013; Smith et al., 2015; Bisby et al., 2010; Lövdén et al., 2011). Types of navigation which may require allocentric processing may be highly relevant to maintain situational awareness and competence in the Armed Forces (see Section 6.1.2). Navigation demands which can require allocentric processing include: using a map and compass; route re-tracing; finding alternative routes; taking shortcuts; exiting buildings without the use of distal cues (i.e. without windows); creating floor plans of buildings; and comparing overhead satellite imagery or maps with landscapes which have changed in their topography (Wolbers & Wiener, 2014; Dudchenko, 2010; Hartley et al., 2007; Bobhot et al., 2007; Erkstrom et al., 2014; Furnman et al., 2014; Banner et al., 2011, etc, and see Sections 1.2.1 and 1.2.2).

What is also interesting to consider in the context of the military is that results in Section 5.4.2 showed that civilians who had had experiences of trauma which they had processed sufficiently to avoid PTSD (the *Trauma Exposed No PTSD* group) were more accurate in their perceptions of how they navigate using allocentric processing than healthy unexposed participants. In contrast, Chapter 6 showed that civilians and veterans who had *not* processed trauma

[39] Within the BDNF literature, there have been many suggestions for trauma therapy improvements, including: boosting BDNF activity in hippocampal-infralimbic circuits (Arnsten et al., 2015; Ahmed, 2007; Wang et al. 2011 with reference to Peters et al., 2010); increasing BDNF signalling (Andero & Ressler, 2012; Felmingham et al., 2013) and increasing BDNF plasma levels (Kurita et al., 2012).

sufficiently to avoid PTSD were not accurate in their application of allocentric processing in navigation. One could extrapolate from this that there is a 'tipping point' in trauma exposure and processing, where exposure shifts from being an advantage for self-assessment in navigation, to a disadvantage. This may be of value for further military research into navigation training and assessment of new recruits and of long-serving, experienced personnel.

Furthermore, Section 6.3 reported findings which revealed that in those with PTSD, having a military background did not increase the accuracy of participants' perceptions of their capacity for allocentric processing in navigation. Even though combat veterans had high self-reported confidence in applying allocentric processing to navigation they did not perform higher as a result (Section 6.3.2). These findings suggest that accuracy in navigation self-assessment in the military may be diminished in those with cumulative unprocessed trauma or undiagnosed PTSD.

8.4.2 ALLOCENTRIC PROCESSING IN THE MILITARY: TRAUMA PROCESSING

A brief review of military mental health literature in Section 6.4.2 and consultation with military professionals (see Section 1.1.3) suggested that the contextualisation of combat experiences was something which was recognised and valued when it came to protecting the mental health and wellbeing of military personnel and their families (KCMHR, 2010; MacManus & Wessely, 2013; MacManus et al., 2014; Dandeker et al., 2010[40]). There was evidence in much of the literature that higher levels of PTSD are consistently reported in those who do not have opportunities to contextualise their experiences during or from tours of duty. This was specifically the case for service personnel who had broken Harmony Guidelines (guidelines which advise personnel to take sufficient breaks in between tours of duty, KCMHR 2010). PTSD was also more highly reported in individuals (usually Reservists) who had not accessed interventions which provided opportunities to share experiences with other serving personnel, such as Third Location Decompression (TLD) and Trauma Risk in Management (TRiM, KCMHR, 2010; MacManus & Wessely, 2013; MacManus et al., 2014; Dandeker et al., 2010). Third Location Decompression (TLD) is an intervention which involves military personnel spending a few days in an alternative location (usually Cyprus) to 'readjust', clean kit, drink alcohol and talk about their (often traumatic) experiences of theatre with colleagues. It functions as an informal unstructured means of trauma exposed personnel contextualising their experiences with one another before returning to the UK where their previous experiences can be far removed from civilian life. TRiM is an assessment process which is common to the military, and to UK emergency responders and even local authorities which involves debriefing attendees of critical incidents to check if employees want to self-report that they have been effected by the trauma exposure and require further support (KCMHR, 2010; Gee, 2013; Palmer, 2012).

However, a key observation reported in this literature was that despite many references in reports and reviews to sharing and contextualising experiences of combat (see KCMHR, 2010),

[40] The British Psychological Society devotes a whole annual conference to the study of individuals' transitions from military to civilian life.

the connection between contextualisation, trauma processing, and the interventions already in place to support trauma processing have not yet been explicitly made. This lack of recognition was reflected a review of Third Location Decompression (TLD) in 2008. TLD was reported as having a positive impact but that this positive impact was seemingly 'inexplicable' and without scientific foundation (Hacker-Hughes et al., 2008). One area of future research could be to assess how existing interventions (such as TLD and TRiM) already use contextualisation to help individuals process trauma and how these interventions might therefore benefit from more formal integration of allocentric processing techniques.

8.4.3 RESEARCHING BDNF AND TRAUMA PROCESSING IN THE MILITARY

Genetic studies in military populations are not uncommon, with twin studies dating back to Gilbertson et al. (2002) and more recently, genome wide association studies (GWAS) being undertaken in the United States (Nievergelta et al., 2015). However, in the research literature there is growing awareness that trauma exposure among individuals with PTSD serving in the military is different from trauma exposure among individuals with PTSD in civilian populations (Gee et al., 2013; KCMHR, 2010; Zhang et al., 2006, 2014; APA, 2013).

Findings reported by Zhang et al. (2006, 2014) have also shed light on the value to genetic research of serving military populations for providing samples in whom environmental factors around trauma exposure are more controlled for than in civilian or non-serving populations. The negative effect of carrying the BDNF met allele for PTSD was demonstrable in a study of homogenous military populations (Zhang et al., 2014) whereas it had not been in a similar earlier study undertaken by the same researchers in diverse and non-combat PTSD populations (Zhang et al., 2006). As explained in Section 7.4.1, the former sample population comprised civilian participants with a range of traumatic experiences who were accessing treatment programs and were at different stages of those programs (Zhang et al., 2006). The latter sample population comprised Special Operations personnel on active service in the US military, who likely shared the same type of traumatic exposure (i.e. that from combat, which may have been repeated, given their experience as Special Operations personnel) and who shared similar constraints in accessing trauma processing interventions. The profile of this latter sample therefore controlled for environmental conditions which (i.e. trauma type, severity and processing), while the former sample population in 2006 had not. Subsequently, there would have been less variation in environmental conditions to mask the effect of the BDNF gene on participants' experiences of PTSD. Serving military populations may therefore prove highly relevant to future research into the role of the BDNF gene in both the manifestation of and resilience to PTSD.

8.4.4 BDNF AND NAVIGATION IN THE MILITARY

The literature reviewed in this thesis (e.g. Lövdén et al., 2011; Banner et al., 2011; Raz et al., 2009; Dennis et al., 2011) and findings reported in Chapter 7 all indicate that, whilst there may be no overall navigation performance disadvantage in carrying the BDNF met allele, there are differences between the genotypes in their approach to navigation and in the accuracy by which individuals perceive their own navigation competence. From these observations, one might

speculate that identifying trainees' BDNF genotypes may enable navigation exercises and self-assessments to be better tailored to suit individuals' approaches to allocentric processing and the military scenarios which demand it.

The value of understanding individual differences in spatial training outcomes has already been recognised in the psychological literature (Uttal et al., 2012). Further neuropsychological and genetic research could explore whether applying more verbal or visual prompts to military navigation training exercises might improve BDNF met carriers' application of allocentric processing and thereby improve training outcomes and navigation performance (as suggested by Lövdén et al., 2011 and in the interpretation of findings from Chapter 7). Such research could also assess whether the accuracy of navigation self-assessments in the military could be improved by more clearly articulating when navigation scenarios are likely to demand allocentric processing. This could improve self-assessment accuracy, particularly for BDNF met carriers who may self-report higher navigation confidence but who may be less accurate in their perception of applying their navigation skills in practice.

8.5 Limitations of the research

There are some key areas of this research, which, if replicated, would benefit from improvement. Possible improvements include: controlling for visuo-spatial ability; finding alternative measures of hippocampal integrity and of BDNF release; and integrating a systems-neuroscience approach to the research.

As explained in Chapter 2 and the Methodology (section 2.5.5), this study was not designed to control for general visuo-spatial ability. Earlier research into PTSD and allocentric spatial processing (Smith et al., 2015) controlled for visuo-spatial ability using a general screening tool measure for learning disabilities and found that participants' scores on this measure provided a unique contribution to memory and perception performance (as a combined score) on the Four Mountains task (Smith et al., 2015). Given these findings by Smith et al. (2015) it would be prudent to control for visuo-spatial ability in future research.

With regards to hippocampal integrity, the current research used a wayfinding paradigm (the Alternative Route by Wiener et al., 2013) which had demonstrated a deleterious impact of aging on allocentric processing (which was deemed to be hippocampal dependent). If this research were to be developed further, other means of measuring of hippocampal integrity, such as neuroimaging techniques to examine hippocampal activation, pattern separation or hippocampal volume could be incorporated (e.g. see Clelland et al., 2009; Ohnishi et al., 2006; Wang et al., 2010; Brooks & Stein, 2015; Gilbertson et al.; 2002; Apfel et al., 2011).

With regards to the BDNF gene, future research would benefit from incorporating measures of new and mature BDNF serum levels, BDNF methylation, BDNF release and hippocampal volume (see Morinobu, 2013; Malan-Müller et al., 2014; Unternaehrer et al. 2012; Fuchikami et al., 2011; Bonne et al., 2011; Autry et al., 2012; Calabrese et al., 2015; Hauck et al., 2010; Jia

et al., 2008; Egan et al., 2003; Pezawas et al., 2004; Bueller et al., 2006; Montag et al., 2008; Chaieb et al., 2013; Gatt et al., 2009; Bremner & Elzinga, 2002; Sapolsky, 2000; Molendijk et al., 2012; Carballelo et al., 2013; Karnik et al., 2010; Richter-Schmidinger et al., 2010; Dalvie et al., 2014; Farhardi et al., 2000).

Finally, future research into the relationship between trauma, navigation and the BDNF gene may benefit from a more systems-neuroscience approach (for example see Byrne et al., 2007). This research has only been able to look at *behaviour* which is typically associated with egocentric and allocentric processing. To fully understand the relationships between trauma, navigation and BDNF, it may important for future research to identify and clarify the specific neural mechanisms and networks associated with egocentric and allocentric processing. Neurobiological models of associative and allocentric processing permeate the trauma and navigation (Voermans et al., 2004; Byrne et al., 2007; Featherstone & McDonald, 2004, 2005; Vasterling & Brewin, 2001; Shin et al., 2011; Shenton & Turetsky, 2010; Rauch, 2006; Wolbers & Wiener, 2014; Fernandez-Seara et al., 2009; Lee & Solivan, 2008). Hippocampal research looking at plasticity and BDNF also relies on an understanding of the neural networks involved in different areas of cognition (e.g. Montag et al., 2008; Neves et al., 2008). However, these neural network models vary greatly, presenting contradictory explanations as to which areas of the brain are responsible for which neural processes. In particular, there is still much work to be done in terms of differentiating between dorsal and ventral streams. Fansleow & Dong (2010) conclude that current discrepancies and "arbitrary definitions" between and within neural networks need to be addressed before any such models can reliably inform our understanding, and this may well be the case for further investigation into trauma processing, navigation and BDNF.

8.6 Future PTSD research

Historical perceptions (and some more recent public perceptions) of post-traumatic stress perceived it as being a 'signature' disease of combat or a "necessary part" of military life (Gee et al., 2013; MacManus & Wessely, 2013; MacManus et al., 2014; Palmer, 2012; KCMHR, 2010; Rona et al., 2009, 2007). This thesis reflects more modern neuropsychological views of post-traumatic stress (and the disorder which may emanate from it) as it being a stage in a natural neurological process of contextualisation and memory encoding. This more 'process-based' account is reflected in revisions made to PTSD theory over the past twenty years which have introduced concepts of neural processing- and allocentric processing in particular (Dalgleish, 2004; Bisby et al., 2010; Brewin & Burgess, 2014; Smith et al., 2015; Selden et al., 1991). Findings from this thesis and from contemporary trauma research suggest that it is more helpful to conceptualise PTSD as a collective description for a stressful experience which occurs *because an individual has not (yet) fully contextualised, encoded and consolidated traumatic experiences.* This concept of PTSD would be in preference to interpreting PTSD as a stress-related disorder which arises as an inevitable consequence of trauma exposure, exacerbated by genetic susceptibility.

To develop this point further, how PTSD is conceptualised in neuropsychological research may well have an influence on how it is perceived in other fields (such as genetics) and therefore the direction of future research. Recent media coverage of the epigenetic role of the $FKBP_5$ gene and PTSD quoted Rachel Yehuda as announcing that if there is a transmitted effect of trauma, "it would be in a stress-related gene that shapes the way we cope with our environment" (*The Guardian*, 2015[41]). One might infer from Yehuda's recent statement and from her previous research (Yehuda et al., 2005, 2006, 2011, 2015) that the role of genetics in the manifestation of PTSD is inherently to do with a transmitted vulnerability to the stress response.

However, as explained previously, other findings in the genetic literature (e.g. Zhang et al., 2006, 2014) have demonstrated that the BDNF gene may influence PTSD not necessarily by virtue of a vulnerability to the stress response but by virtue of the fact that other environmental conditions which effect trauma processing have been controlled (e.g. the extent and severity of trauma exposure and the opportunities individuals have had or not had to process trauma). What is more, findings reported in Section 4.3.2.2 of this study showed that even in those individuals who *do not* exhibit a stress response (i.e. those who have not developed PTSD) their previous trauma exposure affects how they apply hippocampal resources to other areas of cognitive function (i.e. navigation behaviour). This reiterates the point that understanding PTSD is not only about understanding the stress response, but it is also about understanding the *influences over individuals' capacities to process traumatic information,* be they genetic or otherwise.

[41] http://www.theguardian.com/science/2015/aug/21/study-of-holocaust-survivors-finds-trauma-passed-on-to-childrens-genes

8.7 Conclusions

The research reported in this thesis highlights how associative thinking in PTSD can manifest in a different area of an individual's life (spatial processing) and that this manifestation may provide a simple explanation for why some people experience difficulty in navigating after having experienced something traumatic.

Findings from this thesis also provide insights into how individuals' perceptions of their own competence in hippocampal dependent processing differs as a function of factors such as age, gender, experiences of trauma, and genetic profile (i.e. BDNF genotype). This may have practical implications for those professions that rely on individuals being aware of where they are in space and how they can respond to trauma exposure.

The current research has also shown that the BDNF genotype is unlikely to present a clear-cut case of 'advantage versus disadvantage' in terms of hippocampal dependent processing, but that the gene may subtly influence how individuals process information and how they perceive themselves doing so. Further research is recommended to assess the value of gene-based trauma processing and gene-based navigation training interventions in military and civilian settings.

To close, this study has endeavoured to build on long established psychological theories of associative, responsive processing to suggest that cultivating a *non-egocentric*, objective and knowledge-based approach to one's traumatic experiences (and to locating one's place in the environment) has the potential to release individuals from implicit biases, over which they might have otherwise felt they had no control.

In the words of Victor Frankl, Auschwitz survivor, psychiatrist and neurologist (1946),

"Between stimulus and response, there is a space. In that space is our power to choose our response. In our response lies our growth and our freedom."

REFERENCES

Acheson, D.T., Gresack, J. E., and Risbrough, V. B. (2012). Hippocampal dysfunction effects on context memory: possible aetiology for post-traumatic stress disorder. *Neuropharmacology,* 62, 674–685.

Adler, A.B., Bliese, P.D., Mc Gurk, D., Hoge, C.W., Castro, C. A. et al. (2009). Battlemind debriefing and Battlemind training as early interventions with soldiers returning from Iraq. *J Consulting Clin Psychology*. 77, 928-40.

Admon, R., Milad, M.R., Hendler, T. (2013). A causal model of post-traumatic stress disorder: disentangling predisposed from acquired neural abnormalities. *Trends in Cognitive Sciences*, 17, 7, 337-347.

Aguilera, M., Arias, B., Wichers, M., Barrantes-Vidal, N., Moya, J., Villa, H., et al. (2009). Early Adversity and 5-HTT/ BDNF genes: new evidence of gene environment interactions on depressive symptoms in a general population. *Psychol.Med.* 39, 1425–1432.

Ahmed, A. (2007). Post-traumatic stress disorder, resilience and vulnerability. *Advances in Psychiatric Treatment*, 13, 5, 369-375.

Albouy, G., King, B. R., Maquet, P. and Doyon, J. (2013). Hippocampus and striatum: Dynamics and interaction during acquisition and sleep-related motor sequence memory consolidation. *Hippocampus*, 23, 985–1004.

American Psychiatric Association (APA). (1980). *Diagnostic and statistical manual of mental disorders*, (3rd ed.). Washington, DC: Author.

American Psychiatric Association (APA). (2013). *Diagnostic and statistical manual of mental disorders*, (5th ed.). Washington, DC: Author.
http://www.dsm5.org/Documents/PTSD%20Fact%20Sheet.pdf.

Anacker, C., Zunszain, P. A., Cattaneo, A., Carvalho, L. A., Garabedian, M. J., Thuret, S., … Pariante, C. M. (2011). Antidepressants increase human hippocampal neurogenesis by activating the glucocorticoid receptor. *Molecular Psychiatry*, *16*, 7, 738–750.

Andero, R. & Ressler, K.J. (2012). Fear extinction and BDNF: translating animal models of PTSD to the clinic. *Genes, Brain and Behavior*. 11, 5, 503-12.

Andersen, P., Morris, R., Amaral, D., Bliss, T., O'Keefe, J. (Eds). (2007). *The Hippocampus Book.* Oxford University Press: London.

Andersen, S. L., Tomada, A., Vincow, E.S., Valente, E., Polcari, A., Teicher, M.H. (2008). Preliminary evidence for sensitive periods in the effect of childhood sexual abuse on regional brain development. *J Neuropsychiatry Clin Neurosci*, 20, 3, 292-301.

Andridge, R. R., & Little, R. J. A. (2010). A Review of Hot Deck Imputation for Survey Non-response. *International Statistical Review/ Revue Internationale de Statistique*, *78* (1), 40–64.

Anomal, R., de Villers-Sidani, E., Merzenich, M. M., Panizzutti, R. (2013). Manipulation of BDNF Signaling Modifies the Experience-Dependent Plasticity Induced by Pure Tone Exposure during the Critical Period in the Primary Auditory Cortex. *PLoS ONE* 8, 5, e64208. in Doidge, N. (2007) *The brain that changes itself: stories of personal triumph from the frontiers of brain science.* Penguin: London

Apfel, B. A., Ross, J., Hlavin, J., Meyerhoff, D. J., Metzler, T. J, Marmar, C. R., Weiner, M. W., Schuff, N., Neylan, T. C. (2011). Hippocampal volume differences in Gulf War veterans with current versus lifetime posttraumatic stress disorder symptoms. *Biological Psychiatry* 69, 6, 541-548.

Arnold, A. E. G. F., Burles, F., Krivoruchko, T., Liu, I., Rey, C. D., Levy, R. M., et al. (2013). Cognitive mapping in humans and its relationship to other orientation skills. *Exp. Brain Res*. 224, 359–372.

Arnsten, A. Raskind, M.A., Taylor, F.B., Connor, D.F. (2015). The effects of stress exposure on prefrontal cortex: Translating basic research into successful treatments for post-traumatic stress disorder. *Neurobiology of Stress*, 1, 89-99.

Asmundson, G.J.G., Norton, G. R., Allerdings, M. D., Norton, P. J., Larsen, D. L. (1998) Posttraumatic Stress Disorder and Work-Related Injury. *Journal of Anxiety Disorders*, 12, 57–69.

Astur, R. S., St. Germain, S. A., Tolin, D., Ford ,J., Russell, D., and Stevens, M. (2006). Hippocampus function predicts severity of post-traumatic stress disorder. *Cyberpsychol.Behav*. 9, 234–240.

Atwoli, L., Stein, D. J., Koenen, K. C., McLaughlin, K. (2015). Epidemiology of posttraumatic stress disorder: prevalence, correlates and consequences. *Curr Opin Psychiatry*, 28, 307–311

Autry, A. E., & Monteggia, L. M. (2012). Brain-Derived Neurotrophic Factor and Neuropsychiatric Disorders. *Pharmacological Reviews*, *64*, 2, 238–258.

Bagot, R., Parent, C., Bredy, T.W., Zhang, T., Gratton, A., Meaney, M.J. (2007). 'Developmental origins of neurobiological vulnerability for PTSD' in Kirmayer, L. J., Lemelson, R., Barad, M.

(2007). *Understanding Trauma: integrating biological, clinical and cultural perspectives.* Cambridge University Press: Cambridge, UK.

Baker, R., Gale, L., Abbey, G., & Thomas, S. (2013). Emotional processing therapy for post traumatic stress disorder. *Counselling Psychology Quarterly*, 26, 362–385.

Banner, H., Bhat, V., Etchamendy, N., Joober, R., Bohbot, V.D. (2011). The brain-derived neurotrophic factor Val66Met polymorphism is associated with reduced functional magnetic resonance imaging activity in the hippocampus and increased use of caudate nucleus-dependent strategies in a human virtual navigation task. *Eur J Neurosci*, 33, 5, 968-77.

Barrash, J., Damasio, H., Adolphs, R., Tranel, D. (2000). The neuroanatomical correlates of route learning impairment. *Neuropsychologia,* 38, 6, 820-36.

Bastrikova, N., Gardner, G.A., Reece, J.M., Jeromin, A., Dudek, S.M. (2008). "Synapse elimination accompanies functional plasticity in hippocampal neurons". *Proceedings of Natl Acad of Sci of USA,* 105, 8, 3123–27.

Bath, K.G., Jing, D.Q., Dincheva, I., Neeb. C.C., Pattwell,S.S., Chao,M.V., Lee, F.S. Ninan, I. (2012). BDNF Val66Met Impairs Fluoxetine-Induced Enhancement of Adult Hippocampus Plasticity. *Neuropsychopharmacology*, 37, 1297–1304.

Beck, A.T., Steer, R.A. and Brown, G.K. (1996). *Manual for the Beck Depression Inventory-II.* San Antonio, TX: Psychological Corporation.

Beck, J. G., & Coffey, S. F. (2007). Assessment and treatment of PTSD after a motor vehicle collision: Empirical findings and clinical observations. *Professional Psychology, Research and Practice,* 38, 6, 629–639.

Beck, L., Wolter, M., Mungard, N.F., Vohn, R., Staedtgen, M., Kuhlen, T., Sturm, W. (2010). Evaluation of spatial processing in virtual reality using functional magnetic resonance imaging (FMRI). *Cyberpsychol Behav Soc Netw*. 13, 2, 211-5.

Bedard-Gilligan, M. and Zoellner, L.A. (2008). The Utility of the A1 and A2 Criteria in the Diagnosis of PTSD. *Behav Res Ther*. 46, 9, 1062–1069.

De Beni, R., Pazzaglia, F. and Gardini, S. (2006). The role of mental rotation and age in spatial perspective-taking tasks: when age does not impair perspective-taking performance. *Appl. Cognit. Psychol*., 20, 807–821.

Bernstein, D.P, & Fink, L. (1998). *Childhood Trauma Questionnaire: A retrospective self-report manual*, The Psychological Corporation: San Antonio, TX.

Berton, O., McClung, C. A., DiLeone, R. J., Krishnan, V., Renthal, W., Russo, S. J., Graham, D., Tsankova, N. M., Bolanos, C. A., Rios, M., Monteggia, L. M., Self, D. W., Nestler, E. J. (2006). Essential role of BDNF in the mesolimbic dopamine pathway in social defeat stress. *Science,* 311: 864-868.

Beste, C., Baune, B.T., Domschke, K., Falkenstein, M., Konrad, C. (2010). Paradoxical association of the brain-derived-neurotrophic-factor val66met genotype with response inhibition. *Neuroscience*, 166, 178–184.

Bird, C. M., Chan, D., Hartley, T., Pijnenburg, Y., Rossor, M. N., and Burgess, N. (2010). Topographical short-term memory differentiates Alzheimer's disease from frontotemporal lobar degeneration. *Hippocampus* 20, 1154–1169.

Bisby, J. A., King, J. A., Brewin, C. R., Burgess, N., and Curran, H.V. (2010). Acute effects of alcohol on intrusive memory development and viewpoint dependence in spatial memory support a dual representation model. *Biol. Psychiatry,* 68, 280–286.

Bohbot, V.D., Lerch, J., Thorndycraft, B., Iaria, G. & Zijdenbos, A.P. (2007). Gray matter differences correlate with spontaneous strategies in a human virtual navigation task. *J. Neurosci.,* 27, 10078–10083.

Bohbot, V.D., Delbalso, D., Conrad, K., Konishi, K., Leyton, M. (2013). Caudate nucleus-dependent navigational strategies are associated with increased use of addictive drugs. *Hippocampus*, 23, 11, 973-984.

Bonne, O., Gill, J.M., Luckenbaugh, D. A., Collins, C., Owens, M.J., Alesci,S., et al.(2011). Corticotropin- releasing factor,interleukin-6, brain-derived neurotrophic factor, insulin-like growth factor-1,and substance p in the cerebrospinal fluid of civilians with post- traumatic stress disorder before and after treatment with paroxetine. *J.Clin.Psychiatry,* 72, 1124–1128.

Borella, E., Meneghetti, C., Ronconi, L., De Beni, R. (2014). Spatial abilities across the adult life span. *Developmental Psychology*, 50, 2, 384-392.

Brandes, D., Ben-Schachar, G., Gilboa, A., Bonne, O., Freedman, S., Shalev, AY. (2002). PTSD symptoms and cognitive performance in recent trauma survivors. *Psychiatry research,* 110, 3, 231-238.

Bremner, J., Southwick, S., Johnson, D., Yehuda, R., Charney, D. (1993) Childhood physical abuse and combat-related posttraumatic stress disorder in Vietnam veterans. Am J Psychiatry 150(2):235–239

Bremner, J.D. & Elzinga, B.M. (2002). 'Are the neural substrates of memory the final common pathway in posttraumatic stress disorder?' *Journal of Affective Disorders,* 70, 1-17.

Brewin C.R., Dalgleish T., Joseph S. (1996). A dual representation theory of post-traumatic stress disorder. *Psychological Review*, 103, 670–686

Brewin, C.R., Andrews, B. and Valentine, J.D. (2000). Meta-Analysis of Risk Factors for Posttraumatic Stress Disorder in Trauma-Exposed Adults. *Journal of Consulting and Clinical Psychology*, 68, 5, 748-766.

Brewin, C. R., Rose, S., Andrews, B., et al. (2002). Brief screening instrument for post-traumatic stress disorder. *Br. J. Psychiatry*, 181, 158-162.

Brewin, C. & Burgess, N. (2014). Contextualisation in the revised dual representation theory of PTSD: A response to Pearson and colleagues. *J Behav Ther Exp Psychiatry*. 45,1, 217–219.

Brewin, C., Gregory, J. D., Lipton, M., and Burgess, N. (2010). Intrusive images in psychosocial disorders: characteristics, neural mechanisms, and treatment implications. *Psychol. Rev.* 117, 210–232.

Brewin, C. & Holmes, E.A. (2003). Psychological theories of posttraumatic stress disorder. *Clinical Psychology Review*, 23, 339-376.

Brooks, S.J. & Stein, D.J. (2016). A systematic review of the neural bases of psychotherapy for anxiety and related disorders. *Dialogues Clin Neurosci*. 17: 261-276

Browne,T., Hull, L., Horn, O. , Jones, M., Murphy, D. (2007). Explanations for the increase in mental health problems in UK Reserve Forces who have served in Iraq. *Br J Psychiatry,* 190, 484-489.

Bucci, W. (1997). *Psychoanalysis and Cognitive Science: A Multiple Code Theory*. Guildford Press: New York.

Bucci, W. (2001). Pathways of emotional communication. *Psychoanalytic Enquiry*, 21, 40-70.

Buckley, M.G., Smith, A.D., Haselgrove, M. (2015). Learned predictiveness training modulates biases towards using boundary or landmark cues during navigation. *The Quarterly Journal of Experimental Psychology*, 68, 6.

Buckley, M. B., Smith, A. D., & Haselgrove, M. (2016). Blocking spatial navigation across environments that have a different shape. Journal of Experimental Psychology: Animal Learning and Cognition, 42, 51-66.

Bueller, J.A., Aftab, M., Sen, S., Gomez-Hassan, D., Burmeister, M., Zubieta, J.K. (2006). BDNF Val66Met 585 allele is associated with reduced hippocampal volume in healthy subjects. *Biol Psychiatry* 59, 9, 812–5.

Burgess, N. *in press.* Spatial memory: how egocentric and allocentric combine. *Trends in Cognitive Neurosciences.*

Burgess N, Becker S, King JA, O'Keefe J*. (*2001). *Memory for events and their spatial context: models and experiments. Phil. Trans. R. Soc. Lond. B 356, 1493–1503.*

Burgess, N. (2008). *Spatial Cognition and the Brain*. Annals of the New York Academy of Sciences, 1124: 77–97.

Burgess, N., Spiers, H., Paleologou, E. (2005). Orientational manoeuvres in the dark: Dissociating allocentric and egocentric influences on spatial memory*. Cognition* 94, 2, 149-66.

Burns, P.C. (1999). Navigation and the mobility of older drivers. *Journal of gerontol b psychol* Sci Soc Sci, 54: 49-55.

Butler, D.J. & Moffic, H.S. (1999). Post-traumatic stress reactions following motor vehicle accidents. *American Family Physician,* 1, 60, 2, 524-530.

Byrne, P., Becker, S. Burgess, N. (2007). Remembering the past and imagining the future: A neural model of spatial memory and imagery. *Psychol. Rev.,* 114, 340-75.

Calabrese, F., van der Doelen, R.H., Guidotti, G., Racagni ,G., Kozicz, T., Homberg ,J.R., Riva, M.A. (2015). Exposure to early life stress regulates BDNF expression in SERT mutant rats in an anatomically selective fashion. *J Neurochem* 132, 1, 146-54.

Caldwell, W., McInnis, O.A., Mc Quaid, R.J., Liu, G., Stead, J.D., et al. (2013). The Role of the Val66Met Polymorphism of the Brain-Derived Neurotrophic Factor Gene in Coping Strategies. DOI:10.1371/journal.pone.0065547

Campbell, D. G., Felker, B. L., Liu, C.-F., Yano, E. M., Kirchner, J. E., Chan, D., Chaney, E. F. (2007). Prevalence of Depression–PTSD Comorbidity: Implications for Clinical Practice Guidelines and Primary Care-based Interventions. *Journal of General Internal Medicine*, *22*, 6, 711–718.

Campbell, Z., Zakzanis, K.K., Jovanovski, D., Joordens, S., Mraz, R., Graham, S.J. (2009). Utilizing virtual reality to improve the ecological validity of clinical neuropsychology: an FMRI case study elucidating the neural basis of planning by comparing the Tower of London with a three-dimensional navigation task. *Appl Neuropsychol*. 16, 4, 295-306.

Carballedo, A., Morris, D., Zill, P., Fahey, C., Reinhold, E., Meisenzahl, E., Bondy, B., Gill, M., Möller, H.J., Frodl, T.(2013). Brain-derived neurotrophic factor Val66Met polymorphism and early life adversity affect hippocampal volume. *Am J Med Genet B Neuropsychiatr Genet*.162B, 2, 183-90.

Cardoso-Cruz, H., Lima, D., Galhardo, V. (2013). Impaired spatial memory performance in a rat model of neuropathic pain is associated with reduced hippocampus-prefrontal cortex connectivity. *J Neurosci* , 33, 2465–2480.

Casey, B. J.,Glatt, C.E., Tottenham, N., Soliman, F., Bath, K., Amso, D., et al.(2009). Brain-derived neurotrophic factor as a model system for examining gene by environment interactions across development. *Neuroscience,* 164, 108–120.

Cerasa, A., Tongiorgi , E., Fera, F., Gioia, M.C., Valentino, P., Liguori, M., Manna, I,, Zito, G., Passamonti , L., Nistico, R., Quattrone, A .(2010). The effects of BDNF Val66Met polymorphism on brain function in controls and patients with multiple sclerosis: an imaging genetic study. *Behav Brain Res.,* 207, 2, 377–386.

Chaieb, L., Antal, A., Ambrus, G.G., Paulus, W. (2014). Brain-derived neurotrophic factor: its impact upon neuroplasticity and neuroplasticity inducing transcranial brain stimulation protocols. *Neurogenetics*, 15, 1, 1-11.

Chen, Z. Y., Jing, D., Bath, K. G., Ieraci, A., Khan, T.,Siao, C.J., et al.(2006). Genetic variant BDNF (Val66Met) polymorphism alters anxiety-related behavior. *Science* 314, 140–143.

Clarke, S., Kingston, J., James, K., Bolderston, H. and Remington, B. (2016). Acceptance and Commitment Therapy group for treatment-resistant participants: A randomized controlled trial *Journal of Contextual Behavioral Science*, 2212-1447.

Clelland, C. D., Choi, M., Romberg, C., Clemenson, G. D. Jr., Fragniere, A., Tyers, P. et al.(2009). A functional role for adult hippocampal neurogenesis in spatial pattern separation. *Science*, 325, 210–213.

Colzato, L.S., van Muijden, J., Band, G.P., Homme, B. (2011). Genetic Modulation of Training and Transfer in Older Adults: BDNF ValMet Polymorphism is Associated with Wider Useful Field of View. *Frontiers in Psychology*, 2, 199.

Combat Stress (2012). Annual Report 2011–12. [Registered charity206002]. Available online at: http://www.combatstress.org.uk/media/56 674/combat_stress_annual_review_2011-12.pdf.

Conrad, C. D. (2006). What Is the Functional Significance of Chronic Stress-Induced CA3 Dendritic Retraction Within the Hippocampus? *Behavioral and Cognitive Neuroscience Reviews*, *5*, 1, 41–60.

Dalgleish, T. (2004). Cognitive theories of posttraumatic stress disorder: The evolution of multi-representational theorizing. *Psychological Bulletin, 130*, 228-260.

Dalgleish, T. and Power, M.J. (2004) 'Emotion-specific and emotion non-specific components of PTSD: implications for a taxonomy of related psychopathology'. *Behavioural Research and Therapy,* 42, 1069-1088.

Dalvie, S., Stein, D.J., Koenen, K., Cardenas, V., Cuzenz, N. L., Ramesar, R., Fein, G., and Brooks, S.J. (2014). The BDNF Val66Met polymorphism, childhood trauma, and brain volumes in adolescents with alcohol abuse. *BMC Psychiatry*, 14, 328- 336.

Dandeker ,C., Eversden-French, C., Greenberg, N., Hatch, S., Riley, P., van Staden, L., et al. (2010). Laying down their rifles: the changing influences on the retention of volunteer British Army reservists returning from Iraq, 2003–2006. *Armed Forces Soc* , 36, 264–89.

Daugherty, A.M., Yuan, P. Dahle, C.L., Bender, A.R., Yang, Y.,Raz, N. (2015). Path Complexity in Virtual Water Maze Navigation: Differential Associations with Age, Sex, and Regional Brain Volume. *Cereb. Cortex*, 25, 9, 3122-3131.

Davidson, R.J., Kabat-Zinn, J., Schumacher, J., Rosenkranz, M., Muller, D., Santorelli, S.F., Urbanowski, F., Harrington, A. Bonus, K., Sheridan, J.F. (2003). Alterations in Brain and Immune Function Produced by Mindfulness Meditation. *Psychosomatic Medicine* 65, 564 –570.

Davidson, J. R. T., Book, S. W., Colket, J. T., Tupler, L. A., Roth, S., David, D., Hertzberg, M., Mellman, T., Beckham, J. C., Smith, R., Davison, R. M., Katz, R., & Feldman, M. (1997). *Assessment of a new self-rating scale for post-traumatic stress disorder*. Psychological Medicine, 27, 153-160.

De Araujo, I.E., Rolls, E.T., Stringer, S.M. (2001). A view model which accounts for the spatial fields of hippocampal primate spatial view cells and rat place cells. *Hippocampus*.11, 6, 699-706.

Deadwyler, S.A., Bunn, T., Hampson, R.E. (1996). Hippocampal ensemble activity during spatial delayed-non match-to-sample performance in rats. *The Journal of Neuroscience*, 16, 1, 354-372.

Dell'Osso, L., Carmassi, C., Del Debbio, A. , Dell' Osso, M. C., Bianchi, C., da Pozzo, E. et al.(2009).Brain-derived neurotrophic factor plasma levels in patients suffering from post-traumatic stress disorder. *Prog. Neuropsychopharmacol. Biol.Psychiatry,* 33, 899–902.

Dempster, E., Toulopoulou, T., McDonald, C., Bramon, E., Walshe, M., Filbey, F., Wickham, H., Sham, P.C., Murray, R.M. & Collier, D.A. (2005). Association between BDNF val66 met genotype and episodic memory. *Am. J. Med. Genet. B Neuropsychiatr. Genet*., 134B, 73–75.

Dennis, N. A., Cabeza, R., Need, A. C., Waters-Metenier, S., Goldstein, D. B., LaBar, K. S. (2011). Brain-derived neurotrophic factor val66met polymorphism and hippocampal activation during episodic encoding and retrieval tasks. *Hippocampus,* 21, 980–989.

Department of Health (2008). *Code of Practice: Mental Health Act 1983*. The Stationary Office (TSO): London.

DiMaggio, C. & Galea, S. (2006). The behavioral consequences of terrorism: a meta-analysis. *Academic Emergency Medicine*, 13, 559–566.

Dodds, C.M., Henson R.N., Miller, S.R., Nathan, P.J. (2013). Overestimation of the effects of the BDNF val66met polymorphism on episodic memory-related hippocampal function: a critique of a recent meta-analysis*. Neurosci Biobehav Rev.*, 37,4, 739–741.

Doidge, N. (2007). *The Brain that Changes Itself: Stories of Personal Triumph from the Frontiers of Brain Science*. James H. Silberman Books. Penguin: London.

Driscoll, I., Hamilton, D.A., Yeo, R.A., Brooks, W.M., Sutherland, R.J. (2005). Virtual navigation in humans: the impact of age, sex, and hormones on place learning. *Horm Behav*.47, 326–335.

Dror, I.E., Schmitz-Williams, I.C., Smith, W. (2005). Older adults use mental representations that reduce cognitive load: mental rotation utilizes holistic representations and processing. *Exp Aging Res.* 31, 409–4.

Duax, J. M.; Waldron-Perrine, B.; Rauch, S. A. M.; Adams, K. M. (2013). Prolonged exposure therapy for a Vietnam veteran with PTSD and early-stage dementia. *Cognitive and Behavioral Practice*. 20, 1, 64-73.

Dudchenko, P. (2010). *Why people get lost; the psychology and neuroscience of spatial cognition.* Oxford University Press: Oxford.

Duke, L. M. & Vasterling, J. J. (2005). Epidemiological and Methodological Issues in Neuropsychological Research on PTSD. In Vasterling, J. J. & Brewin, C.R. (eds). *Neuropsychology of PTSD: Biological, Cognitive and Clinical Perspectives.* Guildford Press: London.

Duman, R.S. & Monteggia, L. M. (2006). A neurotrophic model for stress-related mood disorders. *Biol. Psychiatry* 59, 1116–1127.

Duric, V., McCarson, K.E. (2005). Hippocampal neurokinin-1 receptor and brain-derived neurotrophic factor gene expression is decreased in rat models of pain and stress. *Neuroscience*, 133, 4, 999-1006.

Duric, V., McCarson, K.E. (2006). Persistent Pain Produces Stress-like Alterations in Hippocampal Neurogenesis and Gene Expression. *The Journal of Pain*, 7, 8, 544-555.

Egan, M. F., Kojima, M., Callicott, J. H., Goldberg, T.E., Kolachana, B.S., Bertolino, A., et al. (2003). The BDNF val66met polymorphism affects activity-dependent secretion of BDNF and human memory and hippocampal function. *Cell,* 112, 257–269.

Ehlers, A. & Clark, D. M. (2000). A cognitive model of post-traumatic stress disorder. *Behav.Res.Ther.* 38, 313–345.

Ehlers, A., Mayou, R.A. & Bryant, B. (1998) Psychological predictors of chronic posttraumatic stress disorder after motor vehicle accidents. *Journal of Abnormal Psychology* , 107, 508-519.

Ehring, T., Ehlers, A., Glucksmanb. E. (2006). Contribution of cognitive factors to the prediction of post-traumatic stress disorder, phobia and depression after motor vehicle accidents. *Behaviour Research and Therapy* 44; 1699–1716.

Eich, E., Handy, T.C., Holmes, E.A., Lerner, J. and Mc Isaac, H. (2011). 'Field and observer perspectives in autobiographical memory'. 14th *Sydney Symposium on Social Psychology*. University of South Wales, 15-17 March 2011.

Eichenbaum H. (1997). How does the brain organize memories. *Science,* 277, 330–332.

Eichenmbaum, H. (2000). A corticol-hioppocampal system for declarative memory. *Nature Re views Neuroscience.* Macmillan Magazines. Vol 1.

Ekstrom, A. D., Aiden, E. G. F., Giuseppe, I. (2014). A critical review of the allocentric spatial representation and its neural underpinnings: Toward a network-based perspective. *Frontiers in Human Neuroscience,* 8, 0803.

Elzinga, B.M. & Bremner, J.D. (2002). Are the neural substrates of memory the final common pathway in posttraumatic stress disorder (PTSD)? *J Affect Disord*.70,1, 1-17.

Elzinga, B. M., Molendijk, M. L., Oude Voshaar, R. C., Bus, B. A., Prickaerts, J., Spinhoven, P., et al. (2011). The impact of childhood abuse and recent stress on serum brain-derived neurotrophic factor and the moderating role of BDNF Val66Met. *Psychopharmacology*, 214, 319–328.

Engel, D., Zomkowski, A. D. E., Lieberknecht, V., Rodrigues, A. L., Gabilan, N. H. (2013). Chronic administration of duloxetine and mirtazapine downregulates proapoptotic proteins and upregulates neurotrophin gene expression in the hippocampus and cerebral cortex of mice. *Journal of Psychiatric Research*, 47, 6, 802-808.

Epstein, S. (1985). The implications of cognitive-experiential self-theory for research in social psychology and personality. *Journal of the Theory of Social Behaviour*, 15, 283-310.

Epstein, R.A., Higgins, S.J., Thompson-Schill, S. (2013). Learning Places from Views: Variation in Scene Processing as a Function of Experience and Navigational Ability. *Journal of Cognitive Neuroscience,* 17, 1, 73–83.

Erickson, K.I., Prakash, R.S., Voss, M.W., Chaddock, L., Heo, S., McLaren, M., Pence, B.T., Martin, S.A., Viera, V.J., Woods, J.A., McAuley, E., and Kramer, A.F. (2010). Brain-derived neurotrophic factor is associated with age-related decline in hippocampal volume. *J Neurosci.,* 30,5368 – 5375.

Erwin, E. (2003). *The Freud Encyclopaedia*. Routledge: London.

Evans, T., Bicanski, A., Bush, D., Burgess, N. (2015). How environment and self-motion combine in neural representations of space. *The Journal of Physiology.* DOI: 10.1113/JP270666

Fanselow, M.S. & Dong, H-W. (2010). Are the Dorsal and Ventral Hippocampus Functionally Distinct Structures? *Neuron,* 65, 7-20.

Farb, N.A., Segal, Z.V., Mayberg, H., Bean, J., McKeon, D., Fatima, Z., Anderson, A.K. (2007). Attending to the present: mindfulness meditation reveals distinct neural modes of self-reference. *Soc Cogn Affect Neurosci*., 2,4, 313-22.

Farhadi, H.F., Mowla, S.J., Petrecca, K., Morris, S.J., Seidah, N.G., Murphy, R.A. (2000). Neurotrophin-3 sorts to the constitutive secretory pathway of hippocampal neurons and is diverted to the regulated secretory pathway by co-expression with brain-derived neurotrophic factor. *J. Neurosci.* 20, 4059–4068.

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, *39*, 175-191.

Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. (2009). Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods*, *41*, 1149-1160.

Featherstone, R, E. & McDonald, R.J. (2004). Dorsal striatum and stimulus response learning: lesions of the dorsolateral, but not dorsomedial, striatum impair acquisition of a simple discrimination task. *Behav Brain Res,* 150:15–23.

Felmingham, K. L., Dobson-Stone, C., Schofield, P. R., Quirk, G. J., and Bryant, R. A. (2013).The brain-derived neurotrophic factor val66met polymorphism predicts response to exposure therapy in post-traumatic stress disorder. *Biol. Psychiatry,* 73, 1059–1063.

Fernandez-Seara, M.A., Aznarez-Sanado, M., Mengual, E., Loayza, F.R., Pastor, M.A. (2009). Continuous performance of a novel motor sequence leads to highly correlated striatal and hippocampal perfusion increases. *Neuroimage,* 47, 1797–1808.

Field, A. P. (2000). *Discovering statistics using SPSS for Windows: advanced techniques for the beginner.* Sage: London.
Field, A.P. (2013). *Discovering statistics using IBM SPSS Statistics: And sex drugs and rock 'n' roll* (4th ed.). Sage: London

Filipas, H. H. & Ullman, S. E. (2006). Child sexual abuse, coping responses, self-blame, posttraumatic stress disorder, and adult sexual re-victimization. *Journal of Interpersonal Violence*, 21, 652–672.

First, M.B., Gibbon, M., Spitzer, R.L., Williams, J.B.W., Benjamin, L.S. (1997). Structured Clinical Interview for DSM-IV Axis II Personality Disorders, (SCID-II). Washington, D.C.: American Psychiatric Press, Inc.

Foa, E. (1995). *Post-Traumatic Stress Diagnostic Scale*. National Computer Systems: Minneapolis.

Foa, E. B. & Kozak, M. J. (1986). Emotional processing of fear - exposure to corrective information. *Psychological Bulletin, 99*, 20-35.

Foa, E.B. & Rothbaum, B.O. (1998). *Treating the trauma of rape: cognitive behavioral therapy for PTSD*. Guilford Press: New York.

Foa, E.B, Cashman L, Jaycox, L.H., Perry, K. (1997).The validation of a self-report measure of PTSD: The PTSD Diagnostic Scale. *Psychological Assessment*, 9, 445–451.

Frank, V. (1946) *Man's Search for Meaning*. Beacon Press: Vienna.

Frankland, P.W., Cestari, V., Filipkowski, R.K., McDonald, R.J. & Silva, A.J. (1998). The dorsal hippocampus is essential for context discrimination but not for contextual conditioning. *Behav. Neurosci*., 112, 863–874. 47

Freud, S. (194, 1936). *The problem of anxiety*. Psychoanalytic Quarterly Press: New York.

Frielingsdorf, H., Bath, K. G., Soliman, F., Difede, J., Casey, B. J., and Lee, F.S. (2010).Variant brain-derived neurotrophic factor Val66Met endophenotypes: implications for post-traumatic stress disorder. *Ann.N.Y.Acad.Sci.* 1208, 150–157.

Fuchikami, M., Morinobu, S., Segawa, M., Okamoto, Y., Yamawaki, S., Ozaki , N. et al. (2012). DNA methylation profiles of the brain-derived neurotrophic factor (BDNF) gene as a potent diagnostic biomarker in major depression. *Plos One*; 6: 8.

Furman, A. J., Clements-Stephens, A. M., Marchette, S.A., & Shelton, A.L. (2014). Persistent and stable biases in spatial learning mechanisms predict navigational style. *Cogn Affect Behav Neurosci*. Special issue. DOI 10.3758/s13415-014-0279-6.

Ganis, G. & Kievit, R. (2015). A New Set of Three-Dimensional Shapes for Investigating Mental Rotation Processes: Validation Data and Stimulus Set. *Open Psychology Data,* 3, 1. [Data set].

Gatt, J. M., Nemeroff, C. B., Dobson-Stone, C., Paul, R. H., Bryant, R. A., Schofield, P. R., et al. (2009). Interactions between BDNF Val66Met polymorphism and early life stress predict brain and arousal pathways to syndromal depression and anxiety. *Mol. Psychiatry* 14, 681–695.

Gee, D. (2013). *The Last Ambush? Aspects of mental health in the British armed forces.* Forces Watch: London

Germain, A., Hall, M., Krakow, B., Shear, M.K., Buysse, D.J. (2005). A brief sleep scale for posttraumatic stress disorder: Pittsburgh Sleep Quality Index Addendum for PTSD. *J Anxiety Disord*.,19, 233–44.

Gerlai, R. (2001). Behavioral tests of hippocampal function: simple paradigms complex problems. *Behav. Brain Res*., 125, 269–277.

Gheysen, F., Van Opstal, F., Roggeman, C., Van Waelvelde, H., Fias, W. (2010). Hippocampal contribution to early and later stages of implicit motor sequence learning. *Exp Brain Res.,* 202, 795–807.

Gilbertson, M. W., Shenton, M. E., Ciszewski, A., Kasai, K., Lasko, N. B., Orr, S. P., et al. (2002). Smaller hippocampal volume predicts pathologic vulnerability to psychological trauma. *Nat. Neurosci*. 5, 1242–1247.

Gilbertson, M. W., Williston, S. K., Paulus, L. A., Lasko, N. B., Gurvits, T. V., Shenton, M. E. (2007). Configural cue performance in identical twins discordant for posttraumatic stress disorder: theoretical implications for the role of hippocampal function. *Biol. Psychiatry* 62, 513–520.

Glazer, D.A., Mason, O., King, J.A., Brewin, C.R. (2013). Contextual memory, psychosis-proneness, and the experience of intrusive imagery. *Cognition and Emotion,* 27, 150–157

Goodman, L.J., Valverde, J., Lim, F., Geschwind, M.D., Federoff, C H.J., Geller, A.I., and Hefti, F. (1996). Regulated release and polarized localization of brain-derived neurotrophic factor in hippocampal secretion. *Mol. Cell. Neurosci.* 7, 223–228.

Gorgoni, M., D'Atri, A., Lauri, G., Rossini, P.M., Ferlazzo, F., De Gennaro, L. (2013). Is Sleep Essential for Neural Plasticity in Humans, and How Does It Affect Motor and Cognitive Recovery? *Neural Plasticity*, 103949, 13.

Gottesman, I .I. & Gould, T. D. (2003).The endophenotype concept in psychiatry: etymology and strategic intentions. *Am.J.Psychiatry* 160, 636–645.

Gray, J. & McNaughton, N. (2003).*The neuropsychology of anxiety: an enquiry into the functions of the septohippocampal system*. 2nd ed. Oxford: Oxford University Press.

Griesel, D., Wesser, M., and Flor, H. (2006). Psychometric Qualities of the German Version of the Post-traumatic Diagnostic Scale (PTDS). *Psychological Assessment*. 18, 3, 262–268.

Guzowski, J.F., Setlow, B., Wagner, E.K., Mc Gaugh, J.L. (2001). Experience-dependent gene expression in the rat hippocampus after spatial learning: a comparison of the immediate-early genes Arc, c-fos, and zif268. *J Neurosci.*15;21, 14; 5089-98.

Hacker Hughes J., Earnshaw, M., Greenberg, N., Eldridge, R., Fear, N., French, C., Deahl, M., Wessely, S. (2008). The use of psychological decompression in military operational environments. *Mil Medicine*, 173: 534-538.

Hajek, T., Kopecek, M., Hoschl, C. (2012). Reduced hippocampal volumes in healthy carriers of brain-derived neurotrophic factor Val66Met polymorphism: meta-analysis. *World J Biol Psychiatry*,13, 3, 178–87.

Halko, M.A., Connors, E.C., Sanchez, J. and Merabet, L.B. (2014). Real world navigation independence in the early blind correlates with differential brain activity associated with virtual navigation. *Hum Brain Mapp*. 35, 6, 2768–2778.

Handley, R., Salkovskis, P. M., Hackmann, A. and Ehlers, A. (2009). *Travel, trauma, and phobia: Treating the survivors of transport-related trauma*. London: Routledge, pp. 31-48.

Hansell, N.K., James, M.R., Duffy, D.L., Birley, A.J., Luciano, M., Geffen, G.M., Wright, M.J., Montgomery, G.W., Martin, N.G. (2007). Effect of the BDNF V166M polymorphism on working memory in healthy adolescents. *Genes Brain& Behavior*, 6, 260–268.

Hanson, R. (2011) The Enlightened Brain: The neuroscience of awakening. Sounds True Inc. Audio Book.

Hariri, A.R., Goldberg, T.E., Mattay, V.S., Kolachana, B.S., Callicott, J.H., Egan, M.F. & Weinberger, D.R. (2003). Brain-derived neurotrophic factor val66met polymorphism affects human memory-related hippocampal activity and predicts memory performance*. J. Neurosci.*, 23, 6690–6694.

Hart, J., Kimbrell, T., Fauver, P., Cherry, B.J., Pitcock, J., Booe, L.Q., Tillman, G., . Freeman, T.W. (2008). Cognitive Dysfunctions Associated With PTSD: Evidence from World War II Prisoners of War. The *Journal of Neuropsychiatry and Clinical Neurosciences*; 20:309-316.

Hartley T., Bird C, M., Chan, D., Cipolotti, L., Husain, M., Vargha-Khadem, F., Burgess, N. (2007). The hippocampus is required for short-term topographical memory in humans. *Hippocampus*, 17, 1, 34-48.

Hartley, T. & Harlow, R. (2012). An association between human hippocampal volume and topographical memory in healthy young adults. *Frontiers in Human Neuroscience* 6, 338.

Hartley, T., Lever, C., Burgess, N., O'Keefe, J. (2013). Space in the brain: how the hippocampal formation supports spatial cognition. *Phil.Trans.R.Soc.B.*369, 201201510.

Hashimoto, R., Moriguchi, Y., Yamashita, F., Mori ,T., Nemoto, K., Okada, T., Hori, H., Noguchi, H,, Kunugi ,H., Ohnishi, T. (2008). Dose-dependent effect of the Val66Met polymorphism of the brain-derived neurotrophic factor gene on memory-related hippocampal activity. *Neurosci Res*. 61,4, 360-7.

Hasler, G., Drevets, W.C., Manji, H.K., Charney, D. S. (2004). Discovering endophenotypes for major depression. *Neuropsychopharmacology*, 29, 1765–1781.

Hauck, S., Kapczinski, F., Roesler, R., de Moura Silveira Jr E., Magalhaes, P.V., Kruel, L.R. et al. (2010). Serum brain-derived neurotrophic factor in patients with trauma psychopathology. *Prog Neuropsychopharmacol Biol Psychiatry,* 34, 459–462.

Hayes, S.C. (2004). Acceptance and Commitment Therapy and the third wave of behavioural and cognitive therapies. *Behavioural Therapy*, 35, 639-665.

Hegarty, M., Richardson, A., Montello, D., Lovelace, K., & Subbiah, I. (2002). Development of a self-report measure of environmental spatial ability. *Intelligence*, 30, 5, 425-447.

Heinonen, I., Kalliokoski, K.K., Hannukainen, J.C., Duncker , D.J., Nuutila, P., Knuuti, J. (2014). Organ-Specific Physiological Responses to Acute Physical Exercise and Long-Term Training in Humans. *Physiology (Bethesda)* 29, 6, 421–436.

Heldt, S.A., Stanek, L., Chhatwal, J.P., Ressler, K.J. (2007). Hippocampus-specific deletion of BDNF in adult mice impairs spatial memory and extinction of aversive memories. *Mol Psychiatry, 1*2, 7, 656–670.

Hemmings, S. M. J., Martin, L.I., Klopper, M., van der Merwe, L. , Aitken, L., De Wit, E. et al. (2012). BDNF val66met and drd2taq1a polymorphisms interact to influence PTSD symptom severity: a preliminary investigation in a South African population. *Progr. Neuropsychopharmacol. Biol. Psychiatry* 40, 273–280.

Hemmings, S.L., Lochner, C., Van der Merwe, L., Cath, D.C., Seedat, S. and Stein, D.J. (2013). BDNF Val66Met modifies the risk of childhood trauma on obsessive-compulsive disorder. *Journal of Psychiatric Research,* 1-7.

Hemmy-Asamsama, O., Dickstein, B.D., Chard, K.N. (2015). Do Scores on the Beck Depression Inventory-II Predict Outcome in Cognitive Processing Therapy? P*sychological Trauma: Theory, Research, Practice, and Policy*. No Pagination Specified.

Hofer, M., Pagliusi, S. R., Hohn, A., Leibrock, J., & Barde, Y. A. (1990). Regional distribution of brain-derived neurotrophic factor mRNA in the adult mouse brain. *The EMBO Journal*, 9, 8, 2459–2464.

Hoge, C. W. (2011). Interventions for War-Related Posttraumatic Stress Disorder: Meeting Veterans Where They Are. *JAMA*, 306, 5, 549-551.

Holmes, E. A., James, E.L., Kilford, E.J., Deeprose, C. (2010). Key Steps in Developing a Cognitive Vaccine against Traumatic Flashbacks: Visuospatial Tetris versus Verbal Pub Quiz. *PLoS ONE,* 5, 11, e13.

Holzel, B.K., Carmody, J., Congleton, C., Yerramsetti, S.M., Gard, T. and Lazar, S.W. (2010). Mindfulness practice leads to increases in regional brain gray matter density. P*sychiatry Research: Neuroimaging,* 191, 36-43.

Horowitz, M.J. (1986). *Stress response syndromes* (2nd ed.). Northvale, NJ: Jason Aronson.

Horowitz, M.J. (ed) (1999). *Essential Papers on PTSD*. New York University Press: New York.

Houston, J.B., Spialek, M.L., Perreault MF. (2015). Coverage of Posttraumatic Stress Disorder (PTSD) in the New York Times, 1950-2012. *J Health Commun. [Epub ahead of print*]

Huang, Z.J., Kirkwood, A., Pizzorusso, T., Porciatti, V., Morales, B., Bear, M.F., Maffei, L., Tonegawa, S. (1999). BDNF regulates the maturation of inhibition and the critical period of plasticity in mouse visual cortex. Cell. 17, 98, 6,739-55.

Iaria, G., Petrides, M., Dagher, A., Pike, B., Bohbot, V.D. (2003). Cognitive strategies dependent on the hippocampus and caudate nucleus in human navigation: Variability and change with practice. *J Neurosci*, 23, 5945–5952.

Jacobs, W.J., Nadel, L. (1985). Stress-induced recovery of fears and phobias. *Psychological Review*, 92, 512–531.

Janoff-Bulman, R. (1992). *Shattered assumptions: Towards a new psychology of trauma*. Free Press: New York.

Janzen, G., Jansen, C. and Turennout, M. V. (2008). Memory consolidation of landmarks in good navigators. *Hippocampus*, 18: 40–47.

Jensen, M.P., Karoly, P., Braver, S., (1986). The measurement of clinical pain intensity: a comparison of six methods. *Pain*, 27, 117-26.

Jia, J.-M., Chen, Q., Zhou, Y., Miao, S., Zheng, J., Zhang, C., & Xiong, Z.-Q. (2008). Brain-derived Neurotrophic Factor-Tropomyosin-related Kinase B Signaling Contributes to Activity-dependent Changes in Synaptic Proteins. *The Journal of Biological Chemistry*, 283, 30, 21242–21250.

Ji, J., & Maren, S.(2008). Differential roles for hippocampal areas CA1and CA3 in the con textual encoding and retrieval of extinguished fear. *Learn.Mem*. 15, 244–251.

Joffe, R.T., Gatt, J.M., Kemp, A.H., Grieve, S., Dobson-Stone, C., Kuan, S. et al. (2009). Brain derived neurotrophic factor Val66Met polymorphism, the five factor model of personality and hippocampal volume: implications for depressive illness. *Hum Brain Mapp*; published online 16 September 2008 (in press).

Jones, E. & Wessely, S. (2005). War Syndromes: The Impact of Culture on Medically Unexplained Symptoms. *Medical History*, 49: 55–78.

Jones, E. & Wessely, S. (2006). Psychological trauma: a historical perspective. *Psychiatry: History, Epidemiology, Treatment,* 5: 7, 217-220.

Kabat-Zinn, J. (2013). *Full Catastrophe Living: How to cope with stress, pain and illness using mindfulness meditation*. Piatkus, US.

Kambeitz, J.P., Bhattacharyya, S. Kambeitz-Ilankovic, L.M., Valli, I., Collier, D.A., McGuire, P. (2012). Effect of BDNF val(66)met polymorphism on declarative memory and its neural substrate: a meta-analysis. *Neurosci Biobehav Rev,* 36, 9, 2165–2177

Kaplan, R., Horner, A.J., Bandettini, P.A., Doeller, C.F., Burgess, N. (2014). Human hippocampal processing of environmental novelty during spatial navigation. *Hippocampus*, 24: 740-750.

Karnik, M.S., Wang, L. Barch, D.M., Morris, J., Csernansky, J.G. (2010). BDNF polymorphism rs6265 and hippocampal structure and memory performance in healthy control subjects. *Psychiatry Res.* 178, 2, 425-429.

Karunakara, U. K., Neuner, F., Schauer, M., et al. (2004). Traumatic events and symptoms of post-traumatic stress disorder amongst Sudanese nationals, refugees and Ugandans in the West Nile. *African Health Sciences*, 4, 83–93.

Kaur, M., Murphy, D., Smith, K.V. (2016) *The Cognitive Behaviour Therapist*, 9, e10. DOI: 10.1017/sS1754470X16000052.

Kemp, A.H., Gordon, E., Rush, A.J., Williams, L.M. (2008). Improving the prediction of treatment response in depression: Integration of clinical, cognitive, psychophysiological, neuroimaging and genetic measures. *CNS Spectrums*, 13, 1066–1086.

Kesner, R.P., Hunsaker, M.R., Warthen, M.W. (2008). The CA3 subregion of the hippocampus is critical for episodic memory processing by means of relational encoding in rats. *Behav Neurosci*.122, 6, 1217-25.

Van Kesteren, M.T.R., Beul, S.F., Takashima, A., Henson, R. Ruiter, D.J., Fernandez, G. (2013). Differential roles for medial prefrontal and medial temporal cortices in schema-dependent encoding: From congruent to incongruent. *Neuropsychologia,* 51, 12, 2352- 2539.

King, J. A., Burgess, N., Hartley, T., Vargha-Khadem, F., & O'Keefe, J. (2002). Human hippocampus and viewpoint dependence in spatial memory. *Hippocampus*, 12, 811–820. DOI: 10.1002/hipo.10070

King, J. A., Trinkler, I., Hartley, T., Vargha-Khadem, F., & Burgess, N. (2004). The hippocampal role in spatial memory and the familiarity-recollection distinction: A case study. Neuropsychology, 18, 405–417.

King's Centre for Military Health Research (KCMHR). (2010) *A fifteen year report: What has been achieved by fifteen years of research into the health of the UK Armed Forces?* KCMHR King's College London: London.

Kirmayer, L. J., Lemelson, R., Barad, M. (2007). *Understanding Trauma: integrating biological, clinical and cultural perspectives.* Cambridge UK: Cambridge University Press.

Kleim, J.A., Chan, S., Pringle, E., Schallert, K., Procaccio, V., Jimenez, R., Cramer, S.C. (2006). BDNF val66met polymorphism is associated with modified experience-dependent plasticity in human motor cortex. *Nat Neurosci.* 9, 735--737.

Klencken, G., Despres, O. and Dufour, A. (2012). What do we know about aging and spatial cognition? Reviews and Perspectives. *Aging Research Reviews* II, 123-135

Knauss, L.G. (2007). Effects of Psychological Stress and Posttraumatic Stress Disorder Symptoms on Cognition: *Madigan Army Medical Center* (Presented at the Pacific Northwest Neuropsychological Society, PNNS Annual Meeting March 3rd 2007).

Koenen, K. C., Amstadter, A.B., and Nugent, N. R. (2009). Gene-environment interaction in post-traumatic stress disorder: an update. *J. Trauma.Stress,* 22, 416–426.

Kolassa, I.T., Kolassa, S., Ertl, V., Papassotiropoulos, A., De Quervain, D.J. (2012). The risk of posttraumatic stress disorder after trauma depends on traumatic load and the catechol-o-methyltransferase Val(158)Met polymorphism. *Biol Psychiatry*, 15, 67,4, 304-8.

Kong, X-Z., Song, Y., Zhen, A., Liu, J. (2016). Genetic Variation in S100B Modulates Neural Processing of Visual Scenes in Han Chinese. *Cereb. Cortex Journal of Neuropathy and Experimental Neurology.* 10.1093.

Kowitz, S. (2011). Thesis: Childhood trauma as a vulnerability to psychopathology after subsequent trauma in adulthood. Monash University, Melbourne Australia. https://view.officeapps.live.com/op/view.aspx?src=http%3A%2F%2Fwww.med.monash.edu.au%2Fpsych%2Fstudents%2Fcurrent%2Fdownload%2Fthesis-cataloguing-v2.xlsx

Krueger, F., Pardini, M., Huey ED, Raymont ,V., et al. (2011).The Role of the Met66 Brain-Derived Neurotrophic Factor Allele in the Recovery of Executive Functioning after Combat-Related Traumatic Brain Injury. *Journal of Neuroscience;* 31, 2, 598–606.

Krueger, R. F., Markon, K. E., Patrick, C. J., Benning, S. D., & Kramer, M. D. (2007). Linking Antisocial Behavior, Substance Use, and Personality: An Integrative Quantitative Model of the Adult Externalizing Spectrum. *Journal of Abnormal Psychology*, *116*(4), 645–666. http://doi.org/10.1037/0021-843X.116.4.645

Kruger, J. and Dunning, D. (1999). Unskilled and Unaware of It: How Difficulties in Recognizing One's Own Incompetence Lead to Inflated Self-Assessments. *Journal of Personality and Social Psychology,* Vol 77, 6, 121-1134.

Kurita, M., Nishino, S., Kato,M., Numata,Y. Sato,T. (2012). Plasma brain-derived neurotrophic factor levels predict the clinical outcome of depression treatment in a naturalistic study. *PLoSONE 7:e39212.*

Lambrey, S., Doeller, C., Berthoz, A., Burgess, N. (2012). Imagining Being Somewhere Else: Neural Basis of Changing Perspective in Space. *Cerebral Cortex*, 22,166—174.

Lanius, R. A., Vermetten, E., Loewenstein, R. J., Brand, B., Schmahl, C., Bremner, J. D., & Spiegel, D. (2010). Emotion modulation in PTSD: Clinical and neurobiological evidence for a dissociative subtype. *American Journal of Psychiatry, 167, 640-647.*

Lang, P.J. (1977). Imagery in therapy: An information-processing analysis of fear. *Behaviour Therapy,* 8, 862-886.

Lang, P.J. (1984). *Cognition in emotion: Concept and action*. In C. Izard., J. Kagan, & R. Zajonc (Eds)., *Emotion, Cognition, & Behavior* (pp. 193-206). Cambridge University Press: New York

Lavebratt. C., Åberg, E., Sjöholm, L.K., Forsell, Y. (2010). Variations in FKBP5 and BDNF genes are suggestively associated with depression in a Swedish population based cohort. *J Affect Disord*; 125: 249.

Lavrakas, P. (2008). *Encyclopaedia of Survey Methods.* Sage: London.

Lawton, C. A. (1994). Gender differences in way-finding strategies: Relationship to spatial ability and spatial anxiety. *Sex Roles*, 30, 765–779.

Le Doux, J.E. (2000). Emotion Circuits in the Brain. *Annual Review of Neuroscience,* 23, 155-184. Vol. 23: 155-184

Lee, H.-J., Kang, R.-H., Lim, S.-W., Paik, J.-W., Choi, M.-J. and Lee, M.-S. (2006). No association between the brain-derived neurotrophic factor gene Val66Met polymorphism and post-traumatic stress disorder. *Stress and Health*, 22: 115–119.

Lee, I. & Solivan, F. (2008). The roles of the medial prefrontal cortex and hippocampus in a spatial paired-association task. *Learn Mem*. 15, 357–367.

Lindauer, R.J., Vlieger, E.J., Jalink, M., Olff, M., Carlier, I.V., Majoie, C.B., den Heeten, G.J., Gersons, B.P. (2004). Smaller hippocampal volume in Dutch police officers with posttraumatic stress disorder. *Biol Psychiatry*, 1, 56, 5, 356-63.

Lindauer, R..J, Olff, M., van Meijel, E.P., Carlier, I.V., Gersons, B.P. (2006) Cortisol,learning, memory, and attention in relation to smaller hippocampal volume in police officers with posttraumatic stress disorder. *Biol Psychiatry*, 15, 59, 2, 171-7.

Lövdén, M., Schaefer, S., Noack, H., Kanowski, M., Kaufmann, J., Tempelmann, C. et al.(2011). Performance-related increases in hippocampal N- acetylaspartate (NAA) induced by spatial navigation training are restricted to BDNF Val homozygotes. *Cereb. Cortex,* 21, 1435–1442.

Lu, B. & Gottschalk, W. (2000).Modulation of hippocampal synaptic protein distribution in the hippocampus of BDNF knockout mice. *Prog. Brain Res. J. Neurosci*. 19, 231–241.

Lubit, R., Rovine, D. DeFrancisci, L, Eth, S. (2003). Impact of trauma on children. *J Psychiatr Pract.* 2003; 9(2):128-38.

Luders, E., Thompson, P.M., Kurth, F. (2015). Larger hippocampal dimensions in meditation practitioners: differential effects in women and men. *Front. Psychol*. 6:186.

Liu, I.Y., Lyons, W.E., Mamounas, L.A., Thompson, R.F. (2004). Brain-derived neurotrophic factor plays a critical role in contextual fear conditioning. *J Neurosci.* 8; 24, 36, 7958-63.

Luo C., Xu H., Li X.M. (2005). Quetiapine reverses the suppression of hippocampal neurogenesis caused by repeated restraint stress. *Brain Res*., 23, 1063, 1, 32-9.

Lyoo, I.K., Kim, J.E., Yoon, S.J., Hwang, J., Bae, S., Kim, D.J. (2011). The neurobiological role of the dorsolateral prefrontal cortex in recovery from trauma. Longitudinal brain imaging study among survivors of the South Korean subway disaster. *Arch Gen Psychiatry*, 68, 7, 701-13.

Mac Manus, D. & Wessely, S. (2013). Veteran mental health services in the UK: Are we headed in the right direction? *Journal of Mental Health*, 22, 4, 301–305.

Mac Manus,D., Jones, N., Wessely, S. , Fear, N.T., Jones, E., Greenberg, N. (2014). The mental health of the UK Armed Forces in the 21st century: resilience in the face of adversity. *JRAMC. J R Army Med Corps*, 0, 1–6.

Maguire, E. A., Gadian, D. G., Johnsrude, I. S., Good, C. D. ,Ashburner, J., Frackowiak, R. S., et al. (2000).Navigation-related structural change in the hippocampi of taxi drivers. *Proc. Natl.Acad.Sci.U.S.A.* 97, 4398–4403.

Malan-Müller, S., Seedat, S., Hemmings, SMJ. (2014). Understanding PTSD: Insights from the methylome. *Genes, Brain and Behavior*, 13, 1, 52–68.

Markon, K.E. & Krueger, R. F. (2005). Categorical and continuous models of liability to externalizing disorders: a direct comparison in NESARC. *Arch Gen Psychiatry*. 2005;62(12):1352-9.

Marmar, C.R., Schlenger, W., Henn-Haase, C., et al. (2015). Course of Posttraumatic Stress Disorder 40 Years After the Vietnam War: Findings From the National Vietnam Veterans Longitudinal Study. *JAMA Psychiatry.* 72, 9, 875-881.

Maren, S. (2008). Pavlovian fear conditioning as a behavioral assay for hippocampus and amygdala function: cautions and caveats. *European Journal of Neuroscience*, 28, 1661–1666.

Maren S. (2001). Neurobiology of Pavlovian fear conditioning. *Annu Rev Neurosci*, 24, 897-931.

Maren, S. (2011). Seeking a Spotless Mind: Extinction, Deconsolidation, and Erasure of Fear Memory, *Neuron*, 70, 5, 9, 830-845.

Mayers, A. (2013). Introduction to Statistics and SPSS in Psychology. Pearson Education. Harlow

Meneghetti, C., Pazzaglia, F. and De Beni, R. (2011). Spatial mental representations derived from survey and route descriptions: When individuals prefer extrinsic frame of reference. *Learning and Individual Differences,* 21, 150–157.

Merzenich, M. M. & Jenkins, W.M. (1995). Cortical plasticity, learning, and learning dysfunction. In Julesz, B. & Kovacs, I. (1995). *Matrurational Windows and Adult Cortical Plasticity.* Addison-Wesley: Reading, M.A. p274-64.

Meyer, T., Smeets, T., Giesbrecht, T.; Quaedflieg, C. W. E. M., Girardelli, M. M., Mackay, G. R. N., Merckelbach, H. (2012). Individual differences in spatial configuration learning predict the occurrence of intrusive memories. *Cogn Affect Behav Neurosci*. 4, 10, 3402.

Miller, J. K., & Wiener, J. M. (2014). PTSD recovery, spatial processing, and the val66met polymorphism. *Frontiers in Human Neuroscience*, *8*, 100.

Ministry of Defence (2014). Defence Science and Technology Laboratory Corporate Plan 2014 – 2019. MOD Corporate Plan. Page 22
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/336266/20140403-Dstl_Corporate_Plan_2014_FINAL_v1_0-O_WEB_VERSION.pdf

Moffat, S.D. (2009). Aging and Spatial Navigation: what do we know and where do we go? *Neuropsychol review*, 19, 478-89.

Moffat, S.D., Zonderman, A.B., Resnick, S.M. (2001). Age differences in spatial memory in a virtual environment navigation task. *Neurobiol Aging,* 22, 5, 787-96.

Molendijk, M.L., Bus, B.A., Spinhoven, P., Kaimatzoglou, A., Oude Voshaar, R.C., Penninx, B.W., van IJzendoorn, M.H., Elzinga, B.M. (2012). A systematic review and meta-analysis on the association between BDNF val(66)met and hippocampal volume - a genuine effect or a Winner's curse? *Am J Med Genet B Neuropsychiatr Genet*. 159B, 6, 731-40.

Montag, C., Reuter, M., Newport, B., et al. (2008). The BDNF Val66Met polymorphism affects amygdala activity in response to emotional stimuli: evidence from a genetic imaging study. *Neuroimage,* 42, 1554-1559.

Morgan, C.A., Grillon, C., Southwick, S.M., Davis, M., Charney, D.S. (1995). Fear-potentiated startle in posttraumatic stress disorder. *Biological Psychiatry*, Volume 38 , Issue 6 , 378 – 385.

Morey, R.A., Hariri, A.R., Gold, A. L., Hauser, M.A., Munger, H.J., Dolcos, F., McCarthy, G. (2011). Serotonin transporter gene polymorphisms and brain function during emotional distraction from cognitive processing in posttraumatic stress disorder. *BMC Psychiatry*, 11, 76.

Morinobu, S. (2013). *Possibility of DNA methylation profiles as a potent diagnostic biomarker in PTSD*. Abstract for the 11th World Congress of Biological Psychiatry (Kyoto, Japan).

Morris, R.G.M. (1981). Spatial localisation does not depend on the presence of local cues. *Learn. Motiv*. 12, 239–260.

Moser, E.I., Kropff, E., Moser, M.B. (2008). Place cells, grid cells, and the brain's spatial representation system. *Annu Rev Neurosci*. 31:69-89.

Mowla, S.J., Pareek, S., Farhadi, H.F., Petrecca, K., Fawcett, J.P., Seidah, N.G., Morris, S.J., Sossin, W.S., Murphy, R.A. (1999). Differential sorting of nerve growth factor and brain-derived neurotrophic factor in hippocampal neurons. *J. Neurosci*. 19, 2069–2080.

Münzer, S. & Hölscher, C. (2011). Entwicklung und Validierung eines Fragebogens zu räumlichen Strategien (Development and Validation of a Self-report Measure of Environmental Spatial Strategies). *Diagnostica,* 57, 3, 111– 125.

Münzer, S. & Stahl, C. (2011) Learning Routes from Visualizations for Indoor Wayfinding: Presentation Modes and Individual Differences. *Spatial Cognition & Computation*, 11:281–312.

Münzer, S. and Hölscher, C. (2011). Entwicklung und Validierungeines Fragebogens zu räumlichen Strategien. *Diagnostica* 57, 3, 111–125.

Murakami, S., Imbe, H., Morikawa, Y., Kubo, C., Senba, E. (2005). Chronic stress, as well as acute stress, reduces BDNF mRNA expression in the rat hippocampus but less robustly. *Neurosci Res*. 53, 2,129-39. PMID: 16024125

Murburg M. (1997). The psychobiology of post-traumatic stress disorder: An overview. A*nn N Y Acad Sci.,* 821: 352-358.

Myers, C.S. (1915) Contribution to the study of shell shock. *The Lancet*, 185, 4772, 316-330.

Nagel, E., Chicherio, C.,Von Oertzen, T., Sander, T., Villringer, A., Heekeren, H.R., Backman, L., Lindenberger, U. (2008). Human aging magnifies genetic effects on executive functioning and working memory. *Front Hum Neurosci* 2:1.

National Health Service (2016): http://www.nhs.uk/Conditions/Post-traumatic-stress-disorder/Pages/Introduction.aspx

Neuner, F., Catani, C., Ruf, M., Schauer, E.,Schauer, M., and Elbert, T. (2008).Narrative exposure therapy for the treatment of traumatized children and adolescents (KidNET):from neurocognitive theory to field intervention. *Child Adolesc.Psychiatr.Clin.N.Am*. 17, 641–664

Neves, G., Cooke, S.F., Bliss, T.V.P. (2008). Synaptic plasticity, memory and the hippocampus: a neural network approach to causality. *Nat Rev Neurosci* 9: 65-75

Nicolle, M.M., Prescott, S., Bizon, J. L . (2003). Emergence of a cue strategy preference on the water maze task in aged C57B6 x SJL F1 hybrid mice. *Learn Mem* 10:520 –524.

Nievergelta C.M., Maihofera, A.X., Mustapica, M., Yurgild, K.A., Schorkc, N.J., Millere, M.W., Logueg, M.W., Geyera, M.A., Risborough, V.B., O'Connor, D.T., Bakerd, D.G. (2015). Genomic predictors of combat stress vulnerability and resilience in U.S. Marines: genome-wide association study across multiple ancestries implicates PRTFDC1 as a potential PTSD gene. *Psychoneuroendocrinology*, 51, 459—471.

Nillson, J. (2012). Allocentric Memory and Hippocampal Function. *Thesis submitted to Newcastle University for the Degree of Doctor of Philosophy in Cognitive Neuroscience.*

Ninan, I., Bath, K.G., Dagar, K., Perez-Castro, R., Plummer, M. R., Lee, F. S., Chao, M.V. (2010). The BDNF Val66Met polymorphism impairs NMDA receptor-dependent synaptic plasticity in the hippocampus. *J Neurosci*. 30, 26, 8866-70.

Norrholm, S. D., Jovanovic, T., Smith, A. K., Binder, E., Klengel, T., Conneely, K., Mercer, K. B., Davis, J. S., Kerley, K., Winkler, J., Gillespie, C. F., Bradley, B. & Ressler, K. J. (2013). Differential Genetic and Epigenetic Regulation of catechol-O-methyltransferase is Associated with Impaired Fear Inhibition in Posttraumatic Stress Disorder. *Front Behav. Neurosci.*, 7, 30.

Notaras, M., Hill, R., van den Buuse, M. (2015). The BDNF gene Val66Met polymorphism as a modifier of psychiatric disorder susceptibility: progress and controversy. *Molecular Psychiatry* 20, 916-930. DOI:10.1038/mp.2015.27

O' Keefe, J. (2015). The Journey to the Hippocampal Cognitive Map. BNA 50th Anniversary Lecture & 2015 Wolstencroft Memorial Award Lecture. *British Neuroscience Association*. Edinburgh. ISSN 1345-8301 2015.

O' Keefe, J. & Dostorovsky, J. (1971). The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat*Brain Research*, 34: 171-175.

O'Keefe, J. & Nadel, L. (1978). *The hippocampus as a cognitive map*. Oxford University Press: Oxford.

Ohnishi, T., Matsuda, H., Hirakata, M., Ugawa, Y. (2006). Navigation ability dependent neural activation in the human brain: An fMRI study. *Neurosci Res,* 55, 361–369.

Oroszi G., Lapteva L., Davis E., Yarboro C. H., Weickert T., Roebuck-Spencer T., et al. (2006). The Met66 allele of the functional Val66Met polymorphism in the brain-derived neurotrophic factor gene confers protection against neurocognitive dysfunction in systemic lupus erythematosus. *Ann. Rheum. Dis*. 65, 1330–1335 10.

Osofsky, J.D. (1995). The effects of exposure to violence on young children. *Am Psychol.* 50(9):782-8. PubMed PMID: 7574189.

Otto, T. & Eichenbaum, H. (1992) Neuronal activity in the hippocampus during delayed non-match to sample performance in rats: Evidence for hippocampal processing in recognition memory. *Hippocampus*, 2, 3, 323–334.

Packard, M. G., & Knowlton, B. J. (2002). Learning and memory functions of the basal ganglia. *Annual Review of Neuroscience*, 25, 563–593.

Poldrack, R. A., Clark, J., Paré-Blagoev, E. J., Shohamy, D., Creso Moyano,J.,Myers, C.,& Gluck, M. A.(2001). Interactive memory systems in the human brain. *Nature*, 414, 546–550.

Poo, M.M. (2001). Neurotrophins as synaptic modulators. *Nat. Rev. Neurosci*. 2, 24–32

Palmer, I. (2012). 'UK extended Medical Assessment Programme for ex-service personnel: the first 150 individuals seen'. *The Psychiatrist Online* 2012, 36:263-27

Palermo,L., Bianchini, F., Iaria, G. , Tanzilli, A. and Guariglia, C. (2012). Assessing Topographical Orientation Skills in Cannabis Users. Research Article: *The Scientific World Journal,* 12, 137071.

Pavlov, I. P. (1927/1960). *Conditional Reflexes.* New York: Dover Publications (the 1960 edition is not an unaltered republication of the 1927 translation by Oxford University Press).

Pazzaglia, F., & De Beni, R. (2001). Strategies of processing spatial information in survey and landmark-centred individuals. *European Journal of Cognitive Psychology*. 13, 493–508

Pazzaglia, F., Cornoldi, C., & De Beni, R. (2000). Differenze individuali nella rappresentazione dello spazio: presentazione di un questionario autovalutativo [Individual differences in representation of space: presentation of questionnaire]. *Giornale Italiano di Psicologia*, 3, 627−650.

Pearson, D.G. (2012). Contextual representations increase analogue traumatic intrusions: evidence against a dual-representation account of peri-traumatic processing. *Journal of Behavior Therapy and Experimental Psychiatry*, 43, 1026–1031.

Pearson D.G., Ross F.D.C., Webster V.L. (2012). The importance of context: evidence that contextual representations increase intrusive memories. *Journal of Behavior Therapy and Experimental Psychiatry*, 43, 573–580.

Perrin, M.A., DiGrande, L., Wheeler, K., Thorpe, L., Farfel, M., Brackbill, R. (2007). Differences in PTSD prevalence and associated risk factors among World Trade Center disaster rescue and recovery workers. *Am J Psychiatry*, 164, 9, 1385-94.

Perroud, N., Courtet, P.,Vincze, I., Jaussent, I., Jollant, F., Bellivier,F.,et al. (2008). Interaction between BDNF Val66Met and childhood trauma on adult's violent suicide attempt. *Genes Brain Behav*. 7, 314–322.

Peters, J., Dieppa-Perea, L. M., Melendez, L. M., Quirk, G. J. (2010). Induction of fear extinction with hippocampal-infralimbic BDNF. *Science,* 328: 1288-1290.

Petryshen, T., Sabeti, P., Aldinger, K., Fry, B., Fan, J., Schaffner, S., Waggoner, S.G., Tahl, A.R, Sklar, P. (2010). Population genetic study of the brain-derived neurotrophic factor (*BDNF*) gene. *Molecular Psychiatry*, *15*, 8, 810–815. DOI:10.1038/mp.2009.24.

Pezawas, L., Verchinsk,i B.A., Mattay, V.S., Callicott, J.H., Kolachana, B.S., Straub, R.E. et al. (2004).The brain-derived neurotrophic factor val66met polymorphism and variation in human cortical morphology. *J Neurosci*, 10, 10099–10102.

Phelps, E.A. (2004). 'Human emotion and memory: interactions of the amygdala and hippocampal complex'. *Current Opinion in Neurobiology*, 14, 198–202

Pitman, R. K., Rasmusson, A. M., Koenen, K. C., Shin, L. M., Orr, S. P.,Gilbertson, M. W., et al. (2012). Biological studies of post-traumatic stress disorder. *Nat.Rev.Neurosci.* 13, 769–787.

Pivac, N., Kozaric-Kovacic, D., Grubisic-Ilic, M., Nedic, G., Rakos, I., Nikolac, M.,et al. (2012). The association between brain - derived neurotrophic factor val66met variants and psychotic symptoms in post-traumatic stress disorder. *WorldJ.Biol.Psychiatry,* 13, 306–311.

Pizarro, J.M., Lumley, L.A., Medina, W., Robison, C.L., Chang, W.E., Alagappan, A., Bah, M.J., Dawood, M.Y., Shah, J.D., Mark, B., Kendall, N., Smith, M.A., Saviolakis, G.A. & Meyerhoff, J.L. (2004). Acute social defeat reduces neurotrophin expression in brain cortical and subcortical areas in mice. *Brain Res* 1025, 10–20.

Pregelj, P., Nedic, G., Paska, A.V., Zupanc, T., Nikolac, M., Balazic,J., et al. (2011). The association between brain-derived neurotrophic factor polymorphism (BDNF Val66Met) and suicide. *J. Affect.Disord*. 128, 287–290.

Pu, L., Bao, G. B., Xu, N-J., Ma, Land Pei, G. (2002) Hippocampal Long-Term Potentiation Is Reduced by Chronic Opiate Treatment and Can Be Restored by Re-Exposure to Opiates. *J. Neurosci.*, *22,* 5, 1914–1921.

Poyner, G. (2010) Psychological Evaluations of Veterans Claiming PTSD Disability with the Department of Veterans Affairs: A Clinician's Viewpoin . *Psychol. Inj. And Law.* Published online: Springer.

Quereshi, S. U., Long, M. E., Bradshaw, R., Pyne, J.M., Magruder, K. M., Kimbrell, T., Hudson, T. J., Jawaid, A., Schulz, P.E. and Kunik, M.E. (2011). Does PTSD Impair Cognition Beyond the Effect of Trauma? *The Journal of Neuropsychiatry and Clinical Neurosciences*, 2, 1, 16-28
Rakofsky, J. J., Ressler, K. J., Dunlop, B.W. (2011). BDNF function as a potential mediator of bipolar disorder and post-traumatic stress disorder comorbidity. *Mol Psychiatry* 17, 1, 22-35.

Rattiner, L. M., Davis, M., French, C.T., and Ressler, K. J. (2004). Brain-derived neurotrophic factor and tyrosine kinase receptor b involvement in amygdala- dependent fear conditioning. *J. Neurosci..* 24, 4796–4806.

Rao, H., Betancourt, L., Giannetta, J.M., Brodsky, N.L., Korczykowski, M., Avants, B.B., Gee, J.C., Wang, J., Hurt, H., Detre, J.A., Farah, M.J. (2010). Early parental care is important for hippocampal maturation: evidence from brain morphology in humans. *Neuroimage,* 1, 49, 1, 1144-50.

Rauch, S.L., Shin, L.M., Phelps, E.A. (2006). Neurocircuitry models of posttraumatic stress disorder and extinction: Human neuroimaging research - Past, present, and future. *Biol. Psychiatry*, 60, 376-82.

Raz, N., Rodrigue, K. M., Kennedy, K. M., & Land, S. (2009). Genetic and Vascular Modifiers of Age-Sensitive Cognitive Skills: Effects of COMT, BDNF, ApoE and Hypertension. *Neuropsychology*, *23*, 1, 105–116.

Reber, P. J., Knowlton, B. J., & Squire, L. R. (1996). Dissociable properties of memory systems: Differences in the flexibility of declarative and nondeclarative knowledge*. Behavioral Neuroscience,* 110, 861–871.

Richardson, L. K., Frueh, C. B., Acierno, R. (2010). Prevalence Estimates of Combat-Related PTSD: A Critical Review. *Aust N Z J Psychiatry*, 44, 1, 4–19. Research Collaboratory for Structural Bioinformatics Protein Data Bank: http://www.rcsb.org/pdb/home/home.do

Richter-Schmidinger, T., Alexopoulos, P., Horn, M., Maus, S., Reichel, M., Rhein, C., Lewczuk, P., Sidiropoulos, C., Kneib, T., Perneczky, R., Doerfler ,A., Kornhuber, J. (2011). Influence of

brain-derived neurotrophic-factor and apolipoprotein E genetic variants on hippocampal volume and memory performance in healthy young adults. *J Neural Transm,* 118, 2, 249–257.

Rodgers, M. K., Sindone, J. A., & Moffat, S. D. (2012). Effects of age on navigation strategy. *Neurobiology of Aging*, 33, 1, 202.

Rona, R. J., Jones, M., Iversen, A., Hull, L., Greenberg, N., Fear, N. T., et al. (2009). The impact of posttraumatic stress disorder on impairment in the UK military at the time of the Iraq war. *Journal of Psychiatric Research,* 43, 6, 649-655.

Rona, R. J., Fear, N. T., Hull, L., Greenberg, N., Earnshaw, M., Hotopf, M., & Wessely, S. (2007). Mental health consequences of overstretch in the UK armed forces: first phase of a cohort study. BMJ : *British Medical Journal*, 335, 7620, 603.

Rosas-Vidal, L.E., Do-Monte, F.H., Sotres-Bayon, F., Quirk, G.J. (2014). Hippocampal–Prefrontal BDNF and Memory for Fear Extinction. *Neuropsychopharmacology*.39, 2161–2169

Rosenzweig, E. S., Barnes, C. A. (2003). Impact of aging on hippocampal function: plasticity, network dynamics, and cognition. *Prog. Neurobiol.* 69, 143–179 10.1016/S0301.

Roth, T.L.; Zoladz, P.R., Sweatt, J.D., Diamond, D.M. (2011). Epigenetic modification of hippocampal *Bdnf* DNA in adult rats in an animal model of post-traumatic stress disorder. *Journal of Psychiatric Research*, 45, 7, 919 – 926.

Rudy, J.W., Huff, N.C., Matus-Amat, P. (2004). Understanding contextual fear conditioning: insights from a two-process model. *Neurosci Biobehav Rev,* 28, 675–685.

Salehi, B., Preuss, N., van der Veen, J.W., Shen, J., Neumeister, A., Drevets, W.C.,Hodgkinson, C., Goldman, D., Wendland, J.R., Singleton, A., Gibbs, J.R., Cookson, M.R., Hasler,G. (2013). Age-modulated association between prefrontal NAA and the BDNF gene. *Int J Neuropsychopharmacol,* 16, 6, 1185 - 93.

Sakata, K., Duke, S.M. (2014). Lack of BDNF expression through promoter IV disturbs expression of monoamine genes in the frontal cortex and hippocampus. *Neuroscience*, 260:265-75.

Sambataro, F., Murty, V., Lemaitre, H., Reed, J., Das, S., Goldberg, T., Mattay, V. (2010). BDNF modulates normal human hippocampal ageing. *Molecular Psychiatry*, 15, 2, 116–118.

Sanchez, M.M., Das, D., Taylor, J.L., Noda, A., Yesavage, J.A. and Salehi, A. (2011). BDNF polymorphism predicts the rate of decline in skilled task performance and hippocampal volume in healthy individuals. *Translational Psychiatry,* 1, 10.

Sarapas, C., Cai, G., Bierer, L.M., Golier, J.A., Galea, S., Ising, M., Rein, T., Schmeidler, J., Müller-Myhsok, B., Uhr, M., Holsboer, F., Buxbaum, J.D., Yehuda, R. (2011). Genetic markers for PTSD risk and resilience among survivors of the World Trade Center attacks. *Dis Markers*, 30, 2-3, 101-10.

Sapolsky, R. M. (2000).Glucocorticoids and hippocampal atrophy in neuropsychiatric disorders. *Arch. Gen.Psychiatry* 57, 925–935.

Schinazi, V.R., Nardi, D., Newcombe, N.S., Shipley, T.F., Epstein, R.A. (2013). Hippocampal Size Predicts Rapid Learning of a Cognitive Map in Humans. *Hippocampus,* 23, 515-528.

Schmidt, U., Holsboer, F. and Rein, T. (2011). 'Epigenetic aspects of posttraumatic stress disorder'. *Disease Markers* 30, 77-87

Schmidt, H.D. & Duman, R.S. (2007). The role of neurotrophic factors in adult hippocampal neurogenesis, antidepressant treatments and animal models of depressive-like behavior. *Behav Pharmacol,* 18, 391-418.

Schmitzer-Torbert, N. (2007). Place and response learning in human virtual navigation: Behavioral measures and gender differences. *Behavioral Neuroscience*, 121, 277–290.

Schofield, P.R.S., Williams, L.M., Paul, R.H., Gatt, J.M., Brown, K., Luty, A. et al. (2009). Disturbances in task-relevant information processing associated with the brain-derived neurotrophic factor Val66Met polymorphism: evidence from cognition, the P300 endophenotype and neuroimaging. *Biol Psychol* 2009 online, 2008.

Scoville, W.B. & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. J *Neurol Neurosurg Psychiatry*; 20:11– 21.

Schomaker, J., van Bronkhorst, L.V., Martijn, M. (2014). Exploring a novel environment improves motivation and promotes recall of words. *Frontiers in Psychology*, 5, http://dx.doi.org/10.3389/fpsyg.2014.00918

Schwabe, L., Dalm, S., Schachinger, H., & Oitzl, M. S. (2008). Chronic stress modulates the use of spatial and stimulus-response learning strategies in mice and man. *Neurobiology of Learning and Memory*, 90, 495-503.

Selden, N . R., Everitt, B. J., Jarrard, L. E., Robbins, T. W. (1991). Complementary roles for the amygdala and hippocampus in aversive conditioning to explicit and contextual cues. *Neuroscience,* 42, 335–350.

Sheeran, T. & Zimmerman, M. (2002). Screening for posttraumatic stress disorder in a general psychiatric outpatient setting. *Journal of Consulting and Clinical Psychology*, 70, 961–966.

Shelton, A. L., Marchette, S. A., & Furman, A. J. (2013). A mechanistic approach to individual differences in spatial learning, memory, and navigation. In B. H. Ross (Ed.). *The psychology of learning and motivation*, 59, 223–259). San Diego, CA: Academic Press.

Shepard, R. & Metzler, J. (1971). Mental rotation of three dimensional objects. *Science*, 171, 972, 701-3.

Shin, L.M., Bush, G., Milad, M.R., Lasko, N.B., Brohawn, K.H., Hughes, K.C., Macklin, M.L., Gold, A.L., Karpf, R.D., Orr, S.P., Rauch, S.L., Pitman, R.K. (2011). Exaggerated activation of dorsal anterior cingulate cortex during cognitive interference: a monozygotic twin study of posttraumatic stress disorder. *Am J Psychiatry*. 168, 9, 979-85.

Siegal, D. (2012). *The Developing Mind.* (2nd edition). The Guildford Press: New York.

Simons, D. J., & Wang, R. F. (1998). Perceiving real-world viewpoint changes. *Psychological Science*, 9, 315–320.

Skelton, K., Ressler, K. J., Norrholm, S. D., Jovanovic, T., & Bradley-Davino, B. (2012). PTSD and Gene Variants: New Pathways and New Thinking. *Neuropharmacology*, *62*, 2, 628–637.

Smith, K., Burgess, N., Brewin, C.R. and King, J.A. (2015). Impaired allocentric spatial processing in posttraumatic stress disorder. *Neurobiology of Learning and Memory,* 119, 69–76.

Soliman, F., Glatt, C.E., Bath, K.G., Levita, L., Jones, R.M., Pattwell, S.S., Jing, D.,Tottenham, N., Amso, D., Somerville, L.H., Voss, H.U., Glover, G., Ballon, D.J., Liston, C.,Teslovich, T., Van Kempen, T., Lee, F.S., Casey, B.J. (2010). A genetic variant BDNF polymorphism alters extinction learning in both mouse and human. *Science,* 12, 327, 5967, 863-6.

Spiers, H.J. & Barry, C. (2015).Neural systems supporting navigation. *Current Opinion in Behavioral Sciences,* 1, 47-55.

Stackman, R.W., Clark, A.S., Taube, J.S. (2002). Hippocampal spatial representations require vestibular input. *Hippocampus*. 12:291--303.

Steel, C., Fowler, D., Holmes, E. A. (2005). Trauma-related intrusions and psychosis: an information processing account. *Behav.Cogn.Psychother*. 33, 139–152.

Strange, B.A. & Dolan, R.J. (2006). Anterior medial temporal lobe in human cognition: Memory for fear and the unexpected*. Cognitive Neuropsychiatry*, 1,3.

Suliman, S., Seedat, S., and Hemmings, S. M. J. (2013). Brain-derived neurotrophic factor (BDNF) protein levels in anxiety disorders: systematic review and meta-regression analysis. *Front. Integr.Neurosci.* 7:55.

Sullivan, T.P. and Holt, L.J. (2008). PTSD Symptom Clusters Are Differentially Related to Substance Use Among Community Women Exposed to Intimate Partner Violence. *J Trauma Stress,* 21, 2, 173–180.

Szeszko, P.R., Lipsky, R., Mentschel, C., Robinson, D., Gunduz-Bruce, H., Sevy, S., et al. (2005). Brain-derived neurotrophic factor val66met polymorphism and volume of the hippocampal formation. *Mol.Psychiatry,* 10, 631–636.

Takei, S., Morinobu, S., Yamamoto,S., Fuchikami, M. , Matsumoto, T., Yamawaki, S. (2011). Enhanced hippocampal BDNF/TrkB signaling in response to fear conditioning in an animal model of posttraumatic stress disorder. *Journal of Psychiatric Research*, 45, 4 , 460 – 468.

Tan, Y.L., Zhou, D.F., Cao, L.Y., Zou, Y. Z., Wu, G.Y., Zhang, X.Y. (2005). Effect of the BDNF Val66Met genotype on episodic memory in schizophrenia. *Schizophr Res*, 77, 355–356.

Tang, Y-Y, Holzel, B.K., Posner, M.I. (2015). The Neuroscience of Mindfulness Meditation, Box 4: Mindfulness meditation and stress. *Nature Reviews Neuroscience*, 16, 213-225.

Taylor, H.A., Tversky, B. (1992). Spatial mental models derived from survey and route descriptions. *Journal of Memory and Language*, 31, 261-292.

Teicher, M.H., Andersen, S.L., Polcari, A., Anderson, C.M., Navalta, C.P., Kim, D.M. (2003). The neurobiological consequences of early stress and childhood maltreatment. *Neuroscience and Biobehavioral Reviews* 27, 33–44.

Teicher, M.H., Anderson, C.M., Polcari, A. (2012). Childhood Maltreatment is Associated with Reduced Volume in Hippocampal Subfields CA3, Dentate Gyrus and Subiculum. *Proceedings of the National Academy of Sciences* 02/2012; 109, 9, E556-72.

Tempesta, D., Mazza, M., Iaria, G., De Gennaro, L., and Ferrara, M. (2011). A specific deficit in spatial memory acquisition in post-traumatic stress disorder and the role of sleep in its consolidation. *Hippocampus,* 22, 1154–1163.

The Guardian (2016): http://www.theguardian.com/society/2016/apr/19/burst-into-tears-emergency-workers-ptsd-post-traumatic-stress-disorder; http://www.theguardian.com/society/video/2014/dec/19/trigger-point-ptsd-video

Thomaes, K., Dorrepaal, E., Draijer, N., de Ruiter, M.B., Elzinga, B.M., Sjoerds, Z., Van Balkom, A.J., Smit, J.H., Veltman, D.J. (2013).Increased anterior cingulate cortex and hippocampus activation in Complex PTSD during encoding of negative words. S*oc Cogn Affect Neurosc*i. 8, 2,190-200.

Thorndyke, P.W., Hayes-Roth, B. (1982). Differences in spatial knowledge acquired from maps and navigation. *Cognitive Psychology*, 14, 560-589.

Tolman, E.C. (1948). Cognitive maps in rats and men. *Psychol. Rev*. 55, 189–208.

Torrents- Roda, D., Fullana, M.A., Arias, B., Bonillo, A., Caseras, X., Andión, O., Mitjans, M., Fañanás, L., Torrubiaa, R. (2012). Acquisition and generalization of fear conditioning are not modulated by the BDNF-val66met polymorphism in humans. *Psychophysiology,* 49, 713–719.

Tsien, J.Z., Huerta, P.T., Tonegawa, S. (1996). The essential role of hippocampal CA1 NMDA receptor-dependent synaptic plasticity in spatial memory. *Cell*, *87, 7,* 1327- 1338.

Tupala E, Hall H, Bergstro¨m K, Mantere T, Ra¨sa¨nen P, Sa¨rkioja T, Hiltunen J, Tiihonen J (2003) Different effect of age on dopamine transporters in the dorsal and ventral striatum of controls and alcoholics. *Synapse* 48:205–211.

Turano, K. A., Munoz, B., Hassan, S. E., Duncan, D. D., Gower, E. W., Roche, K. B.,Keay, L., Munro, C.A., West, S. K. (2009). Poor Sense of Direction Is Associated With Constricted Driving Space in Older Drivers. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, 64B, 3, 348–35.

Unternaehrer, E., Luers, P., Mill, J., Dempster, E., Meyer, A.H., Staehli, S., Lieb, R., Hellhammer, D.H., Meinlschmidt, G. (2012). Dynamic changes in DNA methylation of stress-associated genes (OXTR, BDNF) after acute psychosocial stress. *Translational Psychiatry,* 2, e150.

U.S. Department of Justice (2013). *Crime Scene Investigation: A Guide for Law Enforcement*. National Forensic Science Technology Center, Florida.

Uttal, D. H., Meadow, N. G., Tipton, E., Hand, L. L., Alden, A. R., Warren, C., & Newcombe, N. S. (2012). The Malleability of Spatial Skills: A Meta-Analysis of Training Studies. *Psychological Bulletin.* Advance online publication. DOI: 10.1037/a0028446

Valente, N.L., Vallada, H., Cordeiro, Q., Miguita, K., Bressan, R.A., Andreoli, S.B., Mari, J.J., Mello, M.F. (2011).Candidate-gene approach in posttraumatic stress disorder after urban violence: association analysis of the genes encoding serotonin transporter, dopamine transporter, and BDNF. *J Mol Neurosci.,* 44, 1, 59-67

Van Gerven, D.J.H., Fergeson, T., Skelton, R.W. (2016). Acute stress switches spatial navigation strategy from egocentric to allocentric in a virtual Morris water maze. *Neurobiology of Learning and Memory,* 132; 29-39.

Van der Kolk, B., Brown, P., Vn der Hart. O. (1989). Pierre Janet on post-traumatic stress. *Journal of Traumatic Stress*, 2, 4, 365-378.

Van den Heuvel, L., Suliman, S., Malan-Müller, S., Hemmings, S.; Seedat, S.(2016): Brain-derived neurotrophic factor (BDNF) Val66Met polymorphism and plasma levels in road traffic accident survivors, *Anxiety, Stress, & Coping*, DOI: 10.1080/10615806.2016.1163545

Van Kesteren, M. T. R., Ruiter, D. J., Fernández, G., Henson R. N. (2012). How schema and novelty augment memory formation. *Trends Neurosci*. 35, 211–21910.1016/j.tins.2012.02.001

Vasterling, J.J., Brailey, K., Constans, J., Sutker, P.B. (1998). Attention and Memory Dysfunction in Posttraumatic Stress Disorder. *Neuropsychology,* 12, 1, 125- 133.

Vasterling, J .J. & Brewin, C. R. (2005). Neuropsychology of PTSD: Biological, Cognitive and Clinical Perspectives. London: Guildford Press.

Vermetten, E., Vythilingam, M., Southwick, S. M., Charney, D. S., & Bremner, J. D. (2003). Long-Term Treatment with Paroxetine Increases Verbal Declarative Memory and Hippocampal Volume in Posttraumatic Stress Disorder. *Biological Psychiatry*, *54*(7), 693–702.

Viard, A. Doeller, C.F. Hartley, T., Bird, C.M. , Burgess, N. (2011). Anterior Hippocampus and Goal-Directed Spatial Decision Making. *The Journal of Neuroscience*, 31(12):4613– 4621.

Voermans, N.C.,Petersson,K.M.,Daudey,L.,Weber, B.,Van Spaendonck, K.P., Kremer, H. P.,Ferna´ndez, G. (2004). Interaction between the human hippocampus and the caudate nucleus during route recognition. *Neuron,* 43, 427–435.

Wang, T. (2015). Does BDNF Val66Met Polymorphism Confer Risk for Posttraumatic Stress Disorder. *Neuropsychobiology,* 71, 149-153

Wang, Y., Mathews, C.A., Li, Y., Lin, Z., Xiao, Z. (2011). Brain-derived neurotrophic factor (BDNF) plasma levels in drug-naïve OCD patients are lower than those in healthy people, but are not lower than those in drug-treated OCD patients. *J Affect Disord*. 133, 1-2, 305-10.

Wang, Z., Neylan, T. C., Mueller, S. G., Lenoci, M., Truran, D., Marmar, C. R., et al. (2010). Magnetic resonance imaging of hippocampal subfields in post-traumatic stress disorder. *Arch.Gen. Psychiatry* 67, 296.

Ward, D.C., Summers, M.J., Saunders, N.L., Janssen, P., Stuart, K.E., Vickers, J.C. (2014). APOE and BDNF Val66Met polymorphisms combine to influence episodic memory function in older adults. *Behavioural Brain Research* 271:309-315.
Warrington, E. K. (1996). *The Camden Memory Tests*. Psychology Press: Hove, UK.

Weathers, F.W., Blake, D.D., Schnurr, P.P., Kaloupek, D.G., Marx, B.P., & Keane, T.M. (2013). *The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5)*. Interview available from the National Center for PTSD at www.ptsd.va.gov.

Weathers, F.W., Litz, B.T., Herman, D.S., Huska, J.A. & Keane, T.M. (1993). *The PTSD Checklist (PCL): Reliablity, validity, and diagnostic utility*. Paper presented at the 9th Annual Conference of the ISTSS, San Antonio.

Weber, D.I. (2008). Information processing bias in Post-Traumatic Stress Disorder. *The Open Neuroimaging Journal*, 2008, 2, 29-51.

Wegman, J., Fonteijm, H.M., van Ekert, J., Tyborowska, A., Jansen, C., Janzen, G. (2013). Gray and White Matter Correlates of Navigational Ability in Humans. *Human Brain Mapping*. 00.00.00. Wiley Periodicals, Inc.

Whitford, J.L., Widner,S.C., Mellick, D., Elkins, R.L. (2009). Self-report of drinking compared to objective markers of alcohol consumption. *Am J Drug Alcohol Abuse*, 35, 2, 55 - 8.

Wiener, J.M., Büchner, S. & Hölscher C. (2009). Taxonomy of human wayfinding: A knowledge-based approach. *Spatial Cognition & Computation*, 9, 2, 152-165.

Wiener, J. M., de Condappa, O., Harris, M.A., and Wolbers, T. (2013). Maladaptive bias for extra hippocampal navigation strategies in aging humans. *J. Neurosci.* 33, 6012–6017.DOI: 10.1523/JNEUROSCI.0717-12.2013

Wiener, J.M., Kmecova, H., de Condappa, O. (2012). Route repetition and route retracing: effects of cognitive aging. *Front Aging Neurosci* 4:7.

Wiener, J. M., Kmecova, H., & de Condappa, O. (2012). Route repetition and route retracing: effects of cognitive aging. *Frontiers in Aging Neuroscience*, 4, 7.

Wills, T.J., Cacucci, F., Burgess, N., O'Keefe, J. (2010). Development of the hippocampal cognitive map in preweaning rats. *Science*, 328, 5985, 1573 - 1576.

Wilson, J., Jones, M., Fear, N.T., Hull, L., Hotopf, M., Wessely, S., Rona, R.J. (2009). Is previous psychological health associated with the likelihood of Iraq War deployment? An investigation of the "healthy warrior effect". *Am J Epidemiol*, 1,169, 11; 1362-9.

Wolbers, T. and Wiener, J.M. (2014). Challenges for identifying the neural mechanisms that support spatial navigation: the impact of spatial scale. *Front. Hum. Neurosci*. 8:571.

Wraga, M., Shephard, J.M., Church, J.A., Inati, S., Kosslyn, S. M., (2005). Imagined rotations of self-versus objects: an fMRI study. *Neuropsychologia,* 43, 1351–1361.

Yehuda, R., Daskalakis, N.P., Bierer, L.M., Bader, H.N., Klengel, T., Holsboer, F., Binder, E.B. (2015). Holocaust exposure induced intergenerational effects on FKBP5 methylation. *Biological Psychiatry. (Article in press).*

Yehuda, R., Golier, J. A., Tischler, L., et al. (2005). Learning and memory in aging combat veterans with PTSD. *J Clin Exp Neuropsychol*, 27, 504–515.

Yehuda, R.,Koenen, K.C.,Galea,S.,Flory,J.D. (2011).The role of genes in defining a molecular biology of PTSD. *Dis.Markers*, 30, 67–76.

Yehuda, R., & New York Academy of Sciences. (2006). *Psychobiology of posttraumatic stress disorder: A decade of progress.* Boston: Blackwell Pub. on behalf of the New York Academy of Sciences.

Yule, W., Bolton, D., Udwin, O., Boyle, S., O'Ryan, D., Nurrish, J. (2000). The long-term psychological effects of a disaster experienced in adolescence: I: The incidence and course of PTSD. *J Child Psychol Psychiatry*, 41, 503-11.

Zhang, H., Ozbay, F., Lappalainen, J., Kranzler, H. R., van Dyck, C. H., Charney, D. S., … Gelernter, J. (2006). Brain-Derived Neurotrophic Factor Gene (*BDNF*) Variants and Alzheimer's Disease, Affective Disorders, Posttraumatic Stress Disorder, Schizophrenia and Substance Dependence. *American Journal of Medical Genetics*, *141B*(4), 387–393. http://doi.org/10.1002/ajmg.b.30332

Zhang, L., Benedek, D. M., Fullerton, C.S., Forsten, R. D., Naifeh, J.A., Li, X.X. et al. (2014). Letter to the editor: PTSD risk is associated withBDNFVal66Met and BDNF overexpression. *Mol.Psychiatry* 19, 8–10.

Zhang, L., Li, X.-X., & Hu, X.-Z. (2016). Post-traumatic stress disorder risk and brain-derived neurotrophic factor Val66Met. *World Journal of Psychiatry*, *6*(1), 1–6. DOI: 10.5498/wjp.v6.i1.1

Zoladz, P.R., Diamond, D.M., 2013. Current status on behavioral and biological markers of PTSD: a search for clarity in a conflicting literature'. *Neurosci. Biobehav. Rev*. 37, 860—895.

GLOSSARY

ANOVA: Analysis of Variance

BDNF: Brain Derived Neurotrophic Factor

BPS: British Psychological Society

BU: Bournemouth University

CAPS: Clinical Administered PTSD Scale

CIDI: Composite International Diagnostic Inventory

CRN: Clinical Research Network

DNA: Deoxyribonucleic acid

DOH: Department of Health

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th edition.

ELS: Early life stress

ESRC: Economic and Social Research Council

FRS: Fragebogen Räumliche Strategien" (translated as the 'questionnaire on spatial strategies',

GP: General Practitioner

HPA: hypothalamic pituitary adrenal axis

HWE: Hardy-Weinberg equilibrium

IED: Improvised Explosive Device

IRAS: Integrated Research Application System

KCMHR: King's Centre for Military Health Research

MRC: Medical Research Council

MTL: Medial Temporal Lobe

NAA: Hippocampal N-acetylaspartate

NHS: National Health Service

NIHR: National Institute for Health Research

NMDAR1: N-Methyl-D-Aspartate Receptor Subunit glutamate receptor gene

NRES: National Research Ethics Service

PASAT: Paced Auditory Serial Addition Task

PFMC: Prefrontal Medial Cortex

PIPEDA: Personal Information Protection and Electronic Documents Act

PSS-I: PTSD Symptom Scale Interview

PSQI-A: Pittsburg Sleep Quality Index (PSQI)-Addendum (PSQI-A) for PTSD

PTSD: Post-Traumatic Stress Disorder

RAPM: Raven's Advanced Progressive Matrices

SBSOD: Santa Barbara Sense of Direction questionnaire

SCID: Structured Clinical Interview for the DSMIV

SDQ-S: Sense of Direction Questionnaire

SNR: Standard Numerical Rating scale

TBI: Traumatic Brain Injury

TRiM: Trauma Risk in Management

QSR: Questionnaire of Spatial Representation

UCL: University College London

UK: United Kingdom

WHO: World Health Organisation

WMH: World Mental Health

APPENDIX A: ETHICAL ISSUES

This appendix provides and further information about ethics issues (Section A) to supplement the Methodology (Chapter 2) and official documentation (Section B) from BU, Combat Stress and the NHS granting ethical approval for the study (with approved recruitment material).

A ETHICAL ISSUES RESEARCHING PTSD

The vulnerability of those with PTSD by virtue of their experiences having necessarily been classified as 'traumatic' is perhaps without question. The Code of Practice for the Mental Health Act (1983) listed PTSD as a "clinically recognised condition which could fall within the Act's definition of mental disorder" (2008). Whilst sufferers of PTSD are not specifically classified as 'persons who lack capacity' according to the Mental Capacity Act (2005)[42], The Medical Research Council's (MRC) [43] reference to the 1998 Guidelines for Good Clinical Practice in Clinical Trials (the ethical principles of which have their origin in the Declaration of Helsinki) have been used to guide similar studies into trauma (Smith et al., 2015; Bisby et al. 2010).

Ethical issues considered

In adherence to these principles of good practice, the current study identified areas of concern which were addressed in the application for ethical approval from Bournemouth University, the NHS, and Combat Stress. These included: avoiding harm; informed consent; Human Tissue and DNA; further support; reward and collaboration.

Avoiding harm: In accordance with MRC Guidelines for Good Clinical Practice 1998; 1.15) a 'light touch' on-line clinical questionnaire[44] was used. Selection criteria for the experiments included non-evocative visual imagery and designs which were not designed to generate anxiety (therefore excluding paradigms based on the concept of escape learning). DNA data were collected using self-administered saliva kits to avoid intrusion and larger BU Psychology Laboratories were used to minimise feelings of personal confinement on behalf of the participants.

Informed Consent: In accordance with MRC guidelines (1998;17: 5.4.6) on managing participant expectations, it was clearly articulated to participants that this research was not a clinical trial for- or intervention study of- a PTSD treatment, and that performance on the spatial processing task would not be indicative of any change in the participant's level of clinical need for formal treatment of the PTSD.

[42] http://www.legislation.gov.uk/ukpga/2005/9/contents
[43] MRC 1998 Guidelines for Good Clinical Practice in Clinical Trials : http://www.mrc.ac.uk/research/research-policy-ethics/clinical-research-governance/clinical-trials-regulations/
[44] The PTSD Diagnostic Scale (PDS) by Foa E, B. et al. (1995). National Computer Systems Inc.

Human Tissue and DNA: As a 'new human tissue sample', saliva had to be considered by IRAS under the Human Tissue Act (2004)[45] and this required that the DNA collection (through DNA Genotek, Canada) needed to be in accordance with Data Protection Act 1998. Canada is listed as a country with 'an adequate level of protection' and DNA Genotek's Privacy Policy also adheres to Canadian PIPEDA (Personal Information Protection and Electronic Documents Act) guidelines. Data was also anonymised and participants were assured that no other genetic information will be extracted or stored within or beyond the life of this project.

Further support: As per recommendations in the Department of Health's (DOH) Research Governance Framework (2005; 36)[46], participants were given a long term point of contact for the research and its outcomes as well as comprehensive contact information detailing local and national organisations providing free mental health support. Participants were asked to consent to their General Practitioner (GP) or equivalent clinical professional (in the case of the Dorset NHS Intensive Psychotherapy Clinic and Combat Stress) being informed of their participation in the study.

Reward: In accordance with British Psychological Society (BPS) guidelines (2009; 3.3. iv), University students were offered SONA credits for participation or a £10 cash payment. Combat Stress participants were paid £20 but Dorset Police requested that participants were not financially compensated for legal reasons and in these cases a Combat Stress wrist band and Navigation Skills Personal Profile was offered by way of a 'Thank You' for their time.

Collaboration: The conduct of this research adheres to the British Psychological Society[47] (2009; ii: c) and the policies and practices of BU and UCL. The NHS Research Passport obtained through this IRAS clearance also ensured that the research observed the necessary policies and practices of Dorset NHS Intensive Psychotherapy Service. With reference to the Economic and Social Research Council (ESRC) Framework for Research Ethics (2010; 33), the research project benefitted well from extensive peer (and lay) review by relevant and credible authorities in the field including: directors of intermediaries funding PTSD research programmes; Military psychiatrists and their advisors; National PTSD intermediaries and world-leading UK academics in neuropsychology at UCL and the University of Cambridge.

[45] Human Tissue Act 2004: http://www.legislation.gov.uk/ukpga/2004/30/contents
[46] DOH Research Governance Framework: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/139565/dh_4122427.pdf
[47] BPS Code of Ethics and Conduct: http://www.bps.org.uk/system/files/documents/code_of_ethics_and_conduct.pdf

Managing ethics issues

Amendments and additions to the ethical arrangements requested by the South West NRES in March 2013 included:

i. Inclusion of pain monitoring in participant screening;
ii. Written explanation of how the safety of the researcher would be assured and what trauma exposure (or clinical 'de-briefing') support would be available for the researcher during the study;
iii. Consent to be put in place to be able to contact GPs if a participant appeared to be suffering from depression or anxiety or if a participant disclosed risky behaviour which may cause harm to themselves or to others.

Ethical issues addressed in the study

The ethical issues that arose during the study's testing of over 150 participants were few in number. They included:

I. One case where a BU student who presented as a healthy control scored very highly on the trauma impact screen. Contact details for organisations offering advice and treatment were provided and the student was advised to visit their GP and to inform their tutor that they were seeking mental health support for trauma exposure.
II. Four Police officers also presented as healthy controls but scored very highly on the trauma impact screens as well as sleep disturbance. Again, contact details for organisations offering advice and treatment were provided and the officers were advised to visit their GP and to inform their Trauma Risk Management (TRiM) lead and force Welfare Officer that they were seeking mental health support for work-related trauma exposure.

B DOCUMENTATION

Bournemouth University ethics clearance

Bournemouth University

Initial Research Ethics Checklist

Note: ***All researchers*** must complete this brief checklist to identify any ethical issues associated with their research. Before completing, please refer to the BU *Research Ethics Code of Practice* which can be found at www.bournemouth.ac.uk/researchethics. Project Supervisors or School Research Ethics Representatives can advise on appropriate professional judgement in this review. A list of Representatives can be found at the aforementioned webpage. **Sections 1-5 must be completed by the researcher and Section 6 by the Project Supervisor or School Ethics Representative prior to the commencement of any research.** Approved ethics checklists should be submitted in accordance with the school-specific ethics process and will be stored for audit purposes. Students should also retain a copy for inclusion in their dissertation, which will be checked to ensure that it complies with any ethical constraints identified on the ethics checklist. Please refer to erss.bournemouth.ac.uk/researchsupport/bids/writing/processes.html for school-specific processes.

1 RESEARCHER DETAILS					
Name	Jessica Miller				
Email	millerj@bournemouth.ac.uk				
Status	☒ **Postgraduate**	☐			
School	☐ **BS**	☒ **DEC**	☐ **HSC**	☐ **MS**	☐ **ST**
Degree Framework & Programme	(MPhil/PhD) Neuropsychology				
2 PROJECT DETAILS					
Project Title	PTSD and Spatial Processing				
Project Summary ***Sufficient detail is needed; include methodology, sample, outcomes etc***	*(See below)*				
Proposed Start & End Dates	1/11/12 to 1/11/17				
Project Supervisor	Dr Jan Wiener				
Framework Project Co-ordinator	Prof Sine McDougall				
3 ETHICS REVIEW CHECKLIST – PART A					
I	Is approval from an external Research Ethics Committee (e.g. Local Research Ethics Committee (REC), NHS REC) required/sought?			**Yes**	
II	Is the research solely literature-based?			**No**	

Research Ethics Checklist (Graduate School & CRE) July 2011

III	Does the research involve the use of any dangerous substances, including radioactive materials?	**No**
IV	Does the research involve the use of any potentially dangerous equipment?	**No**
V	Could conflicts of interest arise between the source of funding and the potential outcomes of the research? (see section 8 of BU Research Ethics Code of Practice).	**No**
VI	Is it likely that the research will put any of the following at risk: Living creatures? Stakeholders? Researchers? Participants? The environment? The economy?	**No** **No** **No** **No** **No** **No**
VII	Does the research involve experimentation on any of the following: Animals? Animal tissues? Human tissues (including blood, fluid, skin, cell lines)? Genetically modified organisms?	**No** **No** **No** **No**
VIII	Will the research involve prolonged or repetitive testing?	**No**
IX	Will the research involve the collection of audio, photographic or video materials?	
X	Could the research induce psychological stress or anxiety, cause harm or have negative consequences for the participants or researcher (beyond the risks encountered in normal life)?	**No**
XI	Will the study involve discussion of sensitive topics (e.g. sexual activity, drug use, criminal activity)?	**No**
XII	Will financial inducements be offered (other than reasonable expenses/ compensation for time)?	**No**
XIII	Will it be necessary for the participants to take part in the study without their knowledge / consent at the time?	**No**
XIV	Are there problems with the participant's right to remain anonymous?	**No**
XV	Does the research *specifically* involve participants who may be vulnerable?	**No**
XVI	Might the research involve participants who may lack the capacity to decide or to give informed consent to their involvement?	**No**
4 ETHICS REVIEW CHECKLIST – PART B		
Please give a summary of the ethical issues and any action that will be taken to address these.		

Research Ethics Checklist (Graduate School & CRE) July 2011

Sensitivity
Sufferers of PTSD are not classified as vulnerable according to the Mental Health Act 2005, however their vulnerability by virtue of their condition and experiences requires due care and attention. Contact information for organisations offering support for PTSD sufferers (and those with alcohol or anxiety problems as may be highlighted in the pre-experiment screenings) will be offered in the Information Form (Combat Stress, Alcoholics Anonymous and Anxiety UK, for example) and be advised to discuss this with their GP. Participants who are screened on such sensitive issues (also potentially including recreational drug use) will deserve confirmation of confidentiality and privacy protection and will be given unique ID numbers at screening to depersonalise data. Personal data matched to ID numbers will be kept on a temporary master file only accessible to the immediate research team for the life of the project for analysis and data quality checking purposes only, and will be destroyed on project completion in accordance with the Data Protection Act 1998.

Recording
Audio recordings of initial qualitative interview will be taken. Consent to hold and transcribe audio data under the Data Protection Act 1998 will be sought from participants. Transcribed audio data will also be anonymised, and only ID numbers will be recorded on the audio material and transcripts made thereof.

GP/ Mental Health Professional Diagnosis
Participants suffering from PTSD will be asked for consent to contact their GP/ Mental Health Professional for further confirmation of their PTSD diagnosis. The Consent Form will clearly request confirmation and GP/ Mental Health Professional contact details. If participants do not wish to consent to contact with the GP/ Mental Health Professional, they will be asked to provide further information on diagnosis. If this further information is not sufficient to evidence PTSD for analysis purposes, the participants will be thanked for their time and will not participate further as a member of that sample group. GPs and Mental Health Professionals will be asked by letter to confirm if there is an evidenced history or present exhibition of personal violence for Health and Safety purposes (See Risk Assessment and Hazard and Activity Trawl).

Treatment Interference
Participants in the PTSD groups are likely to be on waiting lists (pre-treatment) or in the early stages of treatment. This is to ensure that the effect of PTSD on navigation has the greatest chance of being assessed accurately. Participants will be clearly informed on the Information Sheet that their participation in the study is for research purposes only and should in no way distract participants from continuing to access their clinical treatment as advised by their GP or Mental Health Professional. Ethics consent will be sought from the clinical body administering the treatment, and this is anticipated to be restricted to Combat Stress (using the registered charity's ethics procedures) and the NHS Trauma Clinics (using IRAS).

Further Contact
There is an opportunity to scope potential interest in a further study looking at the role of genetics in the relationship between PTSD and navigation. Reference to this potential future research will be made in the Consent Forms. Consent for further contact (only) with some participants. Participants will be clearly informed in the Consent Form that any future refusal to participate in a later study in no way invalidates their contribution to this current research project.

5 RESEARCHER STATEMENT

I believe the information I have given is correct. I have read and understood the BU Research Ethics Code of Practice, discussed relevant insurance issues, performed a health & safety evaluation/ risk assessment and discussed any issues/ concerns with the Project Supervisor / School Ethics Representative. I understand that if any substantial changes are made to the research (including methodology, sample etc), then I must notify the Project Supervisor / School Research Ethics Representative and may need to submit a revised Initial Research Ethics Checklist. By submitting this form electronically I am confirming the information is accurate to my best knowledge.		
Signed	JKMiller	31-10-12

6 AFFIRMATION BY PROJECT SUPERVISOR OR SCHOOL RESEARCH ETHICS REPRESENTATIVE

Where there is a potential conflict of interest seek advice from the School Ethics Representative.

Satisfied with the accuracy of the research project ethical statement, I believe that the appropriate action is:

The research project proceeds in its present form	☐ **Yes**	☐ **No**
The research project proposal needs further assessment under the School Ethics procedure*	☐ **Yes**	☑ **No**
The research project needs to be returned to the applicant for modification prior to further action*	☐ **Yes**	☐ **No**

** The School is reminded that it is their responsibility to ensure that no project proceeds without appropriate assessment of ethical issues, which is a stipulated requirement of the University's insurers. In extreme cases, this can require processing by the School or University's Research Ethics Committee or by relevant external bodies.*

Reviewer Signature	Paul Stevens	22 Nov 2012

Additional Comments

Identify any project specific ethical constraints that need to be monitored and observed throughout the project.

Assuming NHS ethics are obtained, then this was approved at the School Ethics Board Meeting 22nd November 2012

PROJECT SUMMARY

Sufficient detail is needed; include methodology, sample, outcomes etc

AIM

The aim of this research is to qualify and quantify the relationship between PTSD and spatial processing in the hippocampus area of the human brain. In doing so, the project will develop a qualitative means of demonstrating preference for navigation strategies and predicting performance in hippocampal-dependant spatial tasks; and will provide practical tests to best demonstrate this. The intentions of this present research are to join together recent research on PTSD and spatial navigation, to test the strength and value of the relationship between them, and to better understand the neuropsychological experience of it.

The research offers benefit to PTSD sufferers and their families, the NHS, support intermediaries, and the Ministry of Defence (MOD). There is much to contribute to the emerging neuroscience research field itself (and within the project there is also an opportunity for participants to indicate interest in potential future research looking at the role of genetics in this relationship between PTSD and spatial processing).

These intentions reflect the principles outlined in Bournemouth University's Research Ethics Code of Practice (2009:4.3, 4.4) and adhere to the British Psychological Society Code of Ethics and Conduct (2009).

OUTCOMES

The intended outcomes of the research will include:

- A Qualitative, Predictive Spatial Processing Paradigm for PTSD (using open-ended interview and the FRS -*Fragebogens zu räumlichen Strategien*- and SBSOD -Santa Barbara Sense of Direction- questionnaires);
- A Quantitative Spatial Processing Test Battery for PTSD (tests may include the Spatial Cognition Lab's 'Alternative Route' Virtual Reality paradigm and mental rotation and perspective tests currently being used by University College London in research also addressing PTSD and navigation); and
- A dataset demonstrating the impact of PTSD on spatial processing experience and performance.

These outputs could later be developed for: recruitment and deployment purposes in the MOD; treatment efficacy measures for the NHS; and psychometric testing for the emergency services. They may also be used in future research investigating the role of DNA in PTSD and spatial processing. Given the British Psychological Society's Code of Ethics and Conduct (and advice therein), the potential misuse or exploitation of these products (i.e. discrimination or negating treatment) will need to be guarded against (2009; 3.1)- upon publication, and possibly via the formation of Intellectual Property Rights agreements. Initial ethics consent for this study is passed to the Bournemouth University Research Ethics Committee, in accordance with recommendations of the Department of Health (2005; 31), and in accordance with BU's Research Ethics Code of Practice (2009; 21.6). Further submission to the ethics clearance of private and public PTSD treatment centres (i.e. Combat Stress Ethics Committee and the IRAS process) may be required for participant recruitment purposes.

OUTLINE OF METHODOLOGY

A 2012 pilot study (recruiting a 'healthy' control group from a 'normal population- mainly BU Students under the SONA and Psychology Research Volunteer Scheme) will develop a qualitative and quantitative framework from which a robust evidence base will be generated to inform a wider 2013-14 study into PTSD, Combat-Related PTSD , Childhood Trauma and Trauma Exposure. N = 20-35 for each group.

Recruitment

The study will require the cooperation of a gatekeeper for initial access to the participants with combat-related post-traumatic stress disorder (CR-PTSD) group, and potentially for the generic (non combat-related) post-traumatic stress disorder group.

The ESRC (2010; section IV; 33) draw attention in their ethics guidance to these types of arrangements, and the importance of gatekeepers' "good standing" (ibid; 13). Care will need to be taken to engage with Combat Stress; NHS Clinics; the network PTSD Resolution UK; and Trauma Response initiatives in the Emergency Services (e.g. Cambridgeshire and the Metropolitan Police) to ensure that sufficient information is provided, that individual consent is sought for each participant as well as on a group basis. Guidance offered by the initiative INVOLVE ('Public Involvement in Clinical Trials' 2012 NIHR) will be useful to ensure that the research maximises the benefits of input from those with experience of PTSD and working with those with PTSD, i.e.: establishing strong working relationships between individuals in the research; ensuring that the members of the public who are involved understand fully the specific research experiments and their value; giving different perspectives to other members of the research team who's specialisms are not PTSD; assisting with dissemination of results for example via charities or patient groups, or by providing a patient story or perspective; helping with future or extended research in the area (such as genetics) by, for example, establishing standard wording or structure for patient information.

The issue of selection bias in PTSD research should be acknowledged[1], as should the reality that PTSD is a highly emotive issue with increasing coverage given current UK military activity in Afghanistan. The need to mitigate against self-selection and volunteer bias in CR-/PTSD groups will be addressed by offering clarity to all participants, that the of their contribution fundamentally lies in their sharing of diagnostic information and the application of their own time and effort on the spatial tasks. The integrity of the research calls only for this, and participants will be verbally reminded in the experiments that there is no good or bad score that can help or hinder the research, and that there are no value judgements being attached to any score- be it negative or positive.

Particpants will be fully briefed with regard to the research aims of the project, including basic definitions (see Information Sheet) of PTSD and spatial processing. Participants will also be offered

---

1 Woodward, S. H., Stegman, W. K., Pavao, J. R., Arsenault, N. J., Hartl, T. L., Drescher, K. D. and Weaver, C. (2007), Self-selection bias in sleep and psychophysiological studies of posttraumatic stress disorder. J. Traum. Stress, 20: 619–623

contacts for further information as to the progress and oucomes of the research and any implications this may have for improving the assessment and monitoring of recovery in PTSD.

Screening

Whilst the research subjects are not classified as a 'vulnerable group' under the Safeguarding Vulnerable Groups Act 2006 or the Mental Capacity Act 2005, sensitivity to the distress of the condition –and the screening required- will nonethless be paramount.

Participants for both the pilot and wider studies will be screened for previous PTSD diagnosis or childhood trauma, brain injury, depression and taking of anti-psychotic drugs, substance and alcohol dependence, sleep quality, alcohol consumption, depression, and the taking of SSRI anti-depressants. Participants will be recruited to relevant groups (I.e. CR-/PTSD; Childhood Trauma + PTSD; Trauma + no PTSD) or excluded (if satisfying criteria for brain injury, alcohol or substance-dependence, or the taking of anti-psychotic medication). This 'screening' will take the form of a simple question and answer format lasting a few minutes. Screens to be used include: Patient Health Questionnaire 9 for depression; PSQI-Addendum for PTSD for sleep quality; and units of alcohol consumed daily/weekly (using NHS guidelines). Further information about that which we will screen for will be sought from GPs Mental Health Professionals in advance, but the screening will be undertaken in person with participants in addition to any information a GP or Mental Health Professional may offer, to ensure consistency of data collection across all participants.

Consent forms will clearly state that this screening is anonymous. All participants will be given a unique ID number which will only be matched to their personal ID on a temporary master file which will be used by the immediate research team only for analysis pruposes of the durtation of the project, and destroyed thereafter in accordance with the Data Protection Act 1998.

Where individuals are excluded from the researc h on the basis of having had childhood trauma or a previous PTSD diagnosis, (for those not recruited to those specificf groups) alcohol or substance dependance, SSRI medication or brain injury, this will be sensitively communicated with reference to the research data parameters and it will be made clear on the information sheet provided that this is not a personal decision or any reflection of any value judgements relating to the criteria.

Screening will also involve the collection of demographic data, including information about 'individual factors' (BPS 2009; 3.3;iii) which will be respected, and which may also call for specific research considerations, e.g. around access and mobility for those with a disability, around the scheduling of experiements around religious festivals etc. Older individuals (i.e. 60+) who's decline in spatial processing decline is likely to be independent of other hippocampal interference) will also be excluded and similar measures to explain exclusion on the basis of age will need to be considered.

Those presenting as combat veterans with CR-PTSD will be asked for their MOD service number. Response times will be judged for malingering/ legitimacy, upon advice from senior military psychiatric personnel (references and details of this advice can be provided on request).

PTSD Symptom Severity

The assessment of PTSD symptom severity that CR-/PTSD participants will experience on first contact with the research team will be no more intrusive than any psychiatric assessment they are likely to have already expereinced to have been diagnosed with CR-/PTSD and be eligible to particpate (such as the SCID- Structured Clinical Interview for the DSM-IV). The assessment will be for research analysis purposes only, not for clinical decision-making. The symptom severity will be taken from the particpants' score on the Davidson Trauma Scale. Childhood Trauma will be assessed on the same principle (ie. for research analysis purposes only and not for clinical decision making) using a Childhood Trauma Questionnaire (e.g. Bernstein, Pearson). Both trauma scales will be administered by the project researcher who is a qualitfied social psychologist (Jessica Miller MPhil *cantab)* who will have received peer training by a clinically trained PhD student , and with advice from the clinical director of NHS Trauma Clinic (Prof Chris Brewin at University college London) . These scales will be administered simply to collect data on symptom severity for analysis purpose, and not in any way for clinical assessment or clinical decision-making.

The BPS call for researchers to inform participants, if, during the course of either screening or data collection, there emerges any "evidence of psychological or physical problem of which they are apparently unaware", if it appears that failrure to do so may endanger their wellbeing (2009; 3.3. viii). Whilst it is unlikely that the initial screening, qualitaitve or quantitative assessment would bring to light any such problems, should any additional anxiety or alcohol problems (for example) emerge through screeining and experiments, that the participant is clearly unaware of, the participant will be informed and contact details for the Student Counselling Service (pilot) and Anxiety UK (all groups) will be provided with the consent forms. Combat Stress contact details will aslo be offered (for CR-PTSD participants). All participants will be encouraged to discuss any issues arising in the screening with their GP or Mental Heatlh Professional. Given that most participants will be accessed through treatment cetres, it is anticipated that their issues will be fully addressed as part of that process.

Partipants will be clearly informed in the Information Form that the study is for research purposes only

and in no way should distract from participants continuing to access their clinical treatment, as advised by their GP or Mental Health Professional.

Qualitative Interview

Participants suffering from PTSD (i.e. in the PTSD group – which includes CR-PTSD- and the Childhood Trauma and PTSD Group) will be asked an open-ended question about their experience of navigation before , and since PTSD. This will be recorded and consent will be sought from participants for audio data to be transcribed. Two navigation questionnaires (FRS and SBSOD) will then be completed. These only take a few minutes to complete and can actually be completed at home before the spatial experiment if necessary.

Spatial Experiment

The spatial experiments will be paper-based, with one 20-30 minute virtual reality paradigm. The tests are not anticipated to be any more challenging than any other virtually simulated interactive games or 'brain training exercises' that participants may have experienced in everyday life. The virtual reality paradigms will not include any evocative imagery or stimulating content which overtly refer in any way to a combat situation or trauma. Similar virtual environments for navigation assessment have already been successfully used with older persons in the Spatial Cognition Lab at Bournmeouth University (2011), for which full ethics clearnace was given. No serious adverse effect (SAE) is anticipated in this experimental paradigm- but processes outlined in the MRC Guidelines for Good Clinical Practice (1998; 1.15) to deal with serious adverse effect will be consulted should this occur. The full duration of the testing phase is expected to be less than 2 hours, with comfort breaks offered to all participants on the hour.

INFORMED CONSENT

The MRC's Good Practice Guide for clinical trials is useful in its articulation that information provided must be 'at a level at which will enable an informed decision by trial participants' to take part in the research (1998;17: 5.4.6). The information that to be provided to participants in order to seek their consent will be made available to the Bournemouth University's Ethics Committee for approval as advised by the MRC's Guidelines for Good Clinical Practice 1998; 5.4.7). The fact that this research crosses many disciplinary boundaries of clinical psychology, neuropsychology, and neurobiology can add to the complexity in terminology between researchers- and therefore, careful use of language and clarity is important when explaining important dynamics of the research and its implications to the participants as members of the public.

Areas where clarity is particularly important include:

- the fact that the research is to understand an effect of PTSD on a brain function, and that the interview and experiment are not a trial of a cure or therapy;
- that any good performance on the spatial processing task is not indicative of any change in the participant's clinical need for formal treatment of the PTSD;
- that further (renegotiated) consent may be sought to obtain consent for genetic research (as per MRC Guidelines 1998;36 and 5.4.4) but refusal of this further contact in no way detracts from their contribution to the present study.

The Department of Health's Research Governance Framework encourages researchers to be open in critical reviews, through 'accepted channels' (2005; 18: 2.4) and that findings must be made accessible to those participating. These research findings will be scrutinized formally through PhD assessment procedures, and reports will be tailored to public and participants in the dissemination period- this will include a report to the intermediary Army of Angels (registered charity number: 1137575), to which the researcher is contractually bound with respect to the UKRIO Research Checklist as referred to in the ESRC Guidelines 2010; 37). Participants and their GPs/ medical referees will also be given a long term point of contact for the research and its outcomes (as per Department of Health's Research Governance Framework 2005; 36).

REWARD

Whilst the intention in this research project is to offer participants reasonable compensation for time and expenses, the investigators are mindful of BPS guidelines urging researchers to "refrain from using financial compensation ...for research participants to risk harm –beyond that which they face in their normal lifestyles" (2009; 3.3. iv).

There is not such anticipated risk of harm in this project, beyond any degree of boredom or frustration they may find with the navigation tasks, which will no doubt vary between individuals, their personalities and their preferences.

Participants will (as per BPS guidance at 3.3. vi) be clearly informed that their right to withdraw from the programme is not affected by the receipt or offer of any financial compensation or other inducements for participation.

The pilot will recruit and reward according to the principles of DEC's psychology research volunteer scheme. Control groups will be sourced as locally as possible to keep travel expenses low. CR-/PTSD

NHS ethics clearance

NHS
Health Research Authority

NRES Committee South West - Cornwall & Plymouth
Bristol Research Ethics Committee Centre
Level 3
Block B
Whitefriars
Lewins Mead
Bristol
BS1 2NT

Telephone: 0117 342 1330
Facsimile: 0117 342 0445

06 March 2013

Ms Jessica K Miller
PhD Candidate
Bournemouth University
P104, Poole House,
Fern Barrow, Talbot Campus, Poole, Dorset
BH12 5BB

Dear Ms Miller

Study title:	**The role of spatial processing and the BDNF polymorphism Val66met in predicting the neurological impact of Post Traumatic Stress Disorder (PTSD), Combat-Related PTSD, and Childhood Trauma.**
REC reference:	**13/SW/0041**
IRAS project ID:	**120945**

Thank you for your letter of 04 March 2013, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator Charlotte Allen, nrescommittee.southwest-cornwall-plymouth@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Advertisement	2	03 March 2013
Evidence of insurance or indemnity		09 July 2012
GP/Consultant Information Sheets	4	03 March 2013
Investigator CV		17 January 2013
Other: CV - Academic Supervisor		
Other: Email from Funder: Army of Angels		25 January 2012
Other: Letter from Funder - Army of Angels		05 February 2013

Participant Consent Form: DNA	2	02 February 2013
Participant Consent Form	3	03 March 2013
Participant Information Sheet: DNA	3	03 March 2013
Participant Information Sheet	3	03 March 2013
Protocol	3	03 March 2013
Questionnaire: SBSOD		
Questionnaire: Generic Pilot Screening		
Questionnaire: Spatial Test: Virtual Reality Sample		
Questionnaire: Alternative Route Instructions - Underground Tunnel		
Questionnaire: Childhood Trauma Screen Questionnaire		
Questionnaire: Cognitive Development Questionnaire		
Questionnaire: PTSD Symptom Severity (DTS)		
Questionnaire: Generic Pilot Screening		03 March 2013
REC application		24 January 2013
Referees or other scientific critique report		07 June 2012
Response to Request for Further Information		04 March 2013

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

13/SW/0041	Please quote this number on all correspondence

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

With the Committee's best wishes for the success of this project.

Yours sincerely

pp.

Canon Ian Ainsworth-Smith
Chair

Email:nrescommittee.southwest-cornwall-plymouth@nhs.net

Enclosures: "After ethical review – guidance for researchers" *(via email)*

Copy to: *Dr Jan Wiener, Bournemouth University*

Prof Sue Clarke, Dorset HealthCare University NHS Foundation Trust

Dorset HealthCare NHS
University NHS Foundation Trust

St Anns Hospital
69 Haven Road
Canford Cliffs
Poole
Dorset
BH13 7LN
Web:
www.dorsethealthcare.nhs.uk

Ms Jessica Miller

P104, Poole House

Fern Barrow

Talbot Campus

Poole

Dorset

BH12 5BB

9 April 2013

Dear Ms Miller

Re: PTSD and Navigation study

Thank you for submitting the above research project to the Dorset Healthcare University NHS Foundation Trust Research & Development department NHS permission to proceed at Bournemouth & Poole.

I am pleased to inform you that NHS permission to proceed for the above research was granted for Dorset Healthcare University NHS Foundation Trust on.

NHS permission was granted on the basis described in the application form, protocol and supporting documentation.

You should notify the Research & Development Office, (R&D) within the same timeframe of notifying the REC and any other regulatory bodies, of the following:

- Amendments (including changes to the local research team) in accordance with guidance on IRAS
- Progress reports
- Changes to the status of the study
- End of study reports

Please do not hesitate to contact the R&D Office on 01202 492128 if you require any additional information or support.

I wish you every success with your research project

Yours sincerely

P. Dill

Paul Dillon

Research Manager

cc Lyn Courtney, Research & Development office

Combat Stress ethics clearance

PATRON: HRH The Prince of Wales KG KT GCB OM AK QSO PC ADC
PRESIDENT: General Sir Reddy Watt KCB KCVO CBE
Head Office: Tyrwhitt House, Oaklawn Road, Leatherhead, Surrey KT22 0BX
Tel: 01372 587100 Fax: 01372 587101
Email: contactus@combatstress.org.uk
Website: www.combatstress.org.uk

COMBAT STRESS
THE ENEMY WITHIN APPEAL

Reply to: Tyrwhitt House
Oaklawn Road
Leatherhead
Surrey KT22 0BX
Tel: (01372) 587107
Fax: (01372) 587081
Email: walter.busuttil@combatstress.org.uk

Dictated 16th April 2013

Ms Jessica Miller
PhD Candidate
Bournemouth University
P104, Poole House
Fern Barrow
Talbot Campus
Poole BH12 5BB

Dear Ms Miller,

I am writing formally to say that the Research & Ethics Committee chaired by Professor Simon Wessely has formally approved your research.

I think we need to have a conversation, in relation to how we pass on the message to veterans, to contact you, I assume you will be able to send me some posters, for us to put on our notice boards for you.

Please remember we have three treatment centres across the country. We also have fourteen clinical Outreach Teams.

I wish you well, in your endeavour.

With best wishes,

Yours sincerely,

Dr Walter Busuttil MB ChB MPhil MRCGP FRCPsych
Consultant Psychiatrist
Medical Director

EX-SERVICES MENTAL WELFARE SOCIETY
Company Limited by Guarantee
Registered in England and Wales No 256353
Charity Registration No 206002
Scotland No SC038828
FundRaising Standards Board

Sample of a recruitment poster (Combat Stress)

APPENDIX B: INFORMATION AND CONSENT FORMS

This appendix provides information sheets and consent forms (A, B, C, D). As explained the Methodology (Chapter 2, Section 2.4), the study began in 2011 but introduced the genetic testing in 2013. Subsequently, supplementary information sheets (B) and supplementary consent forms (D) were provided for collecting saliva samples to analyse Brain-Derived Neurotrophic Factor (BDNF) genotype distribution in the sample population.

A PTSD (Post-Traumatic Stress Disorder) & Navigation Participant Information

Invitation

We would like to invite you to take part in our research study.

Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. We'd suggest this should take about 10 minutes

Talk to others about the study if you wish.

(Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study).

Ask us if there is anything that is not clear.

PART ONE

What is the purpose of the study?

Bournemouth University is undertaking research into the impact that Post-Traumatic Stress Disorder (PTSD) and Combat-Related PTSD may or may not have on spatial processing (the way we navigate around our environment). The intention of this study is to inform those involved in assessing and treating PTSD about further impacts that the condition can have on people's everyday life.

Why have I been invited?

You have been invited to take part because your experiences may be helpful for us to look at navigation in those who have not experienced trauma, or those who have. There may be up to 150 other people participating in the whole study from 2013-16.

Do I have to take part?

It is up to you to decide to join the study. We will describe the study and go through this information sheet. If you agree to take part, we will then ask you to sign a consent form. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you may be receiving in the NHS or privately.

What will happen to me if I take part?

You will actively take part in about 90 minutes of contact time with us, and may be contacted (if you agree that's OK to be) in to give a saliva sample later on (this may be straight away, or later on in the year, depending on when you take part). The research programme lasts from 2013-2016 but we will do our best to involve you as briefly as possible, so as to not inconvenience you.

We will first check with you (either over the 'phone or in person) that you have not had any brain injury, that you are not over 60yrs old, and that you are not taking certain medication. If you have or are, we may thank you for your time and not continue.

If we do continue, we will ask some screening questions about how you are feeling at the moment (sleep, mood, any pain etc). If you have PTSD, we will ask if it's OK to contact your GP to confirm some technical information about the diagnosis for analysis purposes. We will then ask about how you navigate around, using some simple questionnaires. You will then take a picture test which will last about 10 minutes, and then a computer task which will last 25 minutes. (It may be that we ask you some more conversational questions about your experiences, and if that is the case, we may ask to record this using a Dictaphone.)

If, during our time, we think that you may benefit from further support or treatment for your experiences (for depression, anxiety, etc) we will offer to write a letter -with you- to your GP, to ask for more support. The researcher would have a duty to disclose if risky behaviour which might cause harm to you the participant (or to others) was disclosed during the interview.

Expenses and payments

We offer to pay you £10 (estimated at the rate of £6/hr) as a 'Thank You' for your time with us, and to refund any travel expenses you may incur.

What will I have to do?

You will be asked to provide contact information, some basic details about your age, nationality and if you have a disability. You will then meet with us for about 90 minutes for the research. You may then hear from us again to ask if you are interested in offering a saliva sample at a later date. You can also contact us any time to find out more about the research and we can give you feedback on your navigation style if that is of interest to you.

What about diagnosis or treatment?

When you come to us, we will ask if you have been diagnosed with PTSD. If you have, we will ask for your consent to contact your GP for technical information about this diagnosis. If you have not been diagnosed with PTSD but you or we think that you may benefit from further enquiry, we will offer to write with you to your GP- but you will not be asked to continue with the research until you have the diagnosis. If you are receiving treatment for PTSD, we will ask for the date when this started and how long your treatment is for. Your time with us is purely for research purposes and the research does not give any diagnosis or offer any therapeutic treatment for PTSD- but we can offer to help you access support if you or we feel that you need it.

There is currently a wait of six months to receive treatment for PTSD and taking part in the study would not allow you to receive treatment more quickly.

What are the possible disadvantages and risks of taking part?

If you have been exposed to trauma, we will ask you when this occurred and what the nature of the trauma was, and how you feel about it now. There is a chance that this may cause you discomfort, and if so, we offer contact details for support and offer to write with you to your GP. You are also free to withdraw from the research at any time. The computer task is no more challenging than any computer game or brain-training game you may have come across before and only uses pictures of everyday objects and animals, with a neutral setting. We don't anticipate

that any harm or distress will come to you from joining the research, but you are always free to withdraw at any time should you feel uncomfortable.

What are the possible benefits of taking part?

You may feel benefit from understanding better how you navigate around your environment and what your preferred style is- if you would like more feedback on this, please do ask the researcher who will be happy to tell you more.

We cannot promise the study will help you deal with trauma, if you have been exposed to it, but the information we get from this study may go on to inform the treatment of people with childhood trauma, PTSD and Combat-Related PTSD.

What happens when the research study stops?

When the (estimated) 90 minutes research comes to an end, we will offer payment as a thank you for your time. We will also confirm with you if you would like us to write to your GP with you to ask for support, and make arrangements to do so, or we may offer you contact details for further support. We will confirm if it is OK to contact you further about the possibility of giving a saliva sample (for which there is a separate consent form). We will check to see if you'd like some more feedback about your results and navigation style in the future.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

PART TWO

What if relevant new information becomes available?

The research does not involve any therapy or treatment for PTSD, but we do offer contact details for organisations who may know more about PTSD treatment news.

What will happen if I don't want to carry on with the study?

If you withdraw from the study, we will destroy all your identifiable data, but we will need to use the anonymous data collected up to your withdrawal.

What if there is a problem?

If you have a concern about any aspect of this study, you should contact the Chief Investigator who will do their best to answer your questions [email millerj@bournemouth.ac.uk]. If you remain unhappy and wish to complain formally to the supervisor, you can do this by contacting jwiener@bournemouth.ac.uk or by calling 01202 961822.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against [Dorset Healthcare University NHS Foundation Trust] but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Will my taking part in this study be kept confidential?

Yes. Your research data will be collected by hand through the screens and questionnaires, and through the computer game you undertake in the (estimated) 90 minutes contact time. That research data will then be processed and stored securely at Bournemouth University, with your ID being removed from it for analysis and storage. Research data will be kept long term for potential use in future studies, but your personal data will be destroyed at the end of the research programme in 2016. Only the immediate research team will have access to the personal data, and only authorised persons such as researchers, sponsors, and regulatory authorities will have access to the anonymised research data. At no time will your data be able to be associated with you to anyone outside of the immediate research team. Bournemouth University Dorset Healthcare University NHS Foundation Trust comply in full to the Data Protection Act 1998.

What will happen to the results of the research study?

The broad scientific results of the research will be available on the Bournemouth University website: http://microsites.bournemouth.ac.uk/signage/wayfinding-and-ptsd/. Results relevant to you as an individual are available on request to: millerj@bournmeouth.ac.uk.

You may get immediate feedback on the picture task in the 90 minutes you are with the researcher. The intention is to publish the results in medical journals relevant to PTSD, navigation, and the area of the brain which is involved (the hippocampus). You will not be identified in any report/publication unless you have given specific consent to do so.

Who is organising and funding the research?

The research is mainly unfunded, but has received contributions from the Army of Angels (registered charity 1143612), the Bournemouth University Foundation and the Santander BU Travel Grant. The researcher is not being paid for including you in this study. The project is being undertaken as part of a Doctorate in Neuropsychology.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. The project had been reviewed and approved by the Cornwall & Plymouth Research Ethics Committee. The research has also been independently reviewed by senior military psychiatry experts and the medical director of the registered charity Combat Stress. The research is in collaboration with University College London.

Further Information about the Study

PTSD is a complex and debilitating condition that can affect every aspect of a person's life. It is a psychological response to the experience of an event (or events) of an intensely traumatic nature -an event that has provoked intense fear, horror or a sense of helplessness in the individual concerned. These type of events often involve a risk to life – one's own or that of one's colleagues. It is a condition that can affect anyone, regardless of age, gender or culture. (Combat Stress: http://www.combatstress.org.uk/pages/what_is_ptsd.html)

Spatial Processing is about using accurate spatial knowledge and selecting the best strategies to navigate and find our way around their environment. In this project, we use questionnaires and behavioural tasks to investigate how PTSD might or might not affect spatial processing.

Contact Details

For general information about research, visit http://www.bournemouth.ac.uk/prc/ptsd-spatial-processing-and-genetics.html

For specific information about this research project and advice as to whether you should participate, email: millerj@bournemouth.ac.uk.

If you are unhappy with the study, email jwiener@bournemouth.ac.uk or call 01202 961822.

Further information for support

Alcoholics Anonymous: If you need help with a drinking problem either phone our national help line on 0845 769 7555 or contact us by email: help@alcoholics-anonymous.org.uk. These services are staffed by volunteer members of A.A. who will be happy to answer your questions or put you in touch with those who can.

Anxiety UK: If you would like to speak to someone about your anxiety, ring our helpline on 08444 775 774. Our helpline operates from 9:30-5:30, Monday to Friday. The helpline is staffed by volunteers with personal experience of anxiety so you will be speaking with someone who has been there. Alternatively, visit online and email at: http://www.anxietyuk.org.uk/get-help/email-support/

Combat Stress: Helpline 0800 138 1619, by text on 07537 404 719 (standard charges may apply for texts), or email combat.stress@rethink.org. If you or perhaps someone in your family has a problem, then call for an informal chat. Services are free of charge and regardless of War Pension/Armed Forces Compensation Scheme status.

Council for Involuntary Tranquilliser Addiction: Information and support for people addicted to prescription tranquillisers. Helpline: 0151 932 0102

Self-Harm: http://www.siriusproject.org/groups.html is an Information and Support Service with a website signposting users to support groups specialising in self-harm, such as http://self-injury.net/information-recovery/recovery

Talk to Frank: Email and telephone support for young people, parents and carers concerned about drugs. Helpline: 0800 776 600 Email: frank@talktofrank.com Website: www.talktofrank.com

B Supplementary PTSD (Post-Traumatic Stress Disorder) Navigation & DNA Participant Information Sheet

Invitation

We would like to invite you to take part in a further element of our research study.

Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the PTSD and Navigation Information Sheet (as well as this one) with you and answer any questions you have. We'd suggest this should take about 10 minutes Talk to others about the study if you wish.

(Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study). Ask us if there is anything that is not clear.

PART ONE

What is the purpose of the further study?

Bournemouth University is undertaking research into the impact that Post-Traumatic Stress Disorder (PTSD) and Combat-Related PTSD may or may not have on spatial processing (the way we navigate around our environment). We are also taking an initial look at the presence of a gene variation which may have a role to play in the development of the area of the brain which is important for PTSD and navigation. The intention of this DNA collection is to support the main PTSD into navigation.

Why have I been invited?

You have been invited to take part because you took part in the main study into PTSD and Navigation. We are inviting all those who took part to offer an anonymous saliva sample. There may be up to 150 other people participating in the whole study from 2013-16.

Do I have to take part?

It is up to you to decide to join this part of the study. We will describe the study and go through this information sheet. If you agree to take part, we will then ask you to sign a separate DNA consent form. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you may be receiving in the NHS or privately. Your DNA sample will be destroyed if it has not already been depersonalised by the time you withdraw.

What will happen to me if I take part?

You will be invited to come to the University or NHS Clinic and give a saliva sample. The saliva sample itself will only take about 15 minutes to fill an inch of a small container using a cotton bud in your cheek, but you may be with us for up to half an hour in total. You will be asked not to drink any fluids for 30 minutes before your booked time with us.

Expenses and payments

We offer to pay you £10 (estimated at the rate of £6/hr) as a Thank You for your time with us for the main study, and to refund any travel expenses you may incur. If you have to come back to give the DNA sample, we can offer to cover your travel expenses.

What will I have to do?

You will be asked to provide your name, the date you participated in the main study, and not to drink anything 30minutes before you arrive to take the sample.

What about diagnosis or treatment?

Your DNA sample is purely for research purposes and the research does not give any diagnosis or offer any therapeutic treatment for PTSD- but we can offer to help you access support if you or we feel that you need it. The DNA extraction is for one gene only: the met or val variation of the BDNF polymorphism. Its presence does not indicate any medical issue or have any known implications beyond an association with navigation training and with PTSD symptom severity. It is of interest to us for analysis in this area of PTSD and navigation research only. There is currently a wait of six months to receive treatment for PTSD and taking part in the study would not allow you to receive treatment more quickly.

What are the possible disadvantages and risks of taking part

There is no risk of harm to you from providing a saliva sample. It does not hurt and is not uncomfortable and only takes a few minutes, depending on how much saliva you tend to produce. We don't anticipate that any harm or distress will come to you from joining the research, but you are always free to withdraw at any time should you feel uncomfortable.

What are the possible benefits of taking part?

We cannot promise the DNA study or the main study would help you deal with trauma, if you have been exposed to it, but the information we get from this study may help improve the treatment of people with childhood trauma, PTSD and Combat-Related PTSD.

What happens when the research study stops?

We will confirm with you that your DNA will be depersonalised and that only the immediate research team at Bournemouth University and the NHS Trust will be able to access ID associated with the sample. Personal data will be encrypted and the DNA will be stored anonymously by DNA Genotek Canada and destroyed 30 days after the project end.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

PART TWO

What if relevant new information becomes available?

The research does not involve any therapy or treatment for PTSD, but we do offer contact details for organisations who may know more about PTSD treatment news.

What will happen if I don't want to carry on with the study?

If you withdraw from the study, we will destroy all your identifiable data, but we will need to use the anonymous data collected up to your withdrawal. Your DNA sample will be destroyed if it has not already been depersonalised and data from that will not be used.

What if there is a problem?

If you have a concern about any aspect of this study, you should email the Chief Investigator who will do their best to answer your questions at: millerj@bournemouth.ac.uk. If you remain unhappy

and wish to complain formally to the supervisor, you can do this by contacting jwiener@bournemouth.ac.uk or by calling 01202 961822. In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Dorset Healthcare University NHS Foundation Trust but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Will my taking part in this study be kept confidential?

Yes. At no time will your DNA data be able to be associated with you to anyone outside of the immediate research team. Only authorised persons such as researchers, sponsors, and regulatory authorities will have access to your personal research data, which will be encrypted. Your DNA will be depersonalised before sending to your DNA Genotek Canada and destroyed 30 days after the project end. Bournemouth University Dorset Healthcare University NHS Foundation Trust comply in full to the Data Protection Act 1998, and DNA Genotek to equivalent data protection standards as the UK for the purposes of this research.

What will happen to the results of the research study?

The broad scientific results of the research will be available on the Bournemouth University website: http://microsites.bournemouth.ac.uk/signage/wayfinding-and-ptsd/. Results relevant to you as an individual are available on request to: millerj@bournmeouth.ac.uk.

The intention is to publish the results in medical journals relevant to PTSD, navigation, and the area of the brain which is involved (the hippocampus). You will not be identified in any report/publication unless you have given specific consent to do so.

Who is organising and funding the research?

The research is mainly unfunded, but has received contributions from the Army of Angels (registered charity 1143612), the Bournemouth University Foundation and the Santander BU Travel Grant. The researcher is not being paid for including you in this study. The project is being undertaken as part of a Doctorate in Neuropsychology.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. The project had been reviewed and approved by the Cornwall & Plymouth Research Ethics Committee. The research has also been independently reviewed by senior military psychiatry experts and the medical director of the registered charity Combat Stress. The research is in collaboration with University College London.

Contact details

http://www.bournemouth.ac.uk/prc/ptsd-spatial-processing-and-genetics.html

For specific information about this research project and advice as to whether you should participate, email: millerj@bournemouth.ac.uk.

If you are unhappy with the study, email jwiener@bournemouth.ac.uk or call 01202 961822.

About the Study

PTSD is a complex and debilitating condition that can affect every aspect of a person's life. It is a psychological response to the experience of an event (or events) of an intensely traumatic nature -an event that has provoked intense fear, horror or a sense of helplessness in the individual concerned. These type of events often involve a risk to life – one's own or that of one's colleagues.

It is a condition that can affect anyone, regardless of age, gender or culture. (Combat Stress: http://www.combatstress.org.uk/pages/what_is_ptsd.html)

Spatial Processing is about using accurate spatial knowledge and selecting the best strategies to navigate and find our way around their environment. In this project, we use questionnaires and behavioural tasks to investigate how PTSD might or might not affect spatial processing.

DNA and the val66met variation of the BDNF polymorphism has been associated with how well part of the brain (the hippocampus) can benefit from navigation training. That gene has recently been associated with PTSD symptom severity. This suggests further evidence for a connection between the hippocampus, navigation and PTSD. If research can identify who might be able to improve how their hippocampus works through spatial training (by seeing which variation of the gene they carry), this could then be looked at for those with PTSD who's hippocampus does not work so well.

C Consent Form

Title of Project: PTSD and Navigation Study

Your Name:

Name of Researcher:

Please initial box

1. I confirm that I have read and understand the information sheet for the above study (which is dated 020213 and is version 2).	
2. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
3. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without any medical care or legal rights being affected.	
4. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from Bournemouth University, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
5. I agree to my GP being informed of my participation in the study.	
6. I agree to audio recording of any longer responses to questions I may give if this is deemed necessary at the time.	
7. I agree to receive individual feedback from testing.	
8. I agree to take part in the above study.	

Date **Signature**

Name of Person taking consent

Date **Signature**

D Supplementary Consent Form (DNA)

Title of Project: PTSD, DNA and Navigation Study

Your Name:

Name of Researcher:

Please initial box

1. I confirm that I have read and understand the information sheet for the above study (which is dated 020213 and is version 2).	
2. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
3. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without any medical care or legal rights being affected.	
4. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from Bournemouth University, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
5. I agree to my GP being informed of my participation in the study.	
6. I consent to give a saliva sample of DNA which will be de-personalised and then sent as an anonymous sample to DNA Genotek (Canada) which adheres to equivalent data protection measures as the UK where it will be destroyed after 30 days of the project end.	
7. I agree to receive individual feedback from testing.	
8. I agree to take part in the above study.	

Date **Signature**

Name of Person taking consent

Date **Signature**

APPENDIX C: NAVIGATION QUESTIONNAIRES

Santa Barbara Sense of Direction (SBSOD) (Hegarty et al., 2002).

SANTA BARBARA SENSE-OF-DIRECTION SCALE

Sex: F M Today's Date:_____
Age:_____ V. 2

This questionnaire consists of several statements about your spatial and navigational abilities, preferences, and experiences. After each statement, you should circle a number to indicate your level of agreement with the statement. Circle "1" if you strongly agree that the statement applies to you, "7" if you strongly disagree, or some number in between if your agreement is intermediate. Circle "4" if you neither agree nor disagree.

1. I am very good at giving directions.

strongly agree 1 2 3 4 5 6 7 strongly disagree

2. I have a poor memory for where I left things.

strongly agree 1 2 3 4 5 6 7 strongly disagree

3. I am very good at judging distances.

strongly agree 1 2 3 4 5 6 7 strongly disagree

4. My "sense of direction" is very good.

strongly agree 1 2 3 4 5 6 7 strongly disagree

5. I tend to think of my environment in terms of cardinal directions (N, S, E, W).

strongly agree 1 2 3 4 5 6 7 strongly disagree

6. I very easily get lost in a new city.

strongly agree 1 2 3 4 5 6 7 strongly disagree

7. I enjoy reading maps.

strongly agree 1 2 3 4 5 6 7 strongly disagree

8. I have trouble understanding directions.

strongly agree 1 2 3 4 5 6 7 strongly disagree

9. I am very good at reading maps.

strongly agree 1 2 3 4 5 6 7 strongly disagree

10. I don't remember routes very well while riding as a passenger in a car.

strongly agree 1 2 3 4 5 6 7 strongly disagree

11. I don't enjoy giving directions.

strongly agree 1 2 3 4 5 6 7 strongly disagree

12. It's not important to me to know where I am.

strongly agree 1 2 3 4 5 6 7 strongly disagree

13. I usually let someone else do the navigational planning for long trips.

strongly agree 1 2 3 4 5 6 7 strongly disagree

14. I can usually remember a new route after I have traveled it only once.

strongly agree 1 2 3 4 5 6 7 strongly disagree

15. I don't have a very good "mental map" of my environment.

strongly agree 1 2 3 4 5 6 7 strongly disagree

The Questionnaire of Spatial Representation (QSR) (Pazzaglia & De Beni, 2001).

Appendix 1. Questionnaire on Spatial Representation (Pazzaglia et al 2000)

1. Do you think you have a good sense of direction?
   1 (not at all), 2, 3, 4, 5 (very good)
2. Are you considered by your family or friends as having a good sense of direction?
   1 (not at all), 2, 3, 4, 5 (very much)
3. Think about the way you orient yourself in different environments around you. Would you describe yourself as a person:
   (a) who orients him/herself by remembering routes connecting one place to another
   1 (not at all), 2, 3, 4, 5 (very much)
   (b) who orients him/herself by looking for well-known landmarks
   1 (not at all), 2, 3, 4, 5 (very much)
   (c) who tries to create a mental map of the environment
   1 (not at all), 2, 3, 4, 5 (very much)
4. Think of an unfamiliar city. Write the name.....
   Now try to classify your representation of the city:
   (a) survey representation, that is a map-like representation
   1 (not at all), 2, 3, 4, 5 (very much)
   (b) route representation, based on memorizing routes
   1 (not at all), 2, 3, 4, 5 (very much)
   (c) landmark-centred representation, based on memorizing single salient landmarks (such as monuments, buildings, crossroads, etc).
   1 (not at all), 2, 3, 4, 5 (very much)
5. When you are in a natural, open environment (mountains, seaside, country) do you naturally individuate cardinal points, that is where North, South, East, and West are?
   1 (not at all), 2, 3, 4, 5 (very much)
6. When you are in your city do you naturally individuate cardinal points, that is do you find easily where North, South, East, and West are?
   1 (not at all), 2, 3, 4, 5 (very much)
7. Someone is describing for you the route to reach an unfamiliar place. Do you prefer:
   (a) to make an image of the route
   1 (not at all), 2, 3, 4, 5 (very much)
   (b) to remember the description verbally
8. In a complex building (store, museum) do you think spontaneously and easily about your direction in relation to the general structure of the building and the external environment?
   1 (not at all), 2, 3, 4, 5 (very much)
9. When you are inside a building can you easily visualize what there is outside the building in the direction you are looking towards?
   1 (not at all), 2, 3, 4, 5 (very much)
10. When you are in an open space and you are required to indicate a compass direction (north-south-east-west), do you
    (a) point immediately
    (b) need to think before pointing
    (c) have difficulty
11. You are in a complex building (many floors, stairs, corridors) and you have to indicate where the entrance is, do you
    (a) point immediately
    (b) need to think before pointing
    (c) have difficulty

The "Fragebogen Räumliche Strategien" (FRS) (Münzer & Hölscher, 2011).

FRS

This questionnaire consists of statements describing behaviors and preferences for navigation in known and unknown environments. Please indicate how strongly you disagree or agree with each statement by using the following 7-point rating scale:

Strongly Disagree 1 2 3 4 5 6 7 Strongly Agree

For each statement, please mark the position that corresponds to the extent of your disagreement or agreement:

1. In an unknown city, I usually know from which direction I came and in which direction I am going.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

2. If somebody were to ask me for directions in my hometown, I would picture a town map and describe the route based on that map.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

3. While walking through a big building, I usually picture it as a floor plan.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

4. I am very good at pointing toward other nonvisible locations from where I am standing.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

5. In a natural outdoor environment (in the woods or in the mountains) I can remember a route very well if I have walked it before.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

6. I can spontaneously point toward north, south, east and west.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

7. I typically picture my surroundings as a "mental map" (i.e. from an aerial or overhead view).

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

8. I always find my destination without problems.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

9. In a natural outdoor environment (in the woods or in the mountains) I try to understand my surroundings from an aerial (overhead) view.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

10. I can easily find my way in a new environment.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

11. When I'm out and about in my hometown, I can picture my own position as a dot on a "mental map".

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

12. I am very good at remembering how to get somewhere and I don't have trouble finding the way back.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

13. If I have walked a route in a big building once before, I don't have trouble walking it again.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

14. My sense of direction is very good.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

15. From anywhere in my hometown, I can point spontaneously toward prominent buildings and other points of interest.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

16. I can picture my hometown very well from a bird's-eye view, as if it were shown on a map.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

17. In a natural outdoor environment, I can point to north, south, east and west spontaneously.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

18. In a big building I can spontaneously point toward the entrance.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

19. When I move around in a new city, I typically picture it as a map.

Strongly Disagree 1 2 3 4 5 6 7 *Strongly Agree*

APPENDIX D: ALTERNATIVE TRAUMA GROUPINGS

The study assessed the impact of trauma and PTSD using a sample structure of groups comprising: the *Trauma Unexposed,* the *Trauma Exposed* with *No PTSD* and those with *PTSD*). Alternative groupings of trauma status were also evaluated for this study. Basic analyses were undertaken using different trauma delineations to ascertain if these would provide more insight into our understanding of trauma.

Alternative groupings included:

I. 'Trauma exposure *per se*': this differentiated between those who reported trauma exposure and those who reported no trauma exposure (using the Life Events Checklist, Blake et al. 1995). This structure necessarily subsumed both those with PTSD and healthy controls into one group.

II. 'Any trauma now': this differentiated between those who scored above zero on the PTSD Diagnostic Scale (Foa et al. 1995) and those who did not. This structure necessarily subsumed those with trauma exposure and very low PDS scores with those with sub-clinical trauma and those with clinical levels of probable PTSD into one group.

III. 'Trauma impact' groups: this grouped participants by the interquartile range of their PDS score mild, moderate, moderate to severe and severe (Foa et al.1995). This structure would have to integrate an additional group of 'non-scoring' individuals to accommodate participants unexposed to trauma, and this additional group would necessarily have to subsume participants with trauma exposure too if they were not scoring on the PDS.

The sample population was restructured using these groupings to evaluate its usefulness in presenting impairment in spatial processing. As with the main analysis undertaken in Chapter 4 (Section 4.3), repeated measures ANOVAs were conducted the between factor being *trauma group* and the within factor being a standard measure of navigation performance (i.e. same and different direction trial performance in the Alternative Route Paradigm).

Trauma group comprised either: trauma exposed *vs* unexposed; any trauma now *vs* no trauma now; or trauma impact interquartile ranges according to the PTSD Diagnostic Scale: 0 - 20, as mild, 11 – 20 moderate, 21 – 35 moderate to severe and 36 plus, severe (Foa ety al., 1995).

Table D presents the results of the repeated measures ANOVA (main effect of trial, trial and group interaction, and main effect of group) for each of the three alternative grouping structures. Results indicate that these alternative grouping structures do not offer any more clarity on the impact of trauma on spatial processing than the group structure used in the main study in the final row in Table D (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD,* as shown in Section 4.3.1, Chapter 4).

	Main effect of same and different direction trials	**Trauma group and direction trial interaction**	**Main effect of experimental group**
Trauma exposed *vs* unexposed	*F* (1, 138) = 142, *p* < 0.01, η_p^2 **= 0.51**	*F* (1, 138) = 2.57, *p* = 0.11, η_p^2 **= 0.02**	*F* (1, 138) = 15.4, *p* < 0.01, η_p^2 **= 0.10**
Any trauma now *vs* no trauma now	*F* (1, 138) = 190, *p* = .< 0.01, η_p^2 **= 0.58**	*F* (1, 138) = 2.19, *p* = 0.14, η_p^2 **= 0.02**	*F* (1, 138) = 16.2, *p* = < 0.01, η_p^2 **= 0.11**
Trauma impact interquartile ranges	*F* (1, 135) = 189, *p* = < 0.01, η_p^2 **= 0.58**	*F* (4, 135) = .308, *p* = 0.87, η_p^2 **= 0.01**	*F* (4, 135) = 7.71, *p* < 0.01, η_p^2 **= 0.19**
Trauma Unexposed, Trauma Exposed No PTSD, PTSD	*F* (1, 137) =202, *p* < 0.01 , η_p^2 **= 0.60**	*F* (2, 137) = 1.28, *p* = 0.28, η_p^2 **= 0.02**	*F* (2, 137) = 13.4, *p*< 0.01, η_p^2 **= 0.16**

Table D: Results from repeated measures ANOVA with between factors of "alternative trauma groupings" (three alternative analyses according to the grouping) and within factors of same and different approach direction (Alternative Route Paradigm) (*n* = 138).

The alternative groupings were discounted on the basis that they offered no more clarity on the main effect of group than the existing groups do (in the final row in Table D above and at Section 4.3.2 in Chapter 4).

Furthermore, the existing group structure *Trauma Unexposed, Trauma Exposed No PTSD, PTSD)* is a logical development of the sample structure of recent research (Smith et al. 2015; Bisby et al. 2010) which compares PTSD and trauma exposure without PTSD, and makes best use of the new 'unexposed' control group, for which there has been recognition in relevant literature (Yehuda et al., 2015; Wang, 2015). See the Methodology Chapter 2, Section 2.8.1.

APPENDIX E: AUTHOR CORRESPONDENCE

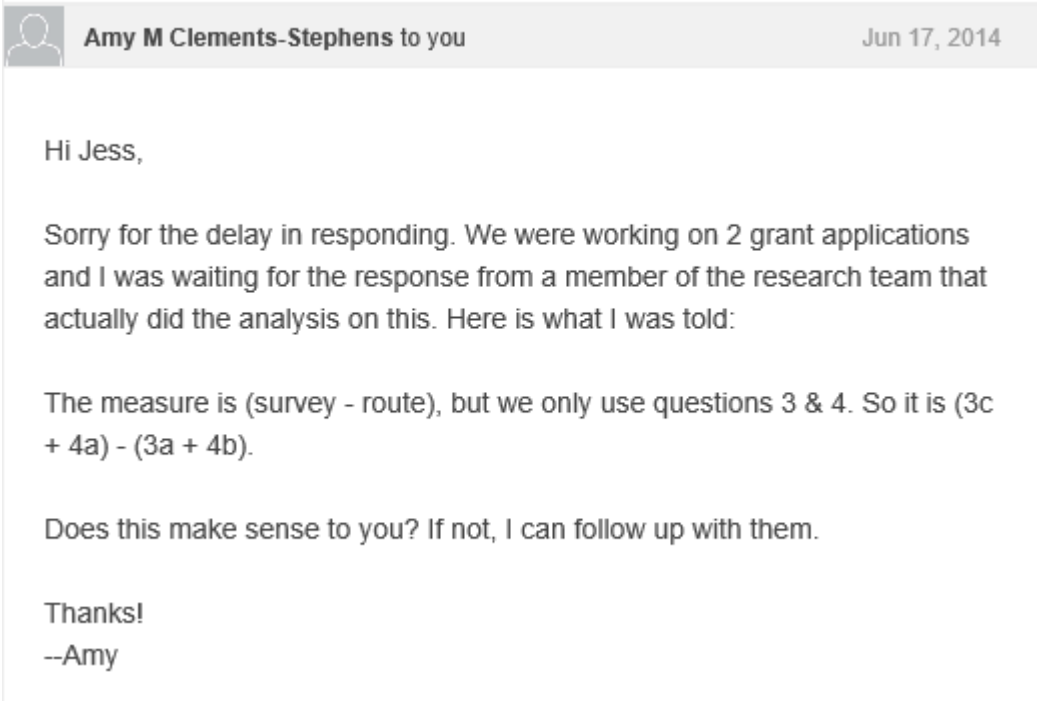
This appendix supplements Chapter 5 (Self-Reported Navigation) with correspondence with authors of navigation questionnaires which confirms the best approach to analysis of self-reported confidence in egocentric and allocentric spatial processing. In section A, Münzer (Münzer & Hölscher, 2011; Münzer & Stahl, 2011) confirms that the allocentric questions have been used to predict spatial learning and in section B, Clements (from Furnman et al., 2014) confirms the key allocentric (survey) and egocentric (route) question numbers.

A EMAIL RE: FRS Questionnaire

Stefan Münzer <stefan.muenzer@[redacted]
Fri 05/10/2012 14:37
To:Jessica Miller. 5 attachments
Dear Jess,
thank you very much for your email and your interest in our questionnaire.
Actually, there is an English version of the questionnaire (I attach it to the mail). I think it can be used and interpreted analogously to the german version. I attach it both in WORD and pdf format. There is a second document that described briefly which items belong to which scales.
Unfortunately, I do not have an English version of the article. Therefore, I will tell you briefly in this email why I think the FRS is an appropriate measure of spatial strategies and sense of direction:
1) both exploratory and confirmatory factor analyses supported the separability of the dimensions/scales of the FRS. The "global-egocentric" scale measures "sense of direction" - a global confidence to find one's way successfully. This global confidence is related to egocentric spatial strategies (route memory and knowing directions from one own's position). Thus, these aspects form a scale together. -- The "survey" scale measures the tendency of the individual to form a mental map which involves "allocentric" views (bird's eye views). Finally, the "cardinal directions" items ask for the competence to identify north/west/south/east while being in an environment. The main difference between the FRS and the SBSOD is thus the multi-dimensionality which is supported by confirmatory factor analysis.
2) The scales predict spatial learning over and above cognitive predictors of spatial ability. We have utilized the FRS in a number of studies, e.g.:
- Both the "global-egocentric" and the "survey" scale predicted spatial overview learning in an unknown, complex, real environment (learning measured with direction estimations)
- Only the "global-egocentric" scale predicted route learning in an unknown, complex, real environment (learning measured as erroneous turns and other indices of uncertainty while walking a route in the real building)
- The "survey" scale predicted spatial overview learning when learning with an interactive virtual model of a complex building (desktop virtual environment) (learning measured with direction estimations)
3) All the items of the FRS went into the development of a larger questionnaire that includes more questions about learning experiences, knowledge of north, usage of GPS-based navigation, etc. This larger questionnaire was developed together with [redacted] and it exists in English and German parallel versions. We collected data in the U.S. and in Germany and I compared the results of separate exploratory factor analyses for the English and the German sample (yet unpublished, more work needs to be done here, admittedly). The factor structure was virtually the same, and the FRS factors were reproduced in both data sets.
Therefore, I am convinced that the FRS-based scales are useful.
I am very much interested in your work and I am very much interested in explanations of differences in spatial / navigation ability between individuals. Therefore, I would like to hear more about your work….
I hope this information is useful for you and I would like to hear more about your research.
all the best,
Stefan

B RESEARCH GATE MESSAGE RE: QSR Questionnaire

https://www.researchgate.net/messages/147256301



Amy M Clements-Stephens to you Jun 17, 2014

Hi Jess,

Sorry for the delay in responding. We were working on 2 grant applications and I was waiting for the response from a member of the research team that actually did the analysis on this. Here is what I was told:

The measure is (survey - route), but we only use questions 3 & 4. So it is (3c + 4a) - (3a + 4b).

Does this make sense to you? If not, I can follow up with them.

Thanks!
--Amy

APPENDIX F: TRAUMA ASSESSMENT

This Appendix provides supplementary information for the Methodology (Chapter 2, Section 2.7.3). The means of assessment below were used to ascertain which participants had been exposed to trauma and which had not (using A: the Life Events Checklist), and which had been affected to either sub-clinical or clinical levels of PTSD from trauma in childhood (using the B: the Brief Trauma Screen) or adulthood (Using C: the PTSD Diagnostic Scale).

A: LIFE EVENTS CHECKLIST (LEC) (Weathers et al., 1995).

- Natural disaster (for example, flood, hurricane, tornado, earthquake)
- Fire or explosion
- Transportation accident (for example, car accident, boat accident, train wreck, plane crash)
- Serious accident at work, home, or during recreational activity
- Exposure to toxic substance (for example, dangerous chemicals, radiation)
- Physical assault (for example, being attacked, hit, slapped, kicked, beaten up)
- Assault with a weapon (for example, being shot, stabbed, threatened with a knife, gun, bomb)
- Sexual assault (rape, attempted rape, made to perform any type of sexual act through force or threat of harm)
- Other unwanted or uncomfortable sexual experience
- Combat or exposure to a war-zone (in the military or as a civilian)
- Captivity (for example, being kidnapped, abducted, held hostage, prisoner of war)
- Life-threatening illness or injury
- Severe human suffering
- Sudden, violent death (for example, homicide, suicide)
- Sudden, unexpected death of someone close to you
- Serious injury, harm, or death you caused to someone else
- Any other very stressful event or experience

Weathers, F.W., Blake, D.D., Schnurr, P.P., Kaloupek, D.G., Marx, B.P., & Keane, T.M. (2013). *The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5)*. Interview available from the National Center for PTSD at www.ptsd.va.gov.

Weathers, F.W., Litz, B.T., Herman, D.S., Huska, J.A. & Keane, T.M. (1993). *The PTSD Checklist (PCL): Reliablity, validity, and diagnostic utility*. Paper presented at the 9th Annual Conference of the ISTSS, San Antonio.

B: BRIEF TRAUMA SCREEN (BTS) (Brewin, 2002).

Instructions:

Please consider the following reactions that sometimes occur after a traumatic event. This questionnaire is concerned with your personal reactions to the traumatic event. Please indicate whether or not you have experienced any of the following AT LEAST TWICE IN THE PAST WEEK.

ITEM	**Yes, at least twice in the past week**	**No**
1. Upsetting thoughts or memories about the event that have come into your mind against your will.		
2. Upsetting dreams about the event.		
3. Acting or feeling as though the event were happening again.		
4. Feeling upset by reminders of the event.		
5. Bodily reactions (such as fast heartbeat, stomach churning, sweatiness, dizziness) when reminded of the event.		
6. Difficulty falling or staying asleep.		
7. Irritability or outbursts of anger.		
8. Difficulty concentrating.		
9. Heightened awareness of potential dangers to yourself and others.		
10. Being jumpy or being startled at something unexpected.		

From Brewin, C. R. et.al. (2002). Brief screening instrument for post-traumatic stress disorder. *British Journal of Psychiatry,* 181, 158 – 162. 'Yes' (scored 1) or ' No' (scored 0): Excellent prediction of a PTSD diagnosis was provided by respondents endorsing at least six re-experiencing or arousal symptoms, in any combination.

C: PTSD DIAGNOSTIC SCALE (PDS) (Foa et al., 1995).

ID :
Date:

Type of Trauma:

Below is a list of problems that people sometimes have after experiencing a stressful event. Choose the answer (0-3) that best describes how often that problem has bothered you IN THE PAST FEW WEEKS.

0 *Not at all or only one time*
1 *Once a week or less/once in a while*
2 *2 to 4 times a week/half the time*
3 *5 or more times a week/almost always*

1. Having upsetting thoughts or images about the traumatic event that came into your head when you didn't want them to 0 1 2 3

2. Having bad dreams or nightmares about the traumatic event 0 1 2 3

3. Reliving the traumatic event, acting or feeling as if it were happening again 0 1 2 3

4. Feeling emotionally upset when you were reminded of the traumatic event (for example, feeling scared, angry, sad, guilty, etc.) 0 1 2 3

5. Experiencing physical reactions when you were reminded of the traumatic event (for example, break into a sweat, heart beating fast) 0 1 2 3

6. Trying not to think about, talk about, or have feelings about the traumatic event 0 1 2 3

7. Trying to avoid activities, people or places that remind you of the traumatic event 0 1 2 3

8. Not being able to remember an important part of the traumatic event 0 1 2 3

9. Having much less interest or participating much less often in important activities 0 1 2 3

10. Feeling distant or cut off from people around you 0 1 2 3

11. Feeling emotionally numb (for example, being unable to cry or unable to have loving feelings) 0 1 2 3

12. Feeling as if your future plans or hopes will not come true (for example, you will not have a career, marriage, children, or a long life) 0 1 2 3

13. Having trouble falling or staying asleep 0 1 2 3

14. Feeling irritable or having fits of anger 0 1 2 3

15. Having trouble concentrating. E.g. Drifting in and out of conversations, losing track of a story on television, forgetting what you read) 0 1 2 3

16. Being overly alert (for example, checking to see who is around you), 0 1 2 3

17. Being jumpy or easily startled (for example, when someone walks up behind you) 0 1 2 3

Foa, E. (1995). *Post-Traumatic Stress Diagnostic Scale*. National Computer Systems: Minneapolis.

APPENDIX G: ALTERNATIVE PERFORMANCE MEASURES

Chapter 2 (the Methodology) introduced the Alternative Route (AR) paradigm and explained that there were alternative performance measures that could have been used in analysis n this study (Section 2.6.1.2). The AR paradigm produces complex and highly detailed data, computing for each participant: the block number (1 to 6), the test number (12 from each block), turn types ('same' and 'different' directions), response times, accuracy and strategy uptake (associative cue, beacon or configural). This appendix describes the performance measures used in the analysis and presents alternative performance measures, along with some basic statistical analysis.

The performance measures used in analysis are detailed below in table G1:

Analysis	Performance Description	Data and analysis	References
Egocentric and allocentric performance	Participants' mean score for being correct in same and different direction trials.	Mean score at same direction trials and different direction trials (calculated in each of the six blocks).	Wiener et al. (2013); Smith et al. (2015); King et al. (2004); Bisby et al. (2010); Lövdén et al. (2011).
		Repeated measures ANOVA with pairwise comparisons, post hoc T-Tests and regression analysis.	
Strategy use	Participants' mean use of each strategy (associative, configural and beacon)	Mean configural/ associative cue/ beacon strategy use (calculated in each of the six blocks).	Wiener et al. (2013); Banner et al. (2011); Furman et al. (2014).
		Repeated measures ANOVAs using strategy by block, per group with pairwise comparisons, post hoc T-Tests and regression analysis.	

Table G1: Selected performance measures for the Alternative Route paradigm (Wiener et al. 2013) for the current study with references. (See Literature Review for more information on measuring allocentric spatial processing and navigation).

The alternative performance measures which were discounted in consultation with the designers of the paradigm (Wiener et al., 2012, 2013) comprised:

I. The mean overall performance measure was discounted because it did not offer any differentiation between allocentric and egocentric (hippocampal *in/* dependent) processing.

II. The 'egocentric controlled' measure subtracts the egocentric (same direction) score from the allocentric (different direction) score and was used by Smith et al. (2015) in the Town Square task. To adapt this for the AR offered no more clarity or accuracy than the measures it already provides.

III. The allocentric improvement score comprised performance on different direction trials in the first two blocks being subtracted from different direction trials in the last two blocks.

IV. Being 'above chance level' in allocentric performance was not commonly used as a specific performance measure in comparable studies (Smith et al. 2015; King et al. 2004; Tempesta et al. 2012; Bisby et al. 2010; Wiener et al. 2013) and did not provide any

further clarity or accuracy when compared with the selected measures for group differences.

V. Response times as a measure was discounted because there is a lack of clarity in the literature to ascertain if response times (such as the Alternative Route paradigm produces) equate to a reliable measure of hippocampal integrity (Wiener et al., 2013).

Table G2 below presents the results of ANOVA between the experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD,* PTSD) using the alternative AR performance measures. Results indicate that the alternative measures which do not provide any more clarity of group differences than those offered in the main analysis and as described at Table G1.

Alternative performance measures by experimental group		**Mean**	***SD* ±**	**N**	**ANOVA analysis**
Mean overall performance throughout the task	*Trauma Unexposed*	.607	.12	33	F (2, 135) = 9.30, p <.001, ηp^2 = 0.12. Significant differences between all groups apart from *Trauma Exposed No PTSD* and *PTSD* group
	Trauma Exposed No PTSD	.597	.11	58	
	PTSD	.514	.11	47	
Egocentric-controlled allocentric performance	*Trauma Unexposed*	-.443	.20	33	F (2, 135) = 1.49, p = 0.23, ηp^2 = 0.02. No significant group differences
	Trauma Exposed No PTSD	-.492	.29	58	
	PTSD	-.405	.25	47	
Allocentric improvement score	*Trauma Unexposed*	.611	.59	33	F (2, 135) = 5.76, p < 01, ηp^2 = 0.08. Significant differences between all groups apart from *Trauma Exposed No PTSD* and *Trauma Unexposed*
	Trauma Exposed No PTSD	.430	.51	58	
	PTSD	.225	.44	47	
Allocentric performance above chance level	*Trauma Unexposed*	.70	.47	33	F (2, 135) = 3.43, p = 0.04, ηp^2 =0.05. Significant difference between *PTSD* group and *Trauma Unexposed* group only
	Trauma Exposed No PTSD	.52	.50	58	
	PTSD	.40	.50	47	

Table G2: Alternative Route paradigm performance between trauma groups (*Trauma Unexposed, Trauma Exposed no PTSD* and *PTSD)* using alternative and discounted measures (n = 137).

APPENDIX H: SUPPLEMENTARY ANALYSIS

This Appendix describes some analysis in more detail to supplement that undertaken in Chapter 4 (PTSD & Navigation) with regard to: clinical and demographic covariates (Section A) and experimental (trauma) group differences in strategy use in the AR paradigm (Section B).

A DEMOGRAPHIC AND CLINICAL FACTORS

Chapter 4 assessed group differences in allocentric navigation performance in the Alternative Route (AR) paradigm. Initial analysis of the demographic and clinical features of the sample population revealed significant differences between experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) in all features: age, gender, the taking of medications, sleep disturbance, pain and PTSD severity (PDS score). As a result of these differences, the demographic and clinical factors needed to be analysed more closely for their influence over allocentric navigation performance using a series of repeated measures ANOVAs.

Repeated measures 6 x 3 ANOVAs for allocentric performance by block for demographic and clinical factors

The first analysis systematically entered each clinical or demographic variable as a covariate in to the repeated measures 6 x 3 ANOVA between experimental groups (*Trauma Unexposed, Trauma Exposed No PTSD, PTSD*) with the within factor 'different direction' score at each block. This assessed the relationship of these variables to allocentric processing across the six blocks of the route learning task. Detailed results of these analyses are provided below.

Age: There was no significant main effect of age, F (1, 134) = 3.10, p = 0.08, η_p^2 = 0.02. The significant main effect of trauma group persisted, F (2, 134) = 3.31, p = 0.04, η_p^2 = 0.05. The significant main effect of block persisted, F (4.12, 134) = 4.02, p < 0.01, η_p^2 = 0.03. There was no significant interaction between block and age, F (4.12, 135) = 0.92, p = 0.46, η_p^2 = 0.01. The significant interaction between block and trauma group persisted, F (8.25, 135) = 2.53, p = 0.01, η_p^2 = 0.04.

Gender: There was no significant main effect of gender, F (1, 134) = 1.89, p = 0.17, η_p^2 = 0.01. The significant main effect of trauma group persisted, F (2, 134) = 5.15, p < 0.01, η_p^2 = 0.07. The significant main effect of block persisted, F (4.13, 135) = 8.07, p < 0.01, η_p^2 = 0.05**.** There was no significant interaction between block and gender, F (4.13, 135) = 2.10, p = 0.08, η_p^2 = 0.02. The significant interaction between block and trauma group persisted, F (8.27, 135) = 3.42 p <0.01, η_p^2 = 0.05.

Medications (Benzodizepines, opiates and SSRIs): There was no significant main effect of either: benzodiazepeines and opiates [F (1, 123) = 2.28, p = 0.13, η_p^2 = 0.02; nor SSRIs [F (1, 135) = 0.90, p = 0.35, η_p^2 = 0.01. The main effect of trauma remained near significant, F (2, 123) = .291, p = 0.06, η_p^2 = 0.045. The significant main effect of block persisted, F (4.21, 135) = 2.62,

p = 0.03, η_p^2 = 0.02. The significant interaction between block and trauma group persisted, F (8.40, 135) = 1.97 p = 0.04, η_p^2 = 0.03.

Pain: There was a significant main effect of pain F (1, 135) = 8.36 p <.001, η_p^2 = 0.07. This resulted in there no longer being a significant main effect of trauma group**,** F (2, 134) = 1.51 p = 0.22, η_p^2 = 0.02. The significant main effect of block persisted, F (4.14, 135) = 1.78, p = 0.13, η_p^2 = 0.01**.** There was no significant interaction between block and pain, F (4.14, 135) = 2.38, p = *0*.13, η_p^2 = 0.01**.** The significant interaction between block and trauma group persisted, F (8.27, 135) = 2.38 p = 0.02, η_p^2 = 0.03.

Sleep quality: There was no significant main effect of sleep disturbance (using the Pittsberg Sleep Quality Index- A), F (1, 129) = .406, p = 0.53, η_p^2 = 0.01. The significant main effect of trauma persisted, F (2, 129) = 3.42, p = 0.04, η_p^2 = 0.05. The significant main effect of block persisted, F (4.15, 129) = 18.9, p < 0.01, η_p^2 = 0.13**.** There was no significant interaction between block and sleep**,** F (8.31, 129) = 2.19, p = 0.3, η_p^2 = 0.03**.**

Post hoc t-tests for gender and allocentric performance by block

Table H1 shows that post hoc t-tests for gender and revealed no significant differences between males (n = 76) and females (n = 62) in allocentric performance in any of the six blocks (1-6).

Allocentric performance (AR)		**F**	**Sig.**	**t**	**df**	**Sig. (2-tailed)**	**Mean Differ-ence**	**Std. Error Differ-ence**	**95% Confidence Interval**	
									Lower	**Upper**
Block 1	Equal variances assumed	2.59	.110	1.17	136	.242	.043	.037	-.029	.115
Block 2	Equal variances assumed	.042	.839	-.762	136	.447	-.034	.044	-.122	.054
Block 3	Equal variances assumed	.272	.603	0.14	136	.892	.007	.053	-.098	.112
Block 4	Equal variances assumed	.002	.966	-0.04	136	.972	-.002	.054	-.109	.105
Block 5	Equal variances assumed	.031	.861	-0.02	136	.982	-.001	.057	-.113	.111
Block 6	Equal variances assumed	1.61	.207	1.05	136	.296	.059	.057	-.053	.171

Table H1: Post hoc t-tests for allocentric performance by block on the Alternative Route (AR) between males (n = 76) and females (n = 72).

Post hoc t-tests for pain, egocentric and allocentric performance by block

Table H2 overleaf shows that post hoc t-tests undertaken for egocentric performance between those who had recorded any pain (n = 36) and those who had not (n = 102) revealed no significant differences between those self-reporting pain and those not in egocentric performance in any block.

Egocentric performance (AR)		F	Sig	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval	
									Lower	Upper
Block 1	Equal variances assumed	.437	.510	1.92	136	.057	.091	.047	-.003	.185
Block 2	Equal variances assumed	.444	.506	-.493	136	.623	-.022	.045	-.110	.066
Block 3	Equal variances assumed	.069	.794	-.257	136	.798	-.011	.043	-.097	.074
Block 4	Equal variances assumed	.813	.369	.875	136	.383	.043	.049	-.054	.140
Block 5	Equal variances assumed	.214	.644	-.684	136	.495	-.032	.047	-.126	.061
Block 6	Equal variances assumed	.193	.662	-.074	136	.941	-.003	.047	-.096	.089

Table H2: Post hoc t-tests for egocentric performance by block on the Alternative Route (AR) between those with (*n* = 36) and without (*n* = 102) any recorded self-reported pain.

Post hoc t-tests were undertaken for allocentric performance between those who had recorded any pain (*n* = 36) and those who had not (*n* = 102). Table H3 shows there were significant differences in allocentric performance in nearly all blocks between those self-reporting pain and those not.

Allocentric performance (AR)			F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval	
										Lower	Upper
Block 1	Equal variances assumed		2.92	.090	-1.10	136	.272	-.046	.041	-.127	.036
Block 2	Equal variances not assumed		15.6	.000	-2.94	82.9	.004	-.125	.043	-.210	-.040
Block 3	Equal variances not assumed		12.05	.001	-3.78	95	.000	-.180	.048	-.275	-.086
Block 4	Equal variances assumed		1.33	.250	-1.90	136	.059	-.115	.061	-.235	.005
Block 5	Equal variances not assumed		6.65	.011	-4.22	81	.000	-.226	.054	-.332	-.119
Block 6	Equal variances assumed		3.11	.080	-2.89	136	.004	-.181	.063	-.305	-.057

Table H3: Post hoc t-tests for allocentric performance by block on the Alternative Route (AR) between those with (*n* = 36) and without (*n* = 102) any recorded self-reported pain.

B STRATEGY USE

CONFIGURAL STRATEGY USE

Table H4 shows that in independent samples t-test between the *Trauma Exposed No PTSD* group and the *PTSD* group for configural strategy use over the six blocks (1-6) of the AR paradigm revealed significantly more use of the configural strategy in those without PTSD.

		F	Sig.	t	df	Sig. (2-tailed)	Mean Differ-ence	Std. Error Difference	95% Confidence Interval	
									Lower	Upper
Block 1	Equal variances assumed	.097	.756	.025	103	.980	.001	.044	-.087	.089
Block 2	Equal variances assumed	.047	.829	.309	103	.758	.017	.055	-.091	.125
Block 3	Equal variances assumed	.348	.557	.692	103	.490	.050	.072	-.093	.193
Block 4	Equal variances assumed	3.760	.055	1.492	103	.139	.109	.073	-.036	.254
Block 5	Equal variances assumed	2.164	.144	2.226	103	**.028**	.158	.071	.017	.298
Block 6	Equal variances assumed	1.185	.279	2.06	103	**.042**	.147	.072	.005	.289

Table H4: Independent samples t-tests between *Trauma Exposed No PTSD* and *PTSD* groups for use of the configural strategy over the six blocks of the Alternative Route paradigm.

Table H5 shows that an independent samples t-test between the *Trauma Exposed No PTSD* group and the *Trauma Unexposed* group for configural strategy use over the six bloxks (1-6) of the AR paradigm revealed significantly higher use of configural strategy in the last block by those unexposed to trauma.

		F	Sig.	t	df	Sig. (2-tailed)	Mean Differ-ence	Std. Error Difference	95% Confidence Interval	
									Lower	Upper
Block 1	Equal variances assumed	.289	.592	-.368	89	.714	-.020	.054	-.127	.087
Block 2	Equal variances not assumed	5.514	.021	-1.73	55.8	.089	-.118	.068	-.253	.018
Block 3	Equal variances assumed	.293	.590	-.210	89	.834	-.016	.077	-.170	.137
Block 4	Equal variances assumed	.005	.946	-.481	89	.631	-.042	.087	-.214	.131
Block 5	Equal variances assumed	.169	.682	-1.11	89	.270	-.097	.087	-.270	.077
Block 6	Equal variances assumed	1.760	.188	-2.34	89	**.021**	-.205	.088	-.379	-.031

Table H5: Independent samples t-tests between *Trauma Exposed No PTSD* and *Trauma Unexposed* groups for use of the configural strategy over the six blocks of the Alternative Route paradigm.

ASSOCIATIVE CUE STRATEGY USE

Table H6 shows that in independent samples t-test between the *Trauma Exposed No PTSD* group and the *Trauma Unexposed* group for associative strategy use over the six blocks (1-6) of the AR paradigm revealed no significant differences in use of the associative cue strategy.

		F	Sig.	t	df	Sig. (2-tailed)	Mean Differ-ence	Std. Error Difference	95% Confidence Interval	
									Lower	Upper
Block 1	Equal variances assumed	.729	.395	-.866	89	.389	-.061	.071	-.202	.079
Block 2	Equal variances assumed	.038	.846	.165	89	.869	.010	.062	-.113	.133
Block 3	Equal variances not assumed	3.99	.049	-1.54	62.0	.129	-.100	.065	-.230	.030
Block 4	Equal variances assumed	.009	.926	-.101	89	.920	-.006	.055	-.115	.104
Block 5	Equal variances assumed	.380	.539	-.215	89	.830	-.011	.052	-.115	.093
Block 6	Equal variances assumed	4.129	.045	-.851	89	.397	-.044	.051	-.145	.058

Table H6: Independent samples t-tests between *Trauma Exposed No PTSD* and *Trauma Unexposed* groups for use of the associative cue strategy over the six blocks of the Alternative Route paradigm.

Table H7 shows that an independent samples t-test between the *Trauma Exposed No PTSD* group and the *PTSD* group for associative strategy use over the six blocks (1-6) of the Alternative Route paradigm showed the *PTSD* group using the strategy significantly more than the group without PTSD from block 2.

		F	Sig.	t	df	Sig. (2-tailed)	Mean Differ-ence	Std. Error Difference	95% Confidence Interval	
									Lower	Upper
Block 1	Equal variances assumed	3.9	.050	-1.73	103	.086	-.117	.067	-.251	.017
Block 2	Equal variances not assumed	15.4	.000	-2.19	80.0	.031	-.151	.069	-.289	-.014
Block 3	Equal variances not assumed	9.8	.002	-1.90	86.1	.060	-.122	.064	-.249	.005
Block 4	Equal variances not assumed	12.2	.001	-2.04	83.5	.045	-.123	.060	-.243	-.003
Block 5	Equal variances not assumed	23.0	.000	-2.13	70.3	.036	-.132	.062	-.256	-.016
Block 6	Equal variances not assumed	29.1	.000	-2.36	65.2	.021	-.135	.057	-.250	-.021

Table H7: Independent samples t-tests between *Trauma Exposed No PTSD* and the *PTSD* groups for use of the associative cue strategy over the six blocks of the Alternative Route paradigm.

APPENDIX I: ADDITIONAL SCREENING QUESTIONS

The Methodology (Chapter 2, Sections 2.3, 2.5.4 and 2.8.2.2) explained that there were some additional questions which were asked of participants to try and gage the extent to which they had had opportunities to improve their allocentric spatial processing (i.e. through navigation training) or to apply themselves to trauma processing (i.e. through talking and or in trauma therapy. This may have helped control for environmental conditions in this diverse study population who had a variety of different trauma exposures and a range of experience of treatment. These additional questions are provided here for information.

In the screening stage of the study, recruited participants were asked questions about a) previous navigation experience (either specific training or undertaking navigation as part of their everyday employment) and b) previous PTSD treatment (therapy).

This information was sought so that one could establish if some participants had had extensively more opportunities to either improve their own performance in hippocampal dependent navigation or to actively engage in trauma processing

For information, the questions comprised:

a) **Have you undertaken navigation training or used navigation in your job? (e.g. cab driver / military) Yes / No**

[If yes please give details of navigation training or experience]

b) **Have you talked through this event or experience with anyone? Yes / No**

Have you received treatment? Yes / No

The quality of data was limited due to several missing values which precludes its inclusion in statistical analysis (see Section 2.5.4 and 2.8.2.2).

[END]