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Developmental Prosopagnosia with Concurrent Topographical Difficulties: A Case Report and Virtual Reality Training Programme

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Abstract

Several neuropsychological case studies report brain-damaged individuals with concurrent impairments in face recognition (i.e. prosopagnosia) and topographical orientation. Recently, individuals with a developmental form of topographical disorientation have also been described, and several case reports of individuals with developmental prosopagnosia provide anecdotal evidence of concurrent navigational difficulties. Clearly, the co-occurrence of these difficulties can exacerbate the negative psychosocial consequences associated with each condition. This paper presents the first detailed case report of an individual (FN) with developmental prosopagnosia alongside difficulties in topographical orientation. FN's performance on an extensive navigational battery indicated that she primarily has difficulties in the formation and retrieval of cognitive maps. We then evaluated the effectiveness of a short-term virtual reality training programme and found that she is able to form a cognitive map of a particular environment following intense overlearning. Surprisingly, FN's performance on a face recognition task also improved following training. While the latter finding was unexpected and requires further exploration, the training programme reported here may help to alleviate some of the compounded negative psychosocial consequences that are associated with difficulties in finding both locations and people.

Keywords: Developmental prosopagnosia; topographical disorientation; navigation; cognitive map; face recognition.

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A Case Report and Virtual Reality Training Programme

1. Introduction

Prosopagnosia is a cognitive condition characterized by a relatively selective deficit in face recognition. While some individuals acquire the disorder following neurological injury or illness (e.g. Damasio, Damasio, & Van Hoesen, 1982; Bate et al., 2015), people with developmental prosopagnosia (DP) fail to develop normal face recognition skills (e.g. Bate, Haslam, Jansari, & Hodgson, 2009; Bate & Cook, 2012; Bennetts, Butcher, Lander, Udale & Bate, 2015; Duchaine & Nakayama, 2006; Jones & Tranel, 2001). DP is sometimes referred to as ‘congenital’ or ‘hereditary’ prosopagnosia (for a discussion of terminology see Bate & Tree, 2017) and has been attributed to a failure to develop the visual recognition mechanisms necessary for successful face recognition, despite intact low-level visual and intellectual functions. While acquired prosopagnosia (AP) is a rare condition, recent reports suggest that DP affects approximately two per cent of the population (Bowles et al., 2009; Bennetts, Murray, Boyce, & Bate, 2017) and in some cases may be genetic in origin (Duchaine, Germine, & Nakayama, 2007; Kennerknecht et al., 2006).

While both AP and DP are characterised by the hallmark symptom of impaired face recognition skills, it is still widely debated whether they are parallel conditions. In part this is because the functional and structural profile of AP is relatively well known in comparison to DP. While more work has focused on theoretically important dissociations within the two conditions (e.g. between face and object recognition or the recognition of facial identity and expression: Bate & Bennetts, 2015; Duchaine & Nakayama, 2005; Fisher, Towler & Eimer, 2017; Humphreys, Avidan & Behrmann, 2007, Palermo et al., 2011), less work has attempted to identify whether the accompanying deficits that are typically associated with AP also hold for DP. This is an important consideration from an assessment and rehabilitation perspective: if other difficulties are commonly associated with DP, it is important that these are assessed and targeted via appropriate intervention techniques.

One common association with AP is topographical disorientation (the inability to orient and navigate in familiar and unfamiliar surroundings: Berthoz, 2001; Wang & Spelke, 2002), where many objective (Hécaen & Angelergues, 1962; Aguirre & D'Esposito, 1999; Landis, Cummings, Benson & Palmer, 1986) and anecdotal (Barton, Press, Keenan, & O'Connor, 2002; Bauer, 1984; Malone, Morris, Kay, & Levin, 1982; Takahashi, Kawamura, Hirayama, Shiota, & Isono, 1995; Schmidt, 2015) reports suggest a long-standing relationship. These difficulties can be underpinned by impaired landmark and/or scene recognition, or by difficulties in the representation of spatial relationships (Aguirre & D'Esposito, 1999; Arnold et al., 2013; De Renzi, 1982; Liu, Levy, Barton, & Iaria, 2011). Although little work has attempted to map these different types of topographical impairment onto particular anatomic or functional subtypes of AP, one recent study concluded that the condition is typically associated with impaired place recognition, together with poor cognitive map formation (mental representations of a person's surrounding, including landmarks and the spatial relations between them: O'Keefe & Nadel, 1978) in cases of occipitotemporal damage (Corrow et al., 2016).

Anecdotal evidence also indicates that topographical disorientation may be prevalent in DP (e.g. Brunsdon, Coltheart, Nickels, & Joy, 2006; Duchaine, Parker, & Nakayama, 2003; Jones & Tranel, 2001; Le Grand et al., 2006; McConachie, 1976), although only two reports to date have formally investigated this possibility. Klargaard, Starrfelt, Peterson and Gerlach (2016) found that four out of nine DPs performed significantly poorer than controls on a memory task that required the retention of topographic information. In the AP paper described above, Corrow and colleagues (2016) also assessed the navigational skills of seven adults with DP. Contrary to the patterns of topographical disorientation observed in the AP participants, atypicalities only emerged on one task (cognitive map formation) in one DP participant, leading the authors to conclude that DP may be a more face-selective disorder than AP. While this certainly may be the case, it is notable that six of the seven DP participants (including the one that displayed atypical performance on the cognitive map test) did not self-report navigational difficulties in an initial interview. Thus, the frequency that topographical disorientation and DP co-occur may be under-represented in this study.

Further, it has recently become clear that topographical disorientation can occur in developmental cases. For instance, Bianchini et al. (2010) described a 22 year-old man with severe developmental topographical disorientation (DTD) who was severely impaired at processing the spatial relationships between the parts of a whole stimulus; and Iaria and Barton (2010) reported 120 people with DTD who had an inability to form cognitive maps. Iaria, Bogod, Fox and Barton (2009) carried out a thorough cognitive and neural examination of a woman with DTD. Behavioural assessments in real-world and virtual reality environments also revealed an inability to form cognitive maps, with a corresponding lack of activation in the hippocampal complex and retrosplenial cortex – regions that were activated in control participants performing the same task. In sum, most reports of DTD to date indicate that the primary impairment in developmental cases may be the formation and retrieval of cognitive maps. However, it remains unclear whether this difficulty is absolute, or if it can at least to some extent be alleviated by over-rehearsal or training within a given environment.

This is a pertinent issue for individuals who simultaneously experience DP and topographical difficulties, given the combined impact of these difficulties on socio-emotional functioning. Indeed, some reports suggest that DP can have detrimental effects on a person's social and occupational interactions (e.g. Yardley, McDermott, Pisarski, Duchaine, &

Nakayama, 2008; Dalrymple et al., 2014), and it is conceivable that the stress and anxiety experienced in such situations would either be further exacerbated by poor navigational skills (e.g. when required to locate a meeting spot and then to subsequently identify a particular person within that location), or increase or bring about the disorientation difficulties themselves. While there have been some attempts to improve face recognition skills in DP (e.g. Bate et al., 2014; DeGutis, Bentin, Robertson, & D'Esposito, 2007; DeGutis, Cohan, & Nakayama, 2014), results are varied and no clear treatment strategy has yet emerged (Bate & Bennetts, 2014). Likewise, few attempts have been made to improve topographical difficulties (but see Brunsdon, Nickels, Coltheart, & Joy, 2007; Bouwmeester, van de Wege, Haaxma, & Snoek, 2015; Davis, 1999; Incoccia et al., 2009), and very little work has specifically focused on cognitive map formation. However, Iaria and colleagues (2009) briefly report preliminary evidence that this skill can be improved in a case of DTD via overtraining in a simplified environment. This report raises the possibility that developmental topographical difficulties are receptive to intervention, and simple training techniques may assist with this particular set of difficulties.

In this paper, we report a detailed case study of an adult female who self-referred to our laboratory complaining of both face recognition and navigational difficulties. We had the opportunity to work with this individual over a period of several months and gathered substantial neuropsychological data. Given that this paper represents the first in-depth report of concurrent DP with topographical difficulties, we initially carried out a detailed neuropsychological investigation to establish the pattern of face-processing deficits and disorientation difficulties that co-present in this individual. Because we found that the primary topographical difficulty was in the formation of cognitive maps, we then evaluated the utility of a virtual reality training programme that aimed to improve this skill. As topographical difficulties have often been associated with prosopagnosia, we additionally assessed whether the training programme also improved face recognition performance.

2. Case history

FN is a 58-year-old right-handed female, who is a member of the clergy. She is educated to postgraduate level and previously worked as a teacher. FN complained of severe difficulties in face recognition where she fails to recognise the faces of family, close friends and colleagues on an everyday basis. She has specific memories of face recognition difficulties in childhood, particularly affecting the recognition of male faces. Given that FN has no medical history of motor, neurological or cognitive developmental delays, nor of neurological or psychiatric illness, her face recognition difficulties appear to be developmental in origin. Unlike some DPs (e.g. Duchaine et al., 2007), she does not believe that any of her relatives also experience face-processing impairments.

FN also reported profound difficulties in topographical orientation. She describes her sense of direction as “awful”, and relies primarily on landmarks to find her way around. When driving she becomes lost very easily and is frequently unable to locate a point of reference to guide her. These conditions initiate panic, causing anxiety and stress. FN’s avoidance of these situations has negatively affected her occupational and social activities. For example, she reports skipping work and social events because she fears losing her way, and often avoids travel to new places.

To compensate for these difficulties, FN plans outings meticulously in advance. She travels stereotyped familiar routes (even when they are not the quickest route available), and prefers to travel on quiet roads so she can stop or turn around easily if needed. FN tries to compensate for her difficulties by using a satellite-navigation system, but finds it very stressful when the presented information does not match visual cues (e.g. when road signs and the device show different road names). FN's topographical difficulties are not limited to driving – when walking in familiar towns she follows pre-defined routes between known landmarks even though she is aware they are not the shortest paths. As a result she often has to amend her schedule (e.g. to skip an errand) because she does not have time to navigate to all the places she wishes to visit. These difficulties appear to be life-long: FN recounted several incidents from childhood where she got severely lost and disoriented in familiar environments, such as the village she grew up in and a department store she visited every week. FN reports that her father may experience similar topographical (but not face-processing) difficulties as he frequently gets lost while driving, even when he has driven a route multiple times.

FN participated in a series of detailed neuropsychological investigations. Informed consent was obtained from the participant, and ethical approval for the study was granted by the institutional ethics committee at Bournemouth University. Four groups of gender-, age- and IQ- (using the Wechsler Test of Adult Reading [WTAR]; Holdnack, 2001) matched participants volunteered to act as control participants for the face-processing and navigational tests that lack published standardization data. Full demographic information is presented for each control group in the relevant section below. Where appropriate, FN's performance was compared to that of controls using Crawford and Garthwaite's (2002) modified *t*-tests for single-case comparisons.

3. Neuropsychological evaluation

We initially administered a series of standard neuropsychological tests assessing general intelligence, memory, executive functioning, language, visuo-perceptual and social functioning abilities (see Table 1). Norms were taken from the appropriate manuals or published papers, referenced below and in Table 1. FN was alert and fully cooperative and motivated. She was fluent and had normal verbal comprehension. No ideomotor, ideative or constructional apraxia was observed. FN underwent a MRI scan which revealed no structural abnormalities.

General cognitive level was tested using the WAIS-III (Wechsler, 1997) seven subtest short-form (Crawford, Allum, & Kinion, 2008). Scores on all subscales were in the average to superior range. General memory ability was tested using the WMS-IV (Wechsler, 2009). FN performed within the average to high average range in most domains, and in the low-average range for visual working memory. Further tests were carried out to examine executive functioning (Wisconsin Card Sorting Test: Heaton et al., 1993), spatial memory (Visual Patterns Test: Della Sala, Gray, Baddeley, & Wilson, 1997; Corsi Block Test: Milner, 1971; Rey's Complex Figure: Rey & Osterrieth, 1993) and language ("Picture Naming" subtest from the Birmingham Object Recognition Battery [BORB]: Riddoch & Humphreys, 1993; WTAR). FN's scores were within the normal range for her age on all tests.

Basic vision was assessed using a standard Snellen letter chart (3m), the Hamilton-Veale contrast sensitivity test, Ishihara's tests for colour deficiency (38 plates; Ishihara, 1996), and the Fly stereo-acuity test (Vision Assessment Corporation, 2007). FN was diagnosed with astigmatism in the right eye at the age of 11 years, and has lost some visual acuity and contrast sensitivity in her right eye (acuity: 20/40; contrast: 10). However, her acuity and contrast sensitivity in her left eye and with both eyes are normal (acuity: 20/20, contrast: 13), her colour and depth perception are normal, and there was no evidence of spatial neglect (FN obtained a perfect score on the Stars Cancellation Test: Wilson, Cockburn, & Halligan, 1987). General visuo-perceptual skills were assessed using five subtests of the BORB and the Visual Object and Space Perception Battery (VOSP: Warrington & James, 1991). Once again, FN performed within the normal range on all subtests (see Table 1).

Because some individuals with autism spectrum disorder also have poor face recognition skills, we carried out some basic tests of socio-emotional functioning: the Autism Spectrum Quotient (AQ: Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001), a 50-item self-report questionnaire; and the Reading the Mind in the Eyes test (RMITE: Baron-Cohen, Wheelwright, Hill, & Plumb 2001), which requires participants to infer what a person is thinking or feeling based on the eye region of their face. FN scored below the published cut-off on the AQ, and within the normal range for the RMITE test – despite the possibility that her poor face-processing skills might influence performance on the latter test (see Table 2). Taken together, the results from the neuropsychological evaluation confirm that FN has normal cognitive, visuospatial, and socio-emotional functioning, and her difficulties with face-processing and topographical orientation do not reflect a more general cognitive, socio-emotional, or visuospatial deficit. However, her relatively lower score on the visual working memory measure may indicate that she has a relative weakness in this process.

4. Face-processing assessment

FN participated in a set of face-processing tests to confirm her prosopagnosia (see Table 2). Her results were compared to 17 age-matched (M = 58.7 years, SD = 4.3) female control participants. None of the control participants reported any difficulties with face recognition or navigation. Note that, due to time constraints and some computer malfunctions, data is not available for all control participants in all tests. The number of control participants for each test is shown in Table 2.

Previous work has indicated that both a clinical interview (Grueter, Grueter, & Carbon, 2008) and objective testing (Bobak, Parris, Gregory, Bennetts, & Bate, 2017; Duchaine, 2008) are necessary to confirm prosopagnosia. FN shared personal anecdotes of instances where she failed to recognize close friends and relatives, and reported apparently lifelong and severe difficulties with face recognition. She stated that she generally relies on context and non-facial cues (e.g., body language, clothing style, characteristic jewellery) to recognise people.

The neuropsychological testing battery presented in Table 2 has been used by other researchers to diagnose DP (e.g. Bate & Cook, 2012; Duchaine et al., 2007; Garrido et al., 2009). Face-processing skills were assessed using the Cambridge Face Memory Test (CFMT: Duchaine & Nakayama, 2006), a famous faces test (Duchaine et al., 2007), and the Cambridge Face Perception Test (CFPT: Duchaine et al., 2007). FN was impaired on all three of these leading diagnostic tests (see Table 2). We also tested her ability to perceive non-identity facial information: expression recognition skills were assessed using the Ekman 60 Faces test and the RMITE, and the perception of age and gender using subtests from the Philadelphia Face Perception Battery (PFPB: Thomas, Lawler, Olsen, & Aguirre, 2008). Like many other DPs (see Bate & Tree, 2017) FN demonstrated intact performance on these tests (see Table 2).

Given the extensive assessment of FN's perceptual abilities described above, it would appear that her difficulties with faces are not caused by low-level visual problems. Indeed, she achieved normal scores on four sub-tests from the BORB that have been used in previous investigations (e.g. Bate et al., 2013; Garrido et al., 2009), and showed no deficits when asked to identify objects from line drawings (BORB: object decision subtest) or silhouettes (VOSP).

5. Navigational skills assessment

FN and a new group of 15 age-matched (M = 56.7 years, SD = 4.5) female controls completed a series of orientation and perspective-taking tasks (see Table 3; once again, not all control participants completed all tasks). A subset of five of the controls (M = 60.0 years, SD = 4.8) also took part in a real-world navigation assessment (section 5.4, Table 4).

5.1. Basic orientation abilities

FN’s basic orientation skills were initially assessed using Benton et al.’s Left-Right Orientation test (Benton, Sivan, Hamsher, Varney, & Spreen, 1993) and the Santa Barbara Sense-of-Direction Scale (Hegarty, Richardson, Montello, Lovelace, & Subbiah, 2002) – a self-report scale of environmental spatial ability used to predict objective measures of these abilities. The scale is highly correlated with tests of spatial knowledge that involve orienting oneself within the environment. While FN demonstrated no left-right confusion, her self-reported sense-of-direction was lower than the control mean by more than 1.5 standard deviations (see Table 3).

5.2. Imagery, mental rotation and perspective taking

Visual imagery abilities are involved in many aspects of topographical cognition (Farah, 1989; Riddoch & Humphreys, 1989). The ability to generate an image from short-term memory was assessed using the Memory of Buildings test (modified from Nori & Giusberti, 2006). Participants are required to study a picture of a building for 10 seconds and then select the studied building from an array containing the target and two distractor buildings. A short version of the Postcard test (see Palermo, Iaria, & Guariglia, 2008) was used to assess FN’s ability to generate images from long-term memory. In this test, participants are presented with photographs of 40 well-known landmarks from around the world and are required to identify them. FN’s performance on the Memory of Buildings test was perfect and she outperformed controls on the Postcards test (see Table 3).

FN’s ability to generate images from long-term memory was also assessed using the O’Clock test (Grossi, Modafferi, Pelosi, & Trojano, 1989). In this test, participants are presented with 32 pairs of digital times and are required to imagine the same times on an analogical clock. For each pair they select the time for which the clock’s hands are furthest apart. FN’s performance on this test was comparable to that of controls (see Table 3).

The Perspective Taking/Spatial Orientation test (Hegarty & Waller, 2004) is a test of participants’ ability to imagine different perspectives or orientations in space. In 12 trials objects are presented in a circular formation with another object in the middle. Participants imagine they are standing at one object, facing another. They are presented with a circle where their current location is presented at the centre, and the object they are facing is placed at 12 o’clock. They are required to draw a line on the circle indicating the direction of a third object from the new perspective. Again, FN’s performance was comparable to controls on this task (see Table 3).

5.3. Map drawing

When FN was in the laboratory she was asked to draw a top-view plan of the two floors of her home from memory. This was compared to an actual plan of her house (see Figure 1). FN does not report any difficulties in navigating her home, and drew the correct number of rooms in the correct locations. However, comparison of the images indicates some inaccuracies in spatial scaling.

< *Insert Figure 1* >

5.4. Navigation

5.4.1. Route-based navigation. In this test FN was asked to learn a route without the aid of a map. FN and the experimenter walked a selected path from a specific place to a given target location, then returned back to the starting location via a different route. The route is displayed in Figure 2a. FN was then asked to follow the same path to the target location that she had travelled with the experimenter. While travelling, no other information or communication was allowed. The route was about 1km in length, and contained five left turns and five right turns. Four out of five age-matched control participants made at least one error, and completed the route in an average time of 473.60 seconds (see Table 4). FN made two experimenter-corrected errors and one self-corrected error, and completed the route in 1062 seconds - a time that was significantly slower than the control participants, $t(4) = 6.38$, $p = .003$, $Z_{CC} = 6.99$.

< Insert Figure 2 and Table 4>

5.4.2. Landmarks-based navigation. The landmark-based navigation task test was similar to the route-based navigation in that FN and the experimenter first travelled a route together, and FN was subsequently asked to navigate the route herself. The route is displayed in Figure 2a. In this case, however, whenever a crossing was reached, the experimenter indicated and named specific landmarks (distinctive buildings, road markings, or other landscape features; locations of landmarks are indicated by number in Figure 2a). FN was asked to name each landmark again as she completed the route herself. The route was about 0.8 km long and contained eight turns (four right, four left). One control participant made four navigation errors (one self-corrected, three experimenter-corrected), and another made three errors (all experimenter-corrected). Age-matched control participants completed this route in an average time of 421.80 seconds. FN reported all landmarks correctly, but made two experimenter-corrected navigation errors. She completed the route in 615 seconds, which was not significantly slower than controls, $t(4) = 2.31$, $p = .082$, $Z_{CC} = 2.57$.

5.4.3. Instruction-based navigation. In this task, FN was taken to a starting location and given a list of instructions for navigation to a given target location. The route is shown in Figure 2a. Each instruction included the name of the street FN was on, the name of the street or landmark to look for, and the direction she needed to turn (e.g., “You are on Fern Barrow. Turn left (following the pedestrian path) when you reach the roundabout at Wallisdown Road”). The list contained twelve instructions that needed to be followed sequentially to reach the target location via the given route. The path was about 0.8 km long and contained eight turns (four right, four left). Only one age-matched control participant made an error (which was experimenter-corrected), and controls completed the route in an average time of 552.20 seconds. FN made one experimenter-corrected error and completed the route in 840 seconds – a time that was significantly longer than control participants, $t(4) = 7.70$, $p = .030$, $Z_{CC} = 7.61$.

5.4.4. Map-based navigation. This test included two tasks: map-following and shortest-route navigation, administered separately. In the map-following task FN was given a map of the neighbourhood surrounding the university, which displayed the selected route from the starting destination to the target location (Figure 2b). FN was asked to follow this route. The path was about 1.5 km long and contained seven turns (four right, three left). Only one age-matched control made a single error (experimenter-corrected), and controls completed the route in an average time of 784.20 seconds. FN made two experimenter-corrected errors and completed the route in 1170 seconds. Performance on both measures was significantly lower than that of controls, $t(4) = 5.42$, $p = .006$, $Z_{CC} = 5.94$ and $t(4) = 3.72$, $p = .021$, $Z_{CC} = 4.07$, respectively.

In the shortest-route navigation task, FN was given the same map (without any route marked) and asked to navigate between a given starting destination and a target location.

Both the starting place and the target location were indicated on the map (these were the same as in the map-following task). FN was required to look at the map and describe the shortest path to the target, then to follow this route to the target location. FN did not choose the shortest route (0.5 km; see dotted line in Figure 2b) – instead she consciously chose a longer route that included streets she had navigated during previous tasks (0.8 km; see solid line in Figure 2b), even after being prompted to only choose the shortest path between the given locations. Nonetheless, she navigated this chosen route without any errors, and within a similar time-frame to age-matched control participants (who uniformly chose the shortest route), $t(4) = 0.18$, $p = .87$, $Z_{CC} = 0.19$.

A separate map-based navigation task was presented to FN in a laboratory-based test (see Table 3). Using the Map Reading test from Module One of the Neuropsychological Spatial Battery (Stern & White, 2001), FN was presented with a map and given a starting location. She then received a series of verbal directions which she was required to follow mentally and was asked to state her destination. FN performed poorly on this test and only completed six of the 12 directions accurately. Norms taken from the testing manual indicate that this performance places her in the 18th percentile.

6. Formation and use of cognitive maps

6.1. Methods

Cognitive maps (mental representations of the environment) are thought to be critical for orientation, and the ability to generate and use these representations has been found to be impaired in all four of the DTD studies reported to date (Iaria et al., 2009; Iaria & Barton, 2010; Bianchini et al., 2010, 2014). A virtual reality cognitive map test (CMT) was created specifically for this study using the software Unity 3D, based on the design of Iaria et al. (2009) and Palermo et al. (2008). The test assesses the ability to generate and use a cognitive map as participants use a three-button keypad (forward, left, right) to navigate via a virtual city containing six landmarks: a cinema, restaurant, pub, hotel, pharmacy and florist (see Figure 3).

< Insert Figure 3 >

In an initial practice phase FN navigated freely within a practice virtual city, in order to become familiar with the software and keypad. Once comfortable with this task three practice trials were administered. Each represented a pre-determined route differing in length, indicated by arrows along the ground. FN was asked to follow each route as quickly and accurately as possible, in order to gain confidence in manoeuvring at speed.

FN then began the learning task using the experimental rather than the practice virtual city. She was instructed to locate the six landmarks while creating a mental image of the city, incorporating the spatial location of each landmark. Every four minutes this task was stopped in order for testing to be carried out. Specifically, using the mental representation she had created, FN was asked to mark the location of each landmark on a top-view schematic image of the city. This task continued until all six landmarks were correctly located.

Once all landmarks had been memorized FN began the retrieval task. In 18 trials she was presented with a starting location represented by one of the six landmarks. A signpost was also presented on the screen, indicating the target destination (one of the remaining five landmarks). FN was required to navigate via the city in order to reach this location as quickly as possible and using the shortest possible route. Five age-matched (M = 56.2 years, SD = 4.3) female control participants also completed this task.

6.2. Results

An initial attempt at the task was aborted after 1080 seconds as FN felt anxious and could not continue. A week later she attempted the test a second time. This time she successfully completed the learning phase, taking 1680 seconds to form a cognitive map of the environment. During this time she explored the environment by covering the same routes several times over. Even though this was FN's second exposure to the task, her performance was still significantly worse than controls who, on their first attempt, took an average time of 1008.00 seconds (SD = 214.66) to form the cognitive map (see Table 5).

For the retrieval task we measured the additional time delay for reaching the target location on each trial by subtracting the fastest possible time (i.e. that of an ideal observer) from each participant's time. When performing the retrieval trials, FN's average delay was 17.33 seconds – a time that exceeded that of the control group with marginal significance (see Table 5).

7. Cognitive map training

7.1. Method

Immediately following the initial CMT assessment FN began a virtual-reality training programme. She completed the same CMT test for a further six sessions, with a 3-4 day break between sessions. The same experimental virtual city and landmarks were used, and the same learning and retrieval tests. However, the practice city and control trials were not included as FN remained adept at manoeuvring with speed and accuracy following the initial assessment. FN also completed a follow-up assessment using the same task one week after training terminated.

We were interested to see whether cognitive map training would also result in an improvement in FN's face-processing skills. Although the training regime encouraged her to overlearn a simply virtual environment, it is possible that more generic gains in the formation and use of cognitive maps (i.e. in spatial processing and visual imagery) would transfer to the recognition of faces. Two new versions of the CFMT (see section 4) were used to assess FN's face recognition skills before and after training. These tasks are fully described in Bate et al. (2014), where they were matched for difficulty, validated, and used in a larger-scale prosopagnosia rehabilitation investigation. For the purposes of this study, we asked 10 gender-, IQ- and age-matched controls to complete the two versions of the CFMT. As found in our previous work, mean scores were very similar (see Table 5) and did not significantly differ between the two versions, $t(9)$ - .355, p = .730.

7.2. Results

Performance in the final training session showed that FN formed a cognitive map of the environment in 240 seconds, and performed the retrieval task with an average delayed time of 6.92 seconds (see Figure 4). Although control participants did not complete the training, we compared FN's performance in the final session to control performance on the standard task. The time that it took FN to correctly form the cognitive map was significantly quicker than controls, while the time it took her to complete the retrieval trials was within the range demonstrated by control participants (see Table 5). A similar pattern of performance was observed at the one-week follow-up session, where FN was significantly quicker than controls in initially creating the cognitive map, and took a similar length of time to complete the retrieval trials (see Table 5). This pattern of findings indicates that FN can acquire and use a cognitive map through intensive overtraining within a simplified environment, and, after seven training sessions, was able to use this map in a similar manner to control participants who had been exposed to the virtual environment within a single session. Although we did not have the opportunity to carry out longer-term assessments on the maintenance or transfer of these gains (the software used for the virtual reality task was no longer available to our group), FN did report benefits in her everyday navigation skills following the training. For example, on one occasion she unexpectedly encountered a diversion while driving – an event that would have previously caused her to feel anxious and panicked. However, on this occasion she was able to picture the diverted route parallel to the road which was closed, and figured out that she would still arrive at her target destination. She felt that she would have not have been able to do this prior to participating in the training.

< *Insert Figure 4* >

Surprisingly, FN's face recognition performance on the CFMT significantly improved following training (see Table 5). While it could be argued that the particular version of the CFMT that was used post-training was easier, this is not supported by control data or previous investigations (Bate et al., 2014). Further, when we asked FN to perform the exact same test again, both one week post-training and after a six-month delay, her score consistently fell within the impaired range (44/72 on both occasions).

8. Discussion

This paper reports an in-depth neuropsychological assessment of an individual presenting with both DP and topographical difficulties. Performance on a battery of navigational assessments indicated a primary impairment in the formation and retrieval of cognitive maps. Importantly, however, a brief period of virtual reality training enabled the woman to successfully create and use a cognitive map of a specific virtual environment. This finding indicates that over-rehearsal of the spatial organization of key environments may assist with everyday topographical orientation in those with developmental difficulties. Surprisingly, the training programme may also have brought about a short-term improvement on a single measure of face memory.

While there have been many reports in the literature of individuals with topographical disorientation alongside AP, very little attention has been directed to the same association in

DP. Despite several anecdotal reports of the relationship, only two investigations have formally investigated this link to date. While Corrow et al. (2016) found little evidence of topographical disorientation in their DP participants, Klargaard et al. (2016) did find impairments in topographical retention in four individuals with DP. The case study reported here is the first in-depth assessment of topographical difficulties alongside DP, and the first evidence of an association between DP and a weakness in cognitive map formation.

Clearly, FN's orientation difficulties cannot be attributed to any low-level deficits in memory, attention or visuospatial processing. Further, FN's basic orientation skills (i.e. her sense of direction and left-right skills) were intact, as were her short- and long-term memory for landmarks and her perspective-taking ability. However, she struggled with navigation in both real-world and virtual environments, where her ability to create and retrieve information from cognitive maps was impaired, including the selection of the shortest route. In addition, she was somewhat slower than controls at navigating a real-world environment by following the experimenter's instructions, by following a map, or by navigating a route that she had walked previously. In sum, the primary navigational difficulty experienced by FN was found to be the formation and retrieval of cognitive maps, potentially alongside a relative difficulty in visual working memory. While previous reports of DTD in the absence of prosopagnosia have followed a similar presentation (e.g. Iaria & Barton, 2010; Iaria et al., 2009), the severity of FN's navigational difficulties does not match these cases. Thus, it is possible that, compared to her high overall IQ, she has a relative weakness in spatial processing and navigation that may be exacerbated by the severe anxiety that she reports when wayfinding. Neuroimaging data would permit more insightful conclusions into the precise underpinnings of her navigational difficulties, and particularly how these compare to cases of DTD in the absence of prosopagnosia. Indeed, one study has linked DTD to a failure to activate the hippocampi (Iaria et al., 2009) – a neural region that is implicated in the use of cognitive maps in orientation tasks (e.g. Janzen, Jansen & van Turennout, 2008; Spiers & Maguire, 2007). A similar study carried out with FN would reveal whether her difficulties have the same aetiology (even if less severe) as published cases of DTD.

Such an investigation would also be of particular value given that topographical disorientation deficits following brain injury appear to have a broad range of underpinnings, where various taxonomies have identified difficulties in landmark and scene recognition, as well as in the processing of spatial relationships or the formation and retrieval of cognitive maps (e.g. Aguirre & D'Esposito, 1999; Arnold et al., 2013; De Renzi, 1982; Liu et al., 2011). This variability in acquired cases is unsurprising given the widespread nature of brain lesions: landmark agnosia has been associated with damage to right ventral temporo-occipital cortex (McCarthy, Evans, & Hodges, 1996; Pai, 1997), scene categorization with the transverse occipital sulcus (Bettencourt & Xu, 2013; Dilks, Julian, Paunov, & Kanwisher, 2013), and both processes to the parahippocampal place area (O'Craven & Kanwisher, 2000; Epstein, Harris, Stanley, & Kanwisher, 1999). Cognitive map formation has been linked to both the right and left hippocampi and the retrosplenial cortex (Iaria et al., 2007).

While few conclusions can be drawn into the precise underpinnings of FN's navigational difficulties, it is also unclear if and how they relate to DP – a condition that also has an unclear pathology, given a variety of structural, functional and connectivity abnormalities have been reported (e.g. Avidan et al., 2014; Behrmann, Avidan, Gao, & Black, 2007; Bentin, Deouell, & Soroker, 1999; Garrido et al., 2009; Song et al., 2015). It is particularly striking that, in the current study, we noted an improvement on a face memory task following the navigational training. Indeed, it is conceivable that there may be some overlap in the cognitive processes that are used in both cognitive map formation and face memory (e.g. more general visual imagery and spatial processing skills). The hippocampus is implicated in the encoding of new faces (Haxby et al., 1996), and lesions to the structure or surrounding area can result in higher-order impairments of face recognition (e.g. associative prosopagnosia or prosopamnesia: Delvenne et al., 2004; Tippett, Miller & Farah, 2000). Notably, FN's performance on the face-processing tasks reported here suggests her prosopagnosia may involve a higher-order impairment, given she did not display any abnormalities in non-identity tests of facial perception (i.e. expression, age or gender recognition). Further, anterior temporal atypicalities have been implicated in some cases of DP (Garrido et al., 2009). However, future replication and exploration of the effect observed here is required before any conclusions can be drawn. This is particularly important given the apparent resistance of prosopagnosia to even long-term intervention (for a review see Bate & Bennetts, 2015), the single case reported in this investigation, and the single measure that was used to assess face memory.

Given that existing evidence mostly appears to restrict developmental topographical difficulties to instances of poor cognitive map formation, a key question is whether the loss of this skill is absolute or simply requires additional rehearsal. Only one attempt to improve cognitive map formation in an individual with DTD has been reported to date, via over-rehearsal of a specific virtual environment (Iaria et al., 2009). In the current study we used a similar virtual reality approach to investigate whether FN can eventually form a cognitive map following repeated rehearsal with that environment. Our findings indicate that after an intense short-term training period, FN was able to successfully use a cognitive map to navigate around that particular environment. Given the simplicity and brief duration of the training, it is certainly possible that FN's difficulties with cognitive map formation reflect a relative weakness (as opposed to a disorder) in spatial memory, potentially exacerbated by hypervigilance and anxiety. This finding raises the possibility that navigational difficulties in individuals such as FN may be particularly responsive to simple intervention techniques.

Having said this, we cannot conclusively assess the effectiveness of our training programme, particularly in terms of generalization. Because we directly replicated the design used by Iaria et al. (2009), we did not ask FN to take part in pre- and post-assessment tasks that were independent of the training programme itself. That is, FN simply repeated the same task in each training session, and the first and the last sessions were used as pre- and post-assessments. While we were also restricted in our design by only having access to one virtual city and set of retrieval tasks, this does mean that a formal baseline and assessment of the generalizability of the navigational gains were not collected. However, it is of note that FN did report some benefits in her everyday navigation skills following completion of the training programme, and her linear improvement throughout the training period (see Figure 4) also supports our claim that she benefited from repeated rehearsal of the task.

While the findings reported here certainly require further exploration and replication, they do suggest that short-term navigational training programmes may provide a promising and simplistic means of assistance for people who experience concurrent DP and navigational difficulties. While the frequency of the relationship between DP and navigational difficulties has yet to be formally uncovered, anecdotal evidence does suggest that many people may experience both types of impairment (e.g. Brunsdon et al., 2006; Duchaine et al., 2003; Jones & Tranel, 2001; Le Grand et al., 2006; McConachie, 1976). Further, DP in isolation has been shown to have severe psychosocial consequences for both adults (Yardley et al., 2008) and children (Dalyrmple et al., 2014), with some individuals reporting severe anxiety, stress or depression when required to recognise faces in social, occupational and educational settings. Likewise, people with topographical difficulties can also experience similar symptoms when attempting to navigate in both novel and familiar buildings and environments (e.g. Iaria et al., 2009). It is certainly conceivable that the combination of these two impairments, as has frequently been reported in AP, might further exacerbate the potential for negative psychosocial consequences, highlighting the practical importance of this investigation.

Nevertheless, it is important for future research to establish the cognitive and neural profile of DP, including its potential subtypes and their links to associated difficulties such as topographical disorientation. This is not only important in terms of progressing our theoretical understanding of the cognitive and neurological underpinnings of the face-processing system, but may also have important implications for the clinical management of the condition.

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Table 1: FN's neuropsychological profile. Unless otherwise marked, all control means and standard deviations are extracted from relevant published norms (see main text for citations).

Test	FN'S score	Control mean	Control SD
General Intelligence			
WAIS III Index scores[a]			
Verbal Comprehension	127	-	-
Perceptual Organisation	111	-	-
Working Memory	117	-	-
Processing Speed	130	-	-
Full scale IQ	125	-	-
Memory			
WMS IV Index scores			
Auditory Memory	115	-	-
Visual Memory	104	-	-
Visual Working Memory	88	-	-
Immediate Memory	115	-	-
Delayed Memory	107	-	-
Executive Functioning			
Wisconsin Card Sorting Test			
Number of categories completed	6	5.46	1.35
Total number of trials administered	75	87.42	19.4
Total number of correct responses	67	67.85	11.51
Total number of errors	8	19.57	10.07
Further Spatial Memory Tests			
Visual patterns test	9/15	9.08	2.25
Corsi block test[b]			
Forward span	6/9	5.3	0.7
Backward span	5/9	5.5	1.1
Rey's complex figure[c]			
Copy	34	31.17	4.43
Delayed recall (20 minutes)	19	16.44	6.08
Language			
Picture Naming (BORB)	15/15	12.7	2.2
WTAR	50/50	-	-
Visuo-perceptual abilities			
BORB			
Length match	27/30	26.9	1.6
Size match	28/30	27.3	2.4
Orientation match	25/30	24.8	2.6
Position of gap match	29/40	35.1	4.0
Object decision (hard version)	57/64	52.4	3.91
VOSP			
Object perception:			
Screening test	20/20	19.92	0.33
Incomplete letters	19/20	18.8	1.4
Silhouettes	25/30	22.2	4.0
Object decision	19/20	17.7	1.9
Progressive silhouettes	10	10.8	2.5

Space perception:			
Dot counting	10/10	9.9	0.2
Position discrimination	19/20	19.6	0.9
Number location	10/10	9.4	1.1
Cube analysis	10/10	9.2	1.2
Social functioning			
Autism Spectrum Quotient	14/50	15.4	5.7

[a]Seven-test short form, scores based on Crawford, Allum, & Kinion (2008). [b]Control scores from Kessels, van den Berg, Ruis, & Brands (2008). [c]Control scores from Fastenau, Denburg, & Hufford (1999).

Table 2: FN's performance on the face-processing tasks. Analyses were conducted using modified *t*-tests for single case comparisons ($p < .05$; two-tailed; Crawford & Garthwaite, 2002). Scores in bold indicate a statistically significant impairment.

Task	**FN**	**Age-matched controls**			**Statistical tests**			
		Mean	**SD**	**n**	***t***	***p***	**% population scoring less than FN**	**Estimated effect size (Z_{cc})**
Face recognition								
CFMT	**28/72**	55.27	11.24	15	-2.35	.034	1.70	-2.43
Famous faces	**43.33%**	89.56%	7.08	17	-6.35	< .001	0.01	-6.53
Face perception								
CFPT[a]	**84**	37.06	10.03	17	4.57	< .001	99.98	4.70
Ekman 60 Faces	48/60	50.82	3.80	17	-0.35	.732	19.91	-0.36
RMITE	28/36	27.71	4.45	17	0.07	.949	52.57	0.07
Gender (PFPB)	45/75	59.42	11.73	12	-1.18	.261	13.07	-1.23
Age (PFPB)	67/75	69.56	3.75	12	-0.32	.757	37.85	-0.33

[a]Higher scores on the CFPT indicate worse performance.

Table 3: FN's performance on the battery of laboratory-based navigational assessments. Analyses were conducted using modified t-tests for single case comparisons ($p < .05$; two-tailed; Crawford & Garthwaite, 2002).

		Age-matched control group			Statistical tests			
Task	**FN**	**Mean**	**SD**	**n**	***t***	***p***	**% population scoring less than FN**	**Estimated effect size (Z_{cc})**
Basic Orientation								
Benton Left-Right Orientation	20/20	19.9	0.3	10	0.31	.758	62.11	0.33
Santa Barbara Sense-of-Direction Scale	33	63.80	16.79	15	-1.78	.097	4.87	-1.83
Imagery								
Memory of Buildings	40/40	38.9	1.2	10	0.87	.405	79.76	0.92
Postcards Test	35/40	23.7	5.14	10	2.10	.066	96.72	2.20
O'Clock Test	30/32	26.7	5.14	10	0.61	.556	72.22	0.64
Perspective taking/spatial orientation test	7/12	5.27	3.47	15	0.48	.637	68.16	0.50
Route-finding								
Map reading[a]	6/12	18th percentile (below average)						

[a]Norms from Stern and White (2001).

Table 4: FN's performance on the battery of real-world navigational assessments. Numbers in bold indicate FN was significantly slower or made significantly more total errors than controls (p < .05; two-tailed). Analyses were conducted using modified t-tests for single case comparisons (Crawford & Garthwaite, 2002).

Navigation test	**Distance (km)**	**FN time (secs)**	**FN errors**[a]			**Control mean time (SD) (secs)**	**Control errors**[a]		
			SC	**EC**	**Total**		**SC**	**EC**	**Total**
Route-based	1.0	**1062**	1	2	3	473.60 (50.32)	0.6 (0.89)	0.8 (1.30)	0.7 (1.05)
Landmark-based	0.8	615	0	2	2	421.80 (73.23)	0.2 (0.45)	1.2 (1.64)	0.7 (1.25)
Instruction-based	0.8	**840**	0	1	1	552.20 (62.35)	0 (0)	0.2 (0.45)	0.1 (0.32)
Map-following	1.5	**1170**	0	2	**2**	784.20 (95.51)	0 (0)	0.2 (0.45)	0.1 (0.32)
Shortest route[b]	0.8	540	0	0	0	514.80 (121.61)	0 (0)	0 (0)	0 (0)

[a]SC = self-corrected error; EC = experimenter-corrected error (i.e., participant asked for help). [b]All controls, but not FN, selected the shortest route (0.5 km).

Table 5: FN's performance on the virtual reality CMT in the first and final training sessions, and at a one-week follow-up session. Her face recognition performance on two different versions of the CMFT are also reported at the pre- and post-training intervals, and the latter test was repeated both one week and six months later. Analyses were conducted using modified *t*-tests for single case comparisons (Crawford & Garthwaite, 2002). Numbers in bold indicate FN performed significantly poorer than controls ($p < .05$; two-tailed).

		Age-matched control group			**Statistical tests**			
Task	**FN**	**Mean**	**SD**	**n**	***t***	***p***	**% population scoring less than FN**	**Estimated effect size (Z_{cc})**
Virtual reality CMT								
Age	57	56.2	4.3	5				
Learning task (seconds)								
Initial assessment	**1680**	1008.00	214.66	5	2.86	.046	97.70	3.31
Final training session	240				-3.27	.031	1.55	-3.58
One-week follow-up	240				-3.27	.031	1.55	-3.58
Retrieval task (seconds)								
Initial assessment	**17.33**	10.45	2.39	5	2.63	.058	97.08	2.88
Final training session	6.92				-1.35	.249	12.44	-1.48
One-week follow-up	9.27				-0.45	.676	33.78	-0.49
CFMT								
Pre-training	**44**/72	61.70	6.20	10	-2.72	.024	1.18	-2.86
Post-training	56/72	62.30	4.58	10	-1.31	.222	11.11	-1.38
One-week follow-up	**44/72**	62.30	4.58	10	-3.81	.004	0.21	-3.97
Six months post-training	**44**/72	62.30	4.58	10	-3.81	.004	0.21	-3.97

Figure Captions

Figure 1: Plans of the (A) lower and (B) upper floors of FN's house. The left-hand images are formal plans of FN's home drawn to scale, and the right-hand images were drawn by FN from memory when she visited our laboratory.

Figure 2: Maps of the routes used to test real-world navigation. A) R1: route-based navigation (solid line); R2: landmark-based navigation (dotted line; numbers indicate locations of landmarks); and R3: instruction-based navigation (dashed line). B) Routes used to test map-based navigation. All routes started and finished in the same location. Map-following route (dashed line); shortest route from start to finish (dotted line); and FN's chosen route in the shortest-route task (solid line).

Figure 3: (A) Example landmarks that were used within the virtual city for the cognitive map test, and (B) the structure of the experimental city, including the location of each landmark where participants performed both the learning and retrieval task.

Figure 4: FN's performance on the retrieval task in each training session and at the one-week follow-up.

Figure 1

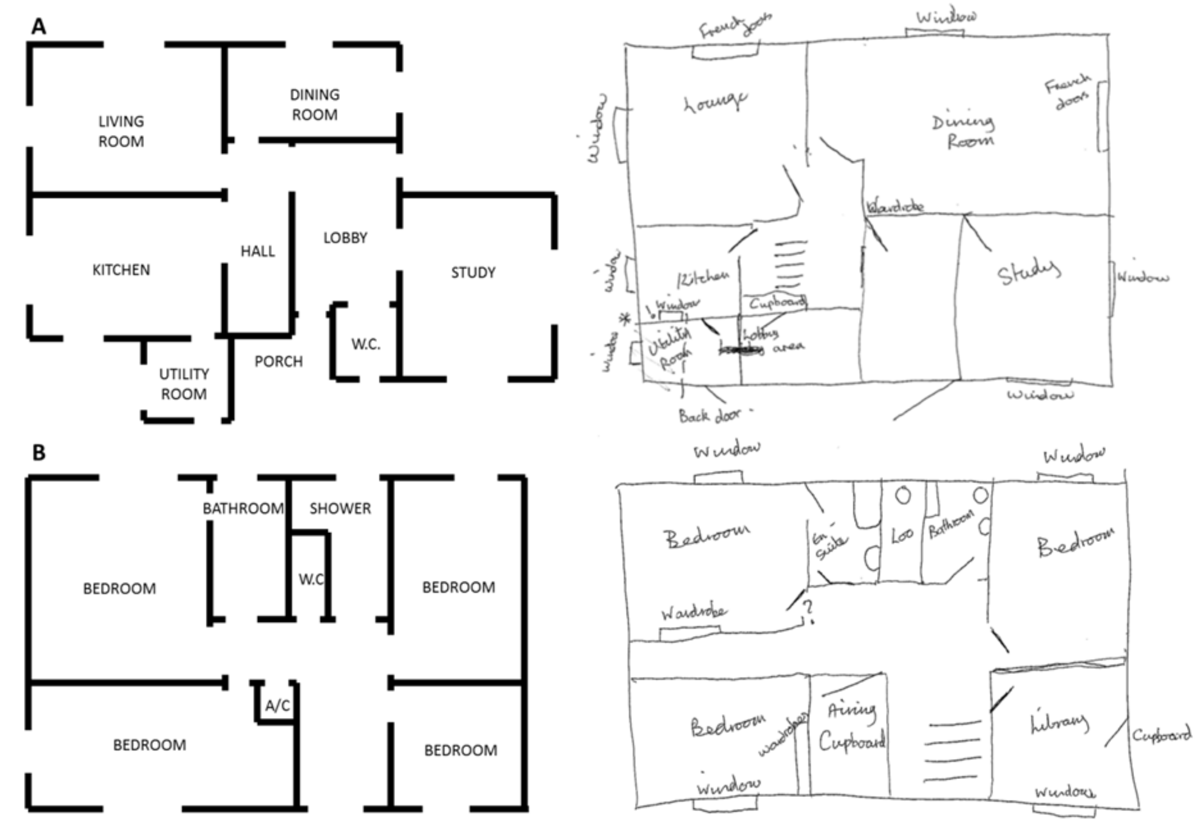
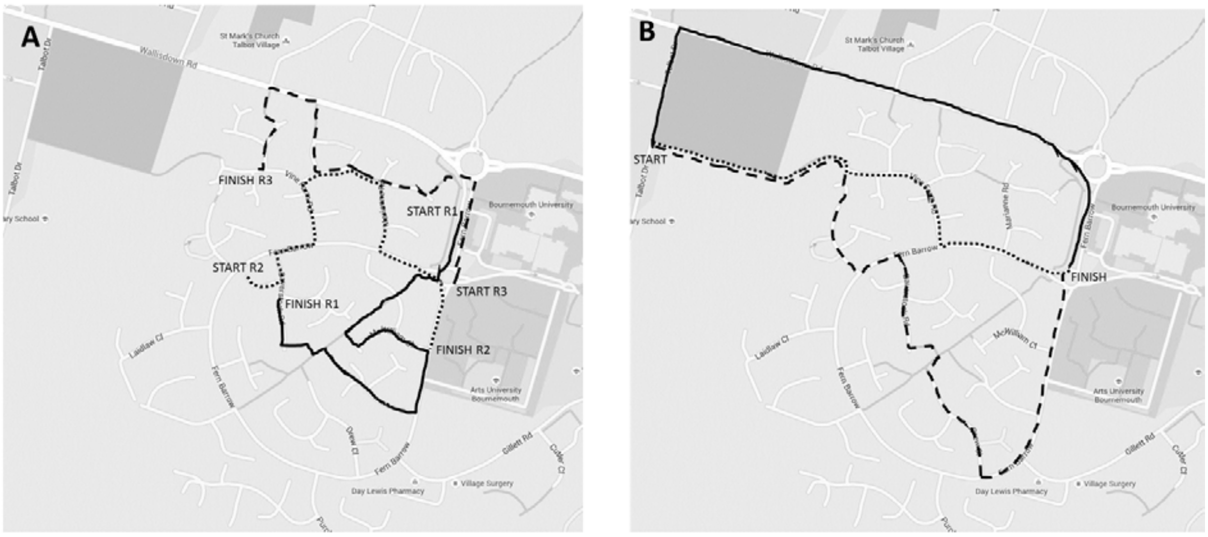

A
LIVING ROOM
DINING ROOM
KITCHEN
HALL
LOBBY
STUDY
W.C.
UTILITY ROOM
PORCH
B
BATHROOM
SHOWER
BEDROOM
W.C
BEDROOM
A/C
BEDROOM
BEDROOM

Figure 2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Wallisdown Rd
St Mark's Church
Talbot Village
Talbot Dr
FINISH R3
START R1
START R2
FINISH R1
START R3
FINISH R2
Bournemouth University
Arts University Bournemouth
Laidlaw Ct
Fern Barrow
Drew Ct
Gillett Rd
Day Lewis Pharmacy
Village Surgery
B
START
FINISH
McWilliam Ct

Figure 3

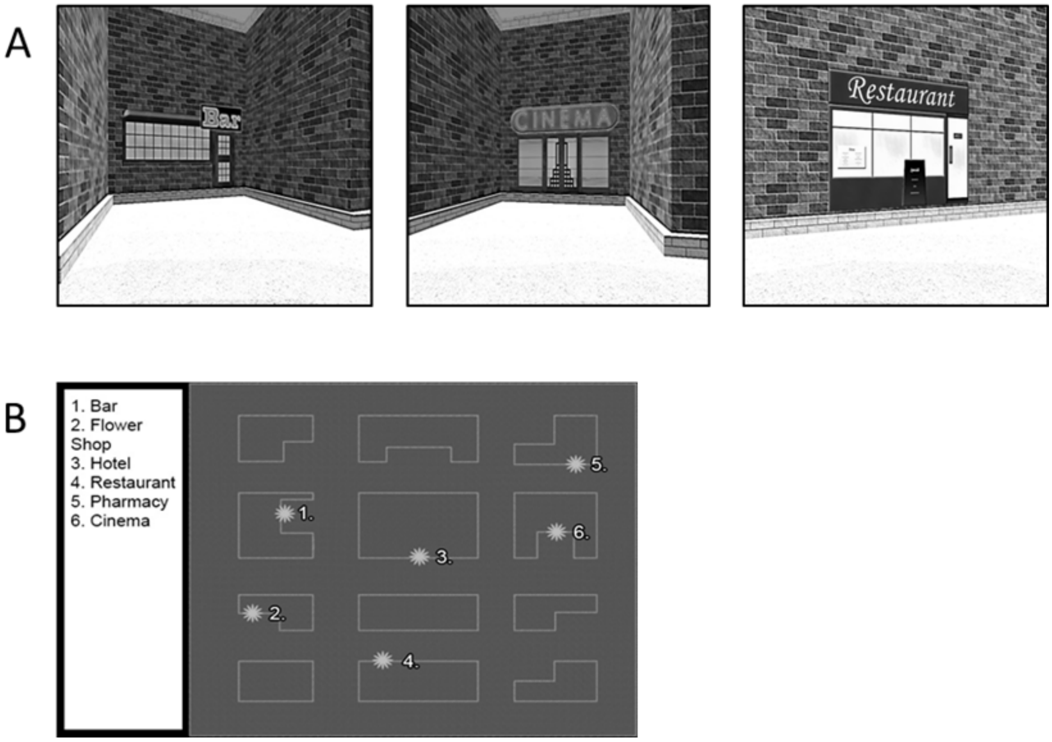
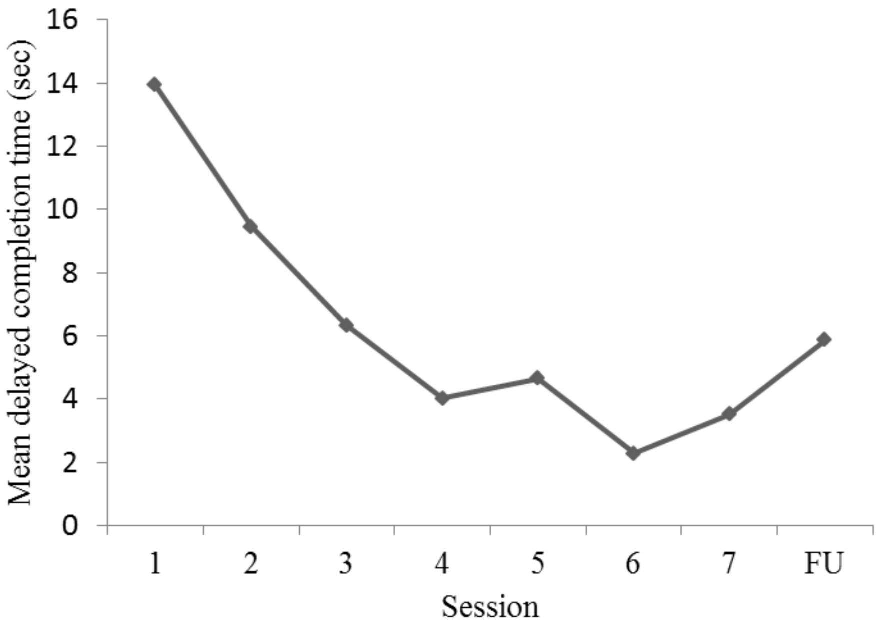

A
Bar
CINEMA
Restaurant
B
1. Bar
2. Flower Shop
3. Hotel
4. Restaurant
5. Pharmacy
6. Cinema
1.
2.
3.
4.
5.
6.

Figure 4


Mean delayed completion time (sec)
16
14
12
10
8
6
4
2
0
1
2
3
4
5
6
7
FU
Session