

The relationship between dissociated measures of inhibition and hypnotic and placebo analgesia effects

Alethea Guestini (MRes) and Benjamin A. Parris (DPhil)*

Department of Psychology

Bournemouth University

*Address for correspondence:

Benjamin A. Parris

Department of Psychology,

Bournemouth University

Talbot Campus

Fern Barrow

Poole

Dorset UK

BH12 5BB

01202 524111

bparris@bournemouth.ac.uk

Word count: 4370

Tables: 2

Figures: 1

Conflicts of Interest and Source of Funding

There are no conflicts of interest to report. The research was not funded and was completed as part of the first author's Masters in Research at Bournemouth University supervised by the lead author.

Abstract

Objective:

The aim of the present research was to assess the relationship between the executive function of inhibition and hypnotic and placebo analgesia.

Method:

In a fully within-subjects experiment, 54 participants performed the Cold Pressor Task under three randomised conditions: 1) hypnotic analgesia; 2) placebo analgesia, and; 3) a control condition. Pain threshold and pain tolerance were used as measures of pain perception in each condition. Analgesia was calculated by subtracting the control conditions from the two critical conditions (hypnosis and placebo). Following recent work indicating doubly-dissociated forms of inhibition, participants also completed: 1) the Stroop task; 2) the Hayling Sentence Completion Task (HSCT) and a matrix reasoning task, in a fixed order.

Results:

Analyses revealed both placebo analgesia (effect sizes $r_B > 0.4$) and hypnotic analgesia (effect sizes $r_B > 0.7$) suggestions were effective. The results also showed that HSCT performance predicted the magnitude of placebo pain threshold ($t(47) = 3.448$, $p < .001$, $BF_{10} = 16.4$), but not hypnotic pain threshold ($t(47) = 0.537$, $p > .5$, $BF_{01} = 3.483$). The results for placebo ($t(47) = 3.126$, $p = .003$) and hypnotic ($t(47) = 0.295$, $p > .7$) pain tolerance and HSCT performance were insensitive ($BF_{10} > 0.3 < 3$). Neither the Stroop task nor matrix reasoning scores predicted analgesic effects ($t_s < 1.6$, $p_s > 0.1$; $BF_{10} < 0.3$).

Conclusion:

The results highlight the efficacy of suggestion on pain perception and show a relationship between performance on the HSCT and the magnitude of the placebo effect. Limitations and directions for future research are discussed.

Key words: Inhibition; Hypnosis; Placebo; Stroop; Hayling Sentence Completion.

Abbreviations: CPT = Cold Pressor Task; HSCT = Hayling Sentence Completion Task.

Introduction

There are overlapping neuroanatomical pathways in the pain and executive function systems, providing the possibility for the two systems to interact (1-5). Such interactions go some way to explaining why pain is a multidimensional experience and why it is dependent on a number of factors that are independent of nociceptive input (6-11). The complexity of the pain experience is reflected, not only in the multifaceted nature of executive functions, which are generally considered to involve, but are not limited to, the processes of inhibition, shifting and updating (12), but also in the influence of the socio-cultural context on pain perception (e.g., 9; 13) as epitomised by analgesia effects observed under suggestion (14).

The importance of inhibition in pain perception

Emerging evidence suggests the importance of inhibition in shaping the perception of pain (15-19). Shackman et al. (2011; 18) have shown that emotion, pain and executive functions share overlapping brain structures, reflecting control processes that are common to all three domains. Pain itself has been described as a control or learning signal (20) that indicates when the body needs rest, or when cognitive control is needed to redistribute resources and attentional focus in response to pain. Haberman et al. (2025; 20) give the example of trying to focus on an important conversation whilst enduring stomach pain. Here executive functions would be marshalled to attenuate the pain sensation. This represents an internal form of pain control that employs executive resources, such as inhibition, to facilitate goal-oriented behaviour.

It has been argued that there is more than one type of inhibition (21-24). Inhibitory control is often dichotomised into response inhibition (also known as prepotent response inhibition) and attentional inhibition (or cognition inhibition; 24-28). Response inhibition refers to the revoking of a prepotent motor response and is often assessed by selective

stopping tasks using manual (button-press) tasks such as stop signal and go/no-go tasks, oculomotor tasks such as the anti-saccade task (24) and, verbal tasks such as the Hayling sentence completion task (29-31). Attentional inhibition has been defined as the stopping or overriding of a mental process (27) or resistance to interference from irrelevant stimuli and is assessed using tasks such as the Flanker task (24) and the Stroop task (32-33).

There is evidence that both response inhibition (16) and attentional inhibition (15;17) are related to pain perception. Karsdorp et al. (2014; 16) reported that poorer response inhibition (as measured by the stop-signal task) was associated with shorter Cold Pressor Test (CPT) immersion durations. Oosterman et al (2016; 17) reported that poorer attention inhibition (a larger Stroop interference score) was related to shorter CPT immersion durations, and decreased pain intensity and unpleasantness ratings. Bjekic et al. (2018; 15) showed that whilst Stroop interference was related to pain experience in the CPT, performance on the stop-signal task was not. Thus, despite some contradictory findings, these measures of response and attention inhibition are related to sensory perception of pain and its control.

Recent research suggests that these two types of inhibition tasks might have relatively well-circumscribed and distinct neural substrates (34-35). Cipolotti et al. (2016; 34) systematically explored the relationship between inhibition, fluid intelligence and lesion location in a neuroimaging study employing voxel-based lesion-symptom mapping. The results from 30 frontal lobe patients of varying aetiologies showed that after accounting for fluid intelligence (as measured by Cattell's Culture Fair Intelligence test, a matrix reasoning test), performance on the Hayling Sentence Completion Test (HSCT; 29), which requires participants to finish a sentence with a word that is not related to the sentence's meaning (e.g., *The captain wanted to stay with the sinking....lamp*) significantly relied on the integrity

of the right Prefrontal Cortex (PFC), specifically the superior and middle frontal gyri. In contrast, performance on the Stroop test (32), which requires participants to name the colour of the ink in which a word is presented (e.g., the word *red* is written in blue ink) relied on the integrity of the superior and middle frontal gyri of the left PFC. The authors noted that these findings are consistent with other findings in the literature (e.g., 21; 22; 36-37). The authors argued that the two measures of inhibition are therefore dissociable components of the executive function of inhibition, supporting Kok's (1999; 23) conclusion that there are multiple forms of inhibition. Here we employ the Hayling Sentence Completion task (29) as a measure of response inhibition, and the Stroop task as a measure of attention inhibition (32-33; 38-40).

Reduction in pain perception under suggestion

Suggestion has been defined as a form of communicable ideation or belief, that once accepted has the capacity to exert profound changes on a person's mood, thoughts, perceptions and behaviors (14). Hypnosis and placebo both involve suggestion (14; 41-42). Within pain studies, research has shown that the placebo phenomenon is powerful enough to cause the release of endogenous opiates (the body's natural painkillers) so that participants report lessor pain scores after being given a placebo to reduce pain (this pain reduction is called placebo analgesia; 43). Like placebo, hypnotic suggestion has also been found to be effective as an analgesic (hypnotic analgesia) which has led to comparisons being drawn between the two phenomena, with hypnosis being described as placebo without deception (44-47), indicating that they are both potentially underpinned by the same executive control mechanisms.

There are indications in the literature however that the two forms of suggestion do not rely on the same executive control functions of the prefrontal cortex (42; 48) and that they do

not correlate (49-50). For example, repetitive Transcranial Magnetic Stimulation (rTMS) of the dorso-lateral prefrontal cortex (PFC) reduces placebo analgesia effects (51), but increases hypnotic suggestibility (52-53). Benedetti (2009; 54) has argued that without a PFC, there are no placebo effects. Support for this position comes from numerous sources (51; 55-58). In contrast, the relationship between hypnotic responding and frontal executive functions is a lot less clear (59-60). This indicates that hypnotic and placebo responding might be underpinned by different executive functions.

The aim of the present study was to investigate whether distinct and recently doubly dissociated inhibitory mechanisms (34) as measured by the Hayling Sentence Completion task (29), and the Stroop task (32-33; 38-40) are related to pain perception under hypnotic and placebo suggestion. Following Cipolotti and colleagues (2016; 34), a measure of fluid intelligence was included in our analysis as a measure of general cognitive ability. We used the Cold Pressor Task (CPT) to induce experimental pain (61). In a fully within-subjects design, participants completed the CPT under three counterbalanced conditions: 1) Placebo analgesia; 2) Hypnotic analgesia; 3) a control condition. They also completed three cognitive tasks: 1) the Hayling Sentence Completion Task; 2) the Stroop task and; 3) Following Cipolotti et al. (2016; 34) a matrix reasoning task was included as a measure of fluid intelligence and general frontal lobe functioning (62). As has been noted above, Stroop task performance has been shown to have a potentially unique relationship to pain perception (at least in the context of Cold Pressor pain; 15; 17) among executive function tasks, indicating that pain can be actively controlled by mechanisms of cognitive/attention inhibition. It was therefore expected that pain perception following hypnotic and/or placebo analgesia suggestions would be related to Stroop task performance. The Hayling Sentence Completion task has previously been investigated in terms of its association with the experience of pain in those with chronic pain (63-64) but as far as we are aware has not been investigated

experimentally in its relationship to pain. However, its double dissociation from the Stroop task, potentially based on its right-sided hemispheric underpinning (compared to the Stroop which is left-sided; 34; 36), makes it a good candidate for a clearly dissociated form of inhibition, and one which has previously been predicted to be associated with pain due to its potential relevance to the descending pain modulatory system (63-64).

Method

Design

This study employed a correlational, fully within-subjects design in which performance on the three cognitive tasks were regressed on our four dependent variables. The four dependant variables (DVs) were: 1) Hypnotic Analgesia for Pain-Threshold (Pain Threshold following Hypnotic Analgesia – Pain Threshold following Control); 2) Hypnotic Analgesia for Pain-Tolerance (Pain Tolerance following Hypnotic Analgesia – Pain Tolerance following Control); 3) Placebo Analgesia for Pain-Threshold (Pain Threshold following Placebo Analgesia – Pain Threshold following Control), and; 4) Placebo Analgesia for Pain-Tolerance (Pain Tolerance following Placebo Analgesia – Pain Tolerance following Control).

Participants

G*Power was used to calculate sample size for linear multiple regression with 4 predictors assuming a medium effect size ($f=0.25$) where power = 0.8. This returned a required sample size of 53 participants. However, sensitivity of all tests was assessed using both frequentist and Bayesian statistical approaches. Participants were recruited from either Bournemouth University's Experiment Participation Scheme, or via advertisements placed on the university campus. Participants on Bournemouth University's Experiment Participation Scheme were given 2 credits (at the standard rate of 1 credit per hour). Other participants were paid £16 for

their time at the standard rate of £8 per hour. Exclusion criteria included those suffering with a heart condition, or any persons taking pain medication for pain conditions (e.g. amitriptyline), as the medication prescribed for both these conditions may have affected pain tolerance levels on the CPT (65-66). Also excluded were those who had suffered a stroke, those suffering with schizophrenia, bi-polar disorder or epilepsy, those taking anti-psychotic and/or anti-depressants and/or anxiety medication.

Of the 54 participants recruited, 6 participants either withdrew or did not fully complete one or more of the executive function tests. The remaining 48 (22 males) participants were aged between 18-48 years ($M = 21.8$, $SD = 5.6$). Participants were also told to abstain from alcohol for 24 hours prior to testing, as well as excluding smoking, drinking coffee/ caffeinated sports drinks and food for 2 hours prior to testing, as these may all have affected executive function' performance (e.g., 65-66). Participants who had participated in research using the CPT before were also excluded, due to prior experience negatively effecting novel placebo-expectation pain reduction (65).

Materials

Cold Pressor Test (CPT) apparatus:

The cold pressor (CP) consisted of a Coleman 36 QT Cooler, containing ice-cold water that contained a large circular bowl that had a circumference large enough for a hand to be rested in, with fingers spread. The bowl was also used to keep the netting and ice pushed towards the inner sides of the CP, thus stopping the ice from touching the participants hand whilst it was immersed in the water. The temperature of the water was maintained at 2 degrees Celsius (C) and did not fluctuate by more than 0.5 degrees C, as small changes could result in pain response variations (67). Additionally, a circulatory water pump by Fluval SEA CP1 (Circulation Pump 1000LPH) was used to prevent a microclimate of warm water building up around the hand

(61). The ice-water level inside the CP was high enough for the hand and wrist to be fully immersed (61).

In the present experiment, two time-points were recorded (in seconds) from when the hand is immersed: 1) Pain-threshold – The participant reports the initial onset of cold pain discomfort (timed from when the hand is initially immersed in the water) and; 2) Pain-tolerance - The time the hand is withdrawn from the water due to intolerance to the pain (timed from when the hand is initially immersed in the water). Following previous studies the maximum time permitted for hand immersion was 180s (61).

In all conditions, in between hand immersions the participants' lower wrist, arm and hand were rested comfortably on an ABLE2 UK LTD cushioned lap rest, covered with a hand-towel and a large sheet of kitchen towel (which was changed each time a cream was applied).

Blood Pressure and Heart rate monitor

Blood pressure (BP; systolic and diastolic) and heart rate (HR) were measured using an Omron M2 Basic Intelli Sense Automatic upper arm blood pressure monitor, as a health and safety check.

Thermometer

Hand temperature was measured using an Acxeon Non-Contact Infrared Forehead-body Thermometer, Digital Laser, Temperature Measurement Gun was used to take temperature reading of the participant's hands (68). A standard size hot water bottle was also used after each immersion; wrapped in a soft, small blanket that participants could slip their hand/s inside to warm up in order to prevent a cumulative cooling effect on the hands, due to repeated immersions (67).

Fluid Intelligence measure

The Matrix Reasoning (MR) Test from the *Wechsler Abbreviated Scale of Intelligence II (WASI)* was used as a measure of fluid intelligence (62). This was a timed test, with 45 seconds being allowed for each item on the test. Each correct answer scored one mark. The manual stated that testing should be discontinued when the participant has made three consecutive incorrect answers. The DV was participants' raw Matrix score.

The Stroop Task (Stroop, 1935)

Following (34) the present study used the Golden and Freshwater (2002; 69) paper version of the Stroop task, which consisted of three A4 pages: 1) Contained five columns of 20 the words 'RED', 'GREEN' and 'BLUE' printed in black ink (Word Score); 2) Contained five columns of 20 coloured crosses 'XXXX' randomly printed in red, green and blue ink (Colour Score); 3) Contained five columns of 20 coloured words, 'RED', 'GREEN' and 'BLUE', written randomly in colours incongruent with the words e.g. the word 'GREEN' written in blue ink (Colour-word Score). For each page (condition) participants had 45 seconds to name aloud the colour of as many items as possible. If the participant had finished the page before the 45 seconds were up they could go back to the beginning of the page and continue saying colours aloud until the time was up. If any items were responded to incorrectly the researcher would say "No", and the participant had to attempt it again before moving on. The researcher marked each correct answer. Following Cipolloti et al. (2016; 34) we used only the number of correct responses from the conflict page (page 3) produced in the 45 second limit as our measure of Stroop task performance.

The Hayling Sentence Completion Task (29)

This test is thought to assess response inhibition/suppression along with strategy generation. Part 1 requires participants to complete 15 sentences using words that are related to the sentence

topic, for example 'Bournemouth can be a very busy...' could be completed by saying the word 'town'. Part 2 required participants to complete 15 sentences using words that were unrelated to the sentence topic, for example 'Bournemouth can be a very busy...' could be completed by saying the word... 'apple' instead of the appropriate word 'town'. After the researcher read a sentence, the participant had to say the missing word as quickly as possible. The researcher made a note of each answer and the time taken. Individuals with frontal-lobe damage may produce suppression errors, and answer with the appropriate word 'town', instead of 'apple' in Part 2 and often they may have longer response times, consequently reducing their scores.

Any error made in Part 2 (category A errors = 3 points and category B errors = 1 point) were calculated and transformed into a scaled score. Part 1 and Part 2 scores can then be calculated and converted to an overall Hayling scaled score (see manual). However, Cipolotti et al. (2016; 34) treated the error and RT scores as independent measures but showed similar effects with both. Following Cipolotti et al. (2016; 34) and to reduce the number of predictors, only the scaled Hayling Suppression Error score was used as a predictor in the present study.

Hypnotic suggestibility screening procedure

The Stanford Hypnotic Susceptibility Scale – Form C (SHSS: C; 70) was used to assess hypnotic suggestibility. Due to the length of testing time, items 6 (DREAM) and 7 (AGE REGRESSION) were omitted. Therefore, in this study, a participant could score between 0 (low hypnotic suggestibility) and 11 (high hypnotic suggestibility).

Procedure

Upon arrival, participants were greeted by two researchers and were asked to read the information sheet about the study and asked if they had any questions about the research. Participants completed a participant details form, also asking them to report which was their

dominant hand and to confirm that they met the inclusion criteria. Participants were then asked to read and complete the consent form. Participants then undertook the executive function tasks in the following order: WASI Block Design; the Hayling Task; the WASI Matrix Reasoning; the Stroop Task.

A different researcher then took the participant through the CPT immediately after the completion of the executive function tasks. A Coleman 36 QT Cooler-box was placed on a large, high-backed chair, where the height was appropriate for the CPT for each participant. This also meant that the box could be moved safely to the left or right side of the participant's seated position, ready for their left/right hand to be immersed. Before beginning the CPT, any necessary adjustments to the water temperature were made to ensure it was at 2 degrees Celsius (C). The participant was then invited to sit down. BP, HR and hand temperature were recorded for a baseline reading. Participants were then instructed by the researcher about the two time-points following immersion (threshold and tolerance) that needed to be recorded by the researcher. Participants were told that the maximum amount of time they could keep their hand in the water for each immersion was 180 seconds, and that they would undertake three, alternating hand immersions in total (one immersion for each of the three conditions). Participants were also instructed on how to place their hand in the bowl, with their fingers spread. The researcher then asked the participant to repeat back the instructions to fully check understanding.

Participants were randomly allocated to one of 6 counterbalanced order conditions in terms of the order in which they completed the CPT conditions (e.g., placebo analgesia-control-hypnotic analgesia / placebo analgesia-hypnotic analgesia-control). The hand (e.g., left hand) participants used for their first CPT condition was counterbalanced between participants, and subsequently alternated in the remaining CPT conditions (e.g., right hand for the second CPT condition and then left hand for the final CPT condition) to deter a practice effect, and the

build-up of coldness on a single hand (61), given that the CPT was used 3 times during the experiment (placebo analgesic condition, hypnotic analgesia condition and control condition). Participants were tested individually for both the executive functions tests and the CPT.

The researcher applied the hand-cream to the participant's hand (either left or right depending on hand counterbalancing), with the relevant information depending on the condition (see below). Each immersion was timed for pain-threshold and pain-tolerance measures, whilst checking and recording the participant's BP and HR. When the participant withdrew their hand at the pain-tolerance point, the researcher wrapped their hand in kitchen towel to dry off the ice-water. The participant was then asked to squeeze their hands tightly into a fist, and then rub their hands together to warm their hands naturally for one minute. Participants' hands were then warmed on a hot-water bottle for two minutes (one minute on each side of the hand) or more if needed until hand temperature had returned to baseline.

In the hypnotic analgesia condition participants underwent a hypnotic induction (taken from the Stanford Hypnotic Susceptibility Scale) after which the participants were given the hypnotic suggestion for painlessness and underwent the hypnotic analgesia condition of the CPT. They were then de-inducted from hypnosis.

Once all three CPT conditions were completed participants were taken through the Stanford Hypnotic Susceptibility Scale to assess hypnotic suggestibility. Once this was complete the participants were thanked for their time and were debriefed about the nature of the placebo condition.

Condition-specific procedures

Control Condition

The hand cream used in the control condition was an E45 cream with no additional odour or colouring, and was dispensed via a white pump-dispenser labelled 'Soft Clean Lotion and Hand

Cleanser'. The researcher covered the nails and in between the fingers with the cream, expressing that "I don't want to miss the nails and in between the fingers".

Placebo Analgesia Condition

It was important that the placebo analgesia "medical" cream differed from the "hand-cream" used in the other two conditions. The placebo hand-cream was in a white pump-dispenser labelled 'Travaricane: Approved for research purposes only' (71) and contained 75% E45 and 25% Conotrane Soothing Cream (to modify the texture of the cream) mixed with roughly 5ml of Thyme Oil (*ThymusVulgaris*) by Health Aid, for a medicinal smell (again following 71), and 2ml of Dr. Oetker (vegan) red food colouring, which when combined with the Conotrane Cream turned pale-pink in colour. The cream was pumped on to the participant's hand and massaged in by the 2nd researcher, who was wearing disposable gloves and a white lab coat. The participant was told by the 2nd researcher that "Travaricane is a very powerful analgesic cream, it has just a light clinical smell and is used by surgeons and GP's for stitches and injections, on the sensitive areas of the face. It is also especially useful, for example, on footballers and rugby player's during bodily injury, as it only takes 30 seconds to start working". The researcher covered the nails and in between the fingers with cream, expressing that "I don't want to miss the nails and in between the fingers as they are also sensitive to the cold".

Hypnotic Analgesia Condition

The 'Soft Clean Lotion and Hand Cleanser' was applied to the participants' hands prior to immersing their hand in the ice-cold water (it was identical to that used in the Control condition). During preparation, the participants were told that "hypnosis is a very powerful tool and is now used on Cancer patients to reduce pain. It is also used by dentists in dentistry,

instead of anaesthesia, and in operations by surgeons, again instead of anaesthesia”. Prior to immersing their hands, the participants were induced into hypnosis and given the following suggestion: “the hand is insensitive to pain and no pain sensation will originate from it.” Participants were told that the hypnotic induction and script for the hypnotic analgesia CPT were taken from an “Oxford University Short Induction Script” to ensure the mainly UK participants recognised the provenance of the induction technique as important. However, the induction was adapted from The Stanford Hypnotic Susceptibility Scale – Form C (SHSS: C; 70) and the hypnotic suggestion was adapted from Casiglia et al.’s (2007; 72) study. The researcher covered the nails and in between the fingers with the cream, expressing that “I don’t want to miss the nails and in between the fingers”.

Timeframe

The data for this project were collected between January 2017 and July 2019.

Ethics

This research was approved by the Institutional Review Board (Bournemouth University’s Science and Technology Research Ethics Panel; Ethics ID: 14034) and informed consent was obtained from participants.

Results

The data were first analysed for evidence of hypnotic and placebo analgesia in the pain threshold and pain tolerance times. Hypnotic analgesia was calculated as the difference (in seconds) between the hypnotic analgesia suggestion condition and the control condition. Likewise, placebo analgesia was calculated as the difference (in seconds) between the placebo analgesia suggestion condition and the control condition. The Shapiro-Wilk test

revealed that these measures of performance were not normally distributed (all $ps < .001$) and we therefore analysed hypnotic and placebo analgesia effects with the Wilcoxon sign-ranked test. See Table 1 for median pain threshold and pain tolerance times in each condition and Figure 1 for box plots of the data in each condition.

Table 1. Medians, Means, Standard Deviations, and Standard Errors for pain threshold and pain tolerance (in seconds) in each condition.

	N	Mean	SD	SE	Median
Placebo Threshold	48	13.1	11.4	1.6	9.5
Control Threshold	48	10.1	13.2	1.9	5.5
Hypnosis Threshold	48	61.5	65.6	9.5	32
Placebo Tolerance	48	77.4	59.2	8.5	46.5
Control Tolerance	48	70.4	63.9	9.2	38
Hypnosis Tolerance	48	107.9	67.5	9.7	90.5

For pain threshold, the effects of both hypnotic analgesia (Median = 19, $W = 5.709$, $p < .001$, $r_B = 0.957$, $BF_{10} = 43818$) and placebo analgesia (Median = 2.5, $W = 4.136$, $p < .001$, $r_B = 0.724$, $BF_{10} = 143$) were shown to be significant. Hypnotic analgesia was larger than placebo analgesia in the present study and indeed many of the participants did not report the onset of pain for the full 3 minutes following the hypnotic suggestion for pain desensitisation (see Figure 1 for box plots for each condition).

For pain tolerance, the effects of both hypnotic analgesia (Median = 8.5, $W = 4.633$, $p < .001$, $r_B = 0.862$, $BF_{10} = 9445$) and placebo analgesia (Median = 2.5, $W = 2.414$, $p = .008$, $r_B = 0.444$, $BF_{10} = 2.89$) were also shown to be significant, albeit where the Bayes Factor for the

latter provided only anecdotal evidence in favour of H1 (see Figure 1 for box plots for each condition).

According to the levels of evidence describe by Jeffreys (1961; 73) and Lee and Wagenmakers (2013; 74), our data provides extreme evidence for hypnotic and placebo analgesic effects on pain threshold and for hypnotic analgesic effects on pain tolerance, but only anecdotal evidence for an effect of placebo analgesia on pain tolerance.

Correlation between Hypnotic and Placebo analgesia

One aim of the present study was to determine whether the magnitudes of hypnotic and placebo analgesia, both involving suggestion, were correlated. Spearman's Rho analysis revealed that they were not related in our data for pain threshold scores ($r = 0.015$, $p = 0.919$) with moderate Bayesian evidence for the null ($BF_{01} = 4.614$) but they were for pain tolerance ($r = 0.487$, $p < 0.001$) with strong Bayesian evidence for the alternative hypothesis ($BF_{10} = 36.024$).

Multiple Regressions

Given the evidence above, we next ran a series of multiple regressions to investigate whether any of the executive function tests predicted the magnitude of the analgesic effects observed in the experiment. See Table 2 for the descriptive statistics for each of the tests and see Figure 1 for the plotted raw times (in seconds) in each condition). In all multiple regressions the predictors were inputted using the Enter method. Frequentist analysis were supplemented with Bayesian equivalents.

Table 2. Descriptive Statistics for the executive function tests.

	Valid	Mean	Std. Error of Mean	Std. Deviation	Minimum	Maximum
Stroop Incongruent stimuli	48	50.5	1.2	8.4	36	76
Hayling Suppression errors (scaled)	48	6.7	0.2	1.1	3	8
Stanford Hypnotic Susceptibility Scale score	48	4.8	0.3	2.1	2	9
Matrix Reasoning	48	19.7	0.5	3.5	9	25

Placebo analgesia for pain threshold

The Durbin-Watson checks for correlations between residuals was between 1 and 3 as required. A residuals plot and standardised residuals (Q-Q) plot revealed that the assumptions of homoscedasticity, normality and linearity were not violated. Tolerance (all $>0.8<1$) and VIF ($>1<1.3$) values were also within acceptable ranges. The model was significant where $F(4, 43) = 3.340$, $p = 0.018$, $R^2 = 0.237$. The adjusted R^2 revealed that the predictor variables predicted 16.6% of the variance. Whilst the overall model was significant, only the Hayling Suppression Scaled Error score was a significant predictor of placebo analgesia, $t(47) = 3.448$, $p < .001$, unstandardized beta = -2.955 where the regression equation is: Placebo analgesia = $19.529 - (2.955 \times \text{Hayling Suppression Error Score})$.

The outcome of this frequentist analysis was supported by a Bayesian multiple regression analysis. A Bayesian multiple regression was carried out using all four predictors as predictors of placebo analgesia. An uninformed uniform prior $[P(M)]$ of 0.125 was set for each of the 16 possible models. Whilst there was moderate evidence for multiple models ($BF_{10} >3<7$) and strong evidence for the model including just Stanford Hypnotic Susceptibility Scale score + Hayling Suppression Errors (Scaled; $BF_{10} = 12.6$), the strongest evidence was for a regression model including only Hayling Suppression Error Score ($BF_{10} = 16.4$) when compared to the null model. Importantly, the $BF_{\text{Inclusion}}$ values were less than 0.8 for all predictors other than Hayling Suppression Errors (Scaled; $BF_{\text{Inclusion}} = 21.9$).

The above results indicate that the higher the Hayling error score, the lower the magnitude of the placebo analgesia effect indicating that pain reduction following placebo analgesia is related to a person's capacity to inhibit the correct sentence completion word.

Hypnotic analgesia for pain threshold

The Durbin-Watson checks for correlations between residuals was between 1 and 3 as required. A residuals plot and standardised residuals (Q-Q) plot revealed that the assumptions of homoscedasticity, normality and linearity were not violated. Tolerance (all $>0.8<1$) and VIF ($>1<1.3$) values were also within acceptable ranges. The model was not significant where $F(4, 43) = 2.009$, $p = 0.11$, $R^2 = 0.157$. The adjusted R^2 revealed that the predictor variables predicted 15.7% of the variance. Whilst the overall model was not significant, the Stanford Hypnotic Susceptibility Scale score was a significant predictor of hypnotic analgesia, $t(47) = 2.127$, $p < .05$, unstandardized beta = 9.606.

Despite the significant result above, the outcome of the frequentist analysis for Stanford Hypnotic Susceptibility Scale score was not supported by a Bayesian multiple regression analysis. An uninformed uniform prior $[P(M)]$ of 0.125 was set for each of the possible models and for none of the models was $BF_{10} > 3$. For Stanford Hypnotic Susceptibility Scale score $BF_{10} = 1.489$, which is insensitive. In contrast, for four of the models there was moderate evidence for the null hypothesis ($BF_{01} > 3 < 6$). All of these models included the Hayling Suppression Errors (Scaled) and indeed included the model with just that predictor where $BF_{01} = 3.483$. The strongest evidence for the null was for the regression model with Stroop Incongruent + Hayling Suppression Error Score ($BF_{01} = 5.522$).

The above results indicate that in contrast to placebo analgesia, hypnotic analgesia is not predicted by Hayling Suppression Errors (Scaled). There was also some evidence that

hypnotic suggestibility predicted hypnotic analgesia in the frequentist analysis of the data ($p < .05$), but this was not supported by the Bayesian analysis of the data.

Placebo analgesia for pain tolerance

The Durbin-Watson checks for correlations between residuals was between 1 and 3 as required. A residuals plot and standardised residuals (Q-Q) plot revealed that the assumptions of homoscedasticity, normality and linearity were not violated. Tolerance (all $> 0.8 < 1$) and VIF ($> 1 < 1.3$) values were also within acceptable ranges. The model was significant where $F(4, 43) = 2.669$, $p = 0.045$, $R^2 = 0.199$. The adjusted R^2 revealed that the predictor variables predict 12.4% of the variance. Whilst the overall model was significant, only the Hayling Suppression Scaled Error score was a significant predictor of placebo analgesia, $t(47) = 3.126$, $p = .003$, unstandardized beta = -25.356 where the regression equation is: Placebo analgesia = $154.963 - (25.356 * \text{Hayling Suppression Error (Scaled)})$.

Despite the significant result above, this outcome of the frequentist analysis was not supported by a Bayesian multiple regression analysis. An uninformed uniform prior $[P(M)]$ of 0.125 was set for each of the possible models and for none of the models was $BF_{10} > 3$. For the model that included only Hayling Suppression Errors (Scaled) $BF_{10} = 0.999$, which is anecdotal. Evidence for the null hypothesis ($BF_{01} > 3 < 9$) was obtained for eight of the models, six of which included Stanford Hypnotic Susceptibility Scale score and five of which included Matrix Reasoning. The models including just the Stanford Hypnotic Susceptibility Scale score or Matrix Reasoning also had $BF_{01} > 3 < 4$.

The above analysis therefore provides some weak evidence in favour of the notion that Hayling Suppression Errors (Scaled) predicts the magnitude of the effect of placebo analgesia on pain tolerance but this was not supported by Bayes Factors. Moderate evidence

was also provided for no relationship between placebo tolerance and hypnotic suggestibility or matrix reasoning.

Hypnotic analgesia for pain tolerance

The Durbin-Watson checks for correlations between residuals was between 1 and 3 as required. A residuals plot and standardised residuals (Q-Q) plot revealed that the assumptions of homoscedasticity, normality and linearity were not violated. Tolerance (all $>0.8 < 1$) and VIF ($> 1 < 1.3$) values were also within acceptable ranges. The model was not significant where $F(4, 43) = 0.623$, $p = 0.623$, $R^2 = 0.055$. The adjusted R^2 revealed that the predictor variables predicted 3.3% of the variance. Furthermore, none of the individual predictors were significant predictors of hypnotic analgesia for tolerance ($ps > .2$).

The outcome of the frequentist analysis was supported by a Bayesian multiple regression analysis. An uninformed uniform prior $[P(M)]$ of 0.125 was set for each of the possible models and for none of the models was $BF_{10} > 0.5$. Evidence for the null hypothesis ($BF_{01} > 3$) was obtained for thirteen of the fifteen models. Furthermore, for two of the models, strong evidence for the null was provided ($BF_{01} > 10$). Specifically, for the model Stanford Hypnotic Susceptibility Scale score + Stroop Incongruent + Hayling Suppression Errors (Scaled) + Matrix Reasoning $BF_{01} = 13.682$, and for the model Stroop Incongruent + Hayling Suppression Errors (Scaled) + Matrix Reasoning, $BF_{01} = 12.425$. For Stanford Hypnotic Susceptibility Scale score, the predictor with the closest p-value to statistical significance, BF_{01} was inconclusive (2.540), but favoured the null.

The above analysis therefore provided strong evidence for no relationship between the chosen measures of executive function and the effect of hypnotic analgesia on pain tolerance. Again, however, the fact that many participants maxed out their submersion times is possibly responsible for this null relationship.

Further analyses

As noted in the introduction, our study was also aimed at testing whether hypnotic suggestibility is related to executive functions and IQ. We therefore ran further multiple regression analyses with the executive function tests as the predictors and hypnotic suggestibility as the dependent variable. The Durbin-Watson checks for correlations between residuals was between 1 and 3 as required. A residuals plot and standardised residuals (Q-Q) plot revealed that the assumptions of homoscedasticity, normality and linearity were not violated. Tolerance (all $>0.8<1$) and VIF ($>1<1.019$) values were also within acceptable ranges. The model was not significant where $F(3, 44) = 1.862$, $p = 0.150$, $R^2 = 0.113$. The adjusted R^2 revealed that the predictor variables predicted 5.2% of the variance. However, one of the individual predictors (Hayling Suppression Errors (Scaled)) was a significant predictor of hypnotic suggestibility.

The outcome of the frequentist analysis was, in the most part, supported by a Bayesian multiple regression analysis. An uninformed uniform prior $[P(M)]$ of 0.125 was set for each of the possible models and for none of the models was $BF_{10} > 3$. However, Hayling Suppression Errors (Scaled) yielded a $BF_{10} = 2.467$, which whilst anecdotal, favours the alternative hypothesis providing weak support for the frequentist analysis of the same data. Moderate evidence for the null hypothesis ($BF_{01} > 3 < 10$) was obtained for three of the seven models (Stroop Incongruent, Matrix Reasoning, and Stroop Incongruent + Matrix Reasoning). For one of the models (Stroop Incongruent + Hayling Suppression Errors (Scaled) + Matrix Reasoning, $BF_{01} = 2.368$ which is anecdotal but favours the null.

This analysis provided weak evidence for a relationship between hypnotic suggestibility and Hayling task performance and moderate evidence for the null hypothesis

for the relationship Matrix Reasoning and hypnotic suggestibility, and Stroop task performance and hypnotic suggestibility.

Discussion

The aim of the present research was to explore executive control functions that underpin pain perception following suggestions for hypnotic and placebo analgesia. In a fully within-subjects design participants completed the Cold Pressor Task (CPT) under three counterbalanced conditions: 1) Placebo analgesia; 2) Hypnotic analgesia; 3) a control condition. They also completed three cognitive tasks: 1) the Hayling Sentence Completion Task; 2) the Stroop task and; 3) a matrix reasoning task.

Analysis first established that the suggestions for both forms of analgesia during the CPT were successful. The placebo analgesia effects sizes were comparable to those observed in previous studies where $r_B = \sim 0.4 - \sim 0.7$ (75-78). Notably, the effect of hypnotic analgesia was larger (r_B 's = 0.86 and 0.96) than that of placebo analgesia in the present study (see also 79), indicating superior pain perception following hypnotic analgesia. However, it was not our intention to directly compare the magnitude of hypnotic and placebo analgesia given the placebo effect itself varies depending on its mode of delivery (e.g., 80). The effect sizes of both analgesic effects were larger than those using different manipulations to increase pain threshold, such as an attention training technique (81), and the normalising effects of methylphenidate on ADHD participants on the CPT (82). Additionally, the CBT-based acceptance approaches to pain control during the CPT have been shown to be much less effective (83) or not affective at all (84) on pain threshold and tolerance. Therefore, these effects are indicative of the potent effects that suggestion can have on pain perception.

Multiple regression analyses showed that HSCT performance predicted the magnitude of placebo analgesia for pain threshold but not pain tolerance and that neither the Stroop task nor matrix reasoning scores predicted CPT performance, where evidence for the null is provided by Bayes Factors. Furthermore, the results show that whilst hypnotic and placebo analgesic effects did not correlate for pain threshold, they did for pain tolerance. Finally, consistent with the literature, some evidence is provided that hypnotic suggestibility correlated with hypnotic analgesia and HSCT performance.

Given that inhibition is likely a heterogeneous mechanism (21-23) we selected two inhibition tasks thought to have distinct neural mechanisms and for which there is evidence of their assessing different forms of inhibition. The Stroop task is thought to measure attention (or cognitive) inhibition (33), and has been shown to have a potentially unique relationship to pain perception (15; 17). The Hayling task has been used as a measure of response inhibition (30-31) and has previously been investigated in terms of its relationship to chronic pain (63-64). Of the inhibition tests we employed, only the HSCT significantly predicted the pain experience; specifically the onset of pain (and somewhat for pain tolerance) in the placebo condition. The poorer the performance on the HSCT, the smaller the placebo analgesia effect. This outcome supports the notion that inhibition plays a role in the perception of pain (15-17; 19; 85) and supports the importance of PFC functions to placebo effects (54). Pain reduction following placebo analgesia is related to a person's ability to inhibit the correct, automatically derived word in the sentence completion task.

It is important to reiterate that we did not employ the selected inhibition tasks because of their neural substrates but based on evidence of their independence. Nevertheless, given that the HSCT is associated with right PFC inhibitory mechanisms (34; 37; 86) it is worth noting that whilst there is some evidence that pain processing has a right PFC bias (87-89); the evidence much more strongly implicates bilateral PFC involvement in pain processing

(88). Equally, whilst there is evidence that placebo analgesia has a right sided PFC bias (90-92) the weight of the evidence favours bilateral PFC involvement (51; 93). It is therefore unlikely that it is the right PFC-mediated nature of the HSCT that is the reason for its predictive utility in the present context. It is therefore likely that its role as a measure of response inhibition is more important than its hemispheric underpinning.

The HSCT involves generating words to complete a sentence. Sometimes ‘that’ word is required to fit with the sentence (Part 1) and sometimes ‘that’ word is required to not be a logical fit to the preceding sentence (Part 2). Both parts likely involve inhibiting incorrect (Part 1) or contextually correct (Part 2) predicted responses with a stronger requirement for inhibition in the latter. The Stroop task can be considered a conflict task in which the irrelevant and relevant dimensions are often presented simultaneously or in close temporal proximity, and therefore for which there is no need for prediction, and the irrelevant dimension is to be ignored (23; 40). The Stroop task involves two visual input channels and attention must be focussed on just one of them (e.g., the colour) and the other channel must be inhibited, making it an attention inhibition task (33). Cipolotti et al. (2016; 34) stated that both the HSCT and the Stroop task involve suppressing a dominant response, but the Stroop task is likely a response inhibition task (40). Indeed Roelofs (33) has shown that the Stroop task is better understood as being an attention / cognitive inhibition task. The two tasks also differ in the involvement of other complex processes such as goal maintenance in the face of a visually presented distraction in the case of the Stroop task, and strategy utilisation in the Hayling test (e.g., successfully choosing a word that does not fit a sentence could be achieved by focussing on objects around the room). Ultimately, it is unclear why the HSCT predicts placebo analgesia whereas the Stroop task does not. This is especially true given that previous research has shown Stroop task performance to be related to pain perception (although the findings so far are mixed with evidence that more Stroop interference is associated with both

more (85) and less (15) pain – see also section below on limitations of the Stroop task employed here). However, most if not all of these tasks are underpinned by neural regions in the descending pain modulatory system (63) and are tapping functions shared by pain, emotion and executive functions (18). Further research is therefore needed to explore the relationship of other inhibition tasks to the analgesic effects of placebo and hypnosis interventions (and their varieties) and to better understand the predictive utility of the HSCT in pain perception. One potential avenue to be explored is that higher-level processing might overlap for language prediction and pain prediction; inhibition of predicted pain and inhibition of a predicted word might rely on the same mechanism.

The present results also showed that neither the Stroop task nor the HSCT predict hypnotic analgesia. As noted above, the relationship between hypnotic responses and the PFC is mixed and it could thus be that hypnotic analgesia operates over different mechanisms than the PFC-mediated placebo analgesia. It is an ongoing debate as to whether hypnotic and placebo responses are related (e.g., 94). Despite the finding that HSCT did not predict hypnotic analgesia, we did observe evidence for a relationship between the magnitude of placebo and hypnotic analgesia on pain tolerance scores. Previous research has reported no such relationship between hypnotic and placebo responding (50; 94; although see also (50) who reported a relationship between placebo analgesia and non-hypnotic suggestibility). One explanation for the difference between the present and previous studies is the employment of an outcome variable that was the same for the placebo and hypnotic responses. For example, in Tasso et al. the placebo response was induced by delivering a suggestion that white noise being played on a compact disc would enhance physiological reactivity, whilst the hypnotic responses were suggestions delivered during a standard hypnotic screening procedure, none of which involve white noise nor suggestions of enhanced reactivity. Similarly, Parsons et al. (2021; 50) employed placebo analgesia for the placebo response but did not employ hypnotic

analgesia for the hypnotic response. In the present study the outcome for both the placebo and hypnotic suggestions was analgesia. It therefore remains possible that correlations between placebo and hypnotic responses are more likely when the placebo and hypnotic responses are in the same modality. Given this potential relationship between these two forms of analgesia, it is even more surprising that they were not predicted by the same form of inhibition. Of course, future research might reveal a measure of inhibition that does predict both forms of analgesia. Nevertheless, the present results indicate that hypnotic and placebo analgesia are related to different forms of inhibitory control.

In the present study we observed a correlation between hypnotic suggestibility and hypnotic analgesia (threshold), although this relationship was not supported by Bayes Factors. This relationship is a common finding in the literature (95-98), although some studies have not observed such a relationship (e.g., 72). The present study also provides weak evidence for a relationship between hypnotic suggestibility and HSCT performance. This relationship could be further explored in future research given the unclear relationship between hypnotic suggestibility and measures of executive function (60).

Limitations

The version of the Stroop task used here, employed to be consistent with Cipolotti et al. (2016; 34) is not ideal (see 40) for two reasons. First, it is a non-computerised, list version in which participants are asked to say aloud the colour of the font of as many Stroop items as possible in a given period of time. Recording of errors and responses is not as precise as a computerised version of the task. Furthermore, following Cipolotti et al. we used participants' performance on the incongruent condition only – it is this measure that was related to left PFC integrity in their patients. However, using just the incongruent condition without a control condition means that performance differences on the incongruent trials could also be driven by simpler response-speed differences (see (40) for a discussion of this).

The Golden and Freshwater (2002; 69) version of the Stroop task employed here does include a baseline condition, a separate sheet for which participants have to name the colour of the font of repeated-letter stimuli (i.e., XXXX), but this is again not ideal (i.e., a better baseline would be a neutral word e.g., the word *table* in red; see (40) for a discussion of this issue). Nevertheless, this baseline condition can be used to calculate a measure of interference (number of correct items in the incongruent list condition minus the number of correct items in the baseline list). To check for the predictive value of this measure of interference in the present study, incongruent only scores were substituted for this measure of interference (incongruent – xxxx sheet). This substitution did not meaningfully change the outcomes of the analyses. Future research could employ a computerised version of the Stroop task with a neutral word baseline for a more precise measure of performance.

Another potential limitation is that the cream used in the placebo condition differed from the other two conditions in potentially important ways. An odour, food colouring and another type of cream were added to the cream in the placebo condition to make it look, smell and feel different from the cream used in the other conditions. The aim was to ensure the placebo cream was believably different from the cream employed in the hypnosis and control conditions and followed the approach taken by Montgomery and Kirsch (1996; 71) in their study on placebo effects in the CPT. One study has shown no effect of different odours on cold pressor pain ratings (compared to water; 99) but no study has as far as we are aware considered the effect of thyme oil. Likewise the colour (100) and texture differences might have played a role in pain relief or even heightening pain.

Another potential limitation of the present study is that roughly half of our participants were male (22 of out 48 participants). Men tend to have higher pain thresholds than women in experimental research (67; 101-102; cf. 103) and so participant gender might be a modifying variable in our study. However, since our study had a fully within-subjects

design it is unlikely that gender would have modified the results with regards to the predictive relationship between the executive function tests and the forms of analgesia. Nevertheless, as with the study by Oosterman et al. (2010; 85) all participants in the present study were examined by female experimenters. Research has shown that male participants report reduced pain experience to female experimenters, whereas women are unaffected by the gender of the experimenter (104-105), although this effect is not always observed on pain experience (67). This means that pain threshold and tolerance values might have been influenced by the presence of a female experimenter, leading to increased immersion times in our male participants. Therefore, to increase immersion times past that which male participants would have had if the experimenter were male, they may have drawn on different inhibition mechanisms. This is speculative and the present study does not have enough male participants to provide a sufficiently powered statistical test of this possibility. A future study could explore this possibility by comparing and contrasting the predictive value of executive functions tests when male participants are tested by male vs. female experimenters.

Finally, the hypnosis condition necessarily involved a hypnotic induction which we estimate resulted in a duration difference of 3-5 minutes on average. This extra time permits the potential for building of greater rapport and trust between the participants and the researcher and could potentially account for the difference in magnitude of the analgesic effect in the two conditions. It is difficult to equate the length of control condition interventions (see also 72; 106 for non-equated intervention durations). The extra time to develop a rapport between the researchers and the participant could modify the mechanism producing the analgesic effect, which could be investigated in future research.

In conclusion, the present study shows the clear and potent effects of both placebo and hypnotic analgesia in pain perception, and especially for the latter for which many

participants did not report the onset of pain before the maximum submersion time allowed was reached. The most important contribution of the present study however is that it provides evidence for a relationship between placebo analgesia and a measure of inhibition as measured by the Hayling Sentence Completion task.

References

1. Abeare, C. A., Cohen, J. L., Axelrod, B. N., Leisen, J. C., Mosley-Williams, A., & Lumley, M. A. (2010). Pain, executive functioning, and affect in patients with rheumatoid arthritis. *The Clinical Journal of Pain*, 26(8), 683–689.
2. Apkarian, A. V., Bushnell, M. C., Treede, R. D., & Zubieta, J. K. (2005). Human brain mechanisms of pain perception and regulation in health and disease. *European Journal of Pain (London, England)*, 9(4), 463–484.
<https://doi.org/10.1016/j.ejpain.2004.11.001>
3. Ashar, Y. K., Chang, L. J., & Wager, T. D. (2017). Brain Mechanisms of the Placebo Effect: An Affective Appraisal Account. *Annual review of clinical psychology*, 13, 73–98.
<https://doi.org/10.1146/annurev-clinpsy-021815-093015>
4. Jefferson, T., Kelly, C. J., & Martina, M. (2021). Differential Rearrangement of Excitatory Inputs to the Medial Prefrontal Cortex in Chronic Pain Models. *Frontiers in neural circuits*, 15, 791043. <https://doi.org/10.3389/fncir.2021.791043>
5. Morogiello, J., Murray, N. G., Hunt, T. N., Harris, B. S., Szekely, B. J., & Shaver, G. W. (2018). The effect of acute pain on executive function. *Journal of Clinical and Translational Research*, 4(2), 113–121.
6. Connelly M, Keefe FJ, Affleck G, Lumley MA, Anderson T, Waters S. Effects of day-to-day affect regulation on the pain experience of patients with rheumatoid arthritis. *Pain*. 2007 Sep;131(1-2):162-70. doi: 10.1016/j.pain.2007.01.002
7. Eccleston C. (1995). Chronic pain and distraction: an experimental investigation into the role of sustained and shifting attention in the processing of chronic persistent pain. *Behaviour Research and Therapy*, 33(4), 391–405. [https://doi.org/10.1016/0005-7967\(94\)00057-q](https://doi.org/10.1016/0005-7967(94)00057-q)

8. Geers, A. L., Wellman, J. A., Fowler, S. L., Helfer, S. G., & France, C. R. (2010). Dispositional optimism predicts placebo analgesia. *The Journal of Pain*, 11(11), 1165–1171. <https://doi.org/10.1016/j.jpain.2010.02.014>
9. Mistiaen, P., van Osch, M., van Vliet, L., Howick, J., Bishop, F. L., Di Blasi, Z., et al. (2016). The effect of patient-practitioner communication on pain: a systematic review. *European Journal of Pain (London, England)*, 20(5), 675–688. <https://doi.org/10.1002/ejp.797>
10. Rischer, K. M., González-Roldán, A. M., Montoya, P., Gigl, S., Anton, F., & van der Meulen, M. (2020). Distraction from pain: The role of selective attention and pain catastrophizing. *European Journal of Pain (London, England)*, 24(10), 1880–1891. <https://doi.org/10.1002/ejp.1634>
11. Weisenberg, M., Raz, T., & Hener, T. (1998). The influence of film-induced mood on pain perception. *Pain*, 76(3), 365–375. [https://doi.org/10.1016/S0304-3959\(98\)00069-4](https://doi.org/10.1016/S0304-3959(98)00069-4)
12. Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: a latent variable analysis. *Cognitive Psychology*, 41(1), 49–100. <https://doi.org/10.1006/cogp.1999.0734>
13. Thompson, T., Terhune, D. B., Oram, C., Sharangparni, J., Rouf, R., Solmi, M., et al. (2019). The effectiveness of hypnosis for pain relief: A systematic review and meta-analysis of 85 controlled experimental trials. *Neuroscience and Biobehavioral Reviews*, 99, 298–310. <https://doi.org/10.1016/j.neubiorev.2019.02.013>
14. Halligan, P. W., & Oakley, D. A. (2014). Hypnosis and beyond: Exploring the broader domain of suggestion. *Psychology of Consciousness: Theory, Research, and Practice*, 1(2), 105–122. <https://doi.org/10.1037/cns0000019>

15. Bjekić, J., Živanović, M., Purić, D., Oosterman, J. M., & Filipović, S. R. (2018). Pain and executive functions: a unique relationship between Stroop task and experimentally induced pain. *Psychological Research*, 82(3), 580–589. <https://doi.org/10.1007/s00426-016-0838-2>
16. Karsdorp, P.A., Geenen, R, Vlaeyen, J.W.S. (2014). Response inhibition predicts painful task duration and performance in healthy individuals performing a cold pressor task in a motivational context. *European Journal of Pain*, 18(1):92–100.
doi:10.1002/j.1532-2149.2013.00348.x
17. Oosterman, J. M., Traxler, J., & Kunz, M. (2016). The influence of executive functioning on facial and subjective pain responses in older adults. *Behavioural Neurology*, 2016, Article 1984827. <https://doi.org/10.1155/2016/1984827>
18. Shackman, A. J., Salomons, T. V., Slagter, H. A., Fox, A. S., Winter, J. J., & Davidson, R. J. (2011). The integration of negative affect, pain and cognitive control in the cingulate cortex. *Nature reviews. Neuroscience*, 12(3), 154–167.
<https://doi.org/10.1038/nrn2994>
19. Zhou, S., Després, O., Pebayle, T., & Dufour, A. (2015). Age-Related Decline in Cognitive Pain Modulation Induced by Distraction: Evidence From Event-Related Potentials. *The Journal of Pain*, 16(9), 862–872.
<https://doi.org/10.1016/j.jpain.2015.05.012>
20. Habermann, M., Strube, A., & Büchel, C. (2025). How control modulates pain. *Trends in cognitive sciences*, 29(1), 60–72. <https://doi.org/10.1016/j.tics.2024.09.014>
21. Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. *Trends in Cognitive Sciences*, 8(4), 170–177.
<https://doi.org/10.1016/j.tics.2004.02.010>

22. Hodgson, T., Chamberlain, M., Parris, B.A., James, M., Gutowski, N., Husain, M., et al. (2007). The role of the ventrolateral frontal cortex in inhibitory oculomotor control. *Brain*, 130(Pt 6), 1525–1537. <https://doi.org/10.1093/brain/awm064>
23. Kok A. (1999). Varieties of inhibition: manifestations in cognition, event-related potentials and aging. *Acta Psychologica*, 101(2-3), 129–158. [https://doi.org/10.1016/s0001-6918\(99\)00003-7](https://doi.org/10.1016/s0001-6918(99)00003-7)
24. Tiego, J., Testa, R., Bellgrove, M. A., Pantelis, C., & Whittle, S. (2018). A hierarchical model of inhibitory control. *Frontiers in Psychology*, 9, 1339.
25. Diamond, A. (2013). Executive functions. *Annual Review of Psychology*, 64(1), 135-168.
26. Gärtner, A., & Strobel, A. (2021). Individual differences in inhibitory control: A latent variable analysis. *Journal of Cognition*, 4(1).
27. MacLeod, C. M. (2007). The concept of inhibition in cognition. In D. S. Gorfein & C. M. MacLeod (Eds.), *Inhibition in cognition*(pp. 3–23). American Psychological Association. <https://doi.org/10.1037/11587-001>
28. Nigg, J. T. (2000). On inhibition/disinhibition in developmental psychopathology: views from cognitive and personality psychology and a working inhibition taxonomy. *Psychological bulletin*, 126(2), 220.
29. Burgess, P. W., & Shallice, T. (1996). Response suppression, initiation and strategy use following frontal lobe lesions. *Neuropsychologia*, 34(4), 263–272. [https://doi.org/10.1016/0028-3932\(95\)00104-2](https://doi.org/10.1016/0028-3932(95)00104-2)
30. Van der Linden, M., Ceschi, G., Zermatten, A., Dunker, D., & Perroud, A. (2005). Investigation of response inhibition in obsessive-compulsive disorder using the Hayling task. *Journal of the International Neuropsychological Society : JINS*, 11(6), 776–783. <https://doi.org/10.1017/S1355617705050927>

31. Siquier, A., & Andrés, P. (2021). Cognitive and Behavioral Inhibition Deficits in Parkinson's Disease: The Hayling Test as a Reliable Marker. *Frontiers in aging neuroscience*, 12, 621603. <https://doi.org/10.3389/fnagi.2020.621603>
32. Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology*, 18(6), 643–662. <https://doi.org/10.1037/h0054651>
33. Roelofs, A. (2021). How attention controls naming: Lessons from Wundt 2.0. *Journal of Experimental Psychology: General*, 150(10), 1927.
34. Cipolotti, L., Spanò, B., Healy, C., Tudor-Sfetea, C., Chan, E., White, M., et al. (2016). Inhibition processes are dissociable and lateralized in human prefrontal cortex. *Neuropsychologia*, 93(Pt A), 1–12.
<https://doi.org/10.1016/j.neuropsychologia.2016.09.018>
35. Moore, M. J., Byrne, J., Gibson, E. C., Ford, L., & Robinson, G., A. (2024). Hayling and Stroop tests tap dissociable deficits and network-level neural correlates. *Brain Structure and Function*, 229(4), 879-896.
36. Parris, B. A., Wadsley, M. G., Hasshim, N., Benattayallah, A., Augustinova, M., & Ferrand, L. (2019). An fMRI study of response and semantic conflict in the Stroop task. *Frontiers in Psychology*, 10, 2426. <https://doi.org/10.3389/fpsyg.2019.02426>.
37. Robinson, G. A., Cipolotti, L., Walker, D. G., Biggs, V., Bozzali, M., & Shallice, T. (2015). Verbal suppression and strategy use: a role for the right lateral prefrontal cortex? *Brain*, 138(Pt 4), 1084–1096. <https://doi.org/10.1093/brain/awv003>
38. Hasshim, N., & Parris, B. A. (2014). Two-to-one color-response mapping and the presence of semantic conflict in the Stroop task. *Frontiers in Psychology*, 5, 1157.
<https://doi.org/10.3389/fpsyg.2014.01157>
39. Palfi, B., Parris, B. A., McLatchie, N., Zekecs, Z., Dienes, Z. (2021). Can unconscious intentions be more effective than conscious intentions? Test of the role of

metacognition in hypnotic response. *Cortex*, 135, 219-239.

<https://doi.org/10.1016/j.cortex.2020.11.006>

40. Parris, B. A., Hasshim, N., Wadsley, M., Augustinova, M., & Ferrand, L. (2022). The loci of Stroop effects: a critical review of methods and evidence for levels of processing contributing to color-word Stroop effects and the implications for the loci of attentional selection. *Psychological Research*, 86(4), 1029–1053. <https://doi.org/10.1007/s00426-021-01554-x>

41. Cardeña, E., & Spiegel, D. (1991). Suggestibility, absorption, and dissociation: An integrative model of hypnosis. In J. F. Schumaker (Ed.), *Human suggestibility: Advances in theory, research, and application* (pp. 93–107). Taylor & Frances/Routledge.

42. Parris B. A. (2016). The Prefrontal Cortex and Suggestion: Hypnosis vs. Placebo Effects. *Frontiers in Psychology*, 7, 415. <https://doi.org/10.3389/fpsyg.2016.00415>

43. Zubieta, J. K., Bueller, J. A., Jackson, L. R., Scott, D. J., Xu, Y., Koeppe, R. A., et al. (2005). Placebo effects mediated by endogenous opioid activity on mu-opioid receptors. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 25(34), 7754–7762. <https://doi.org/10.1523/JNEUROSCI.0439-05.2005>

44. Wickless, C., & Kirsch, I. (1989). Effects of verbal and experiential expectancy manipulations on hypnotic susceptibility. *Journal of Personality and Social Psychology*, 57(5), 762–768. <https://doi.org/10.1037/0022-3514.57.5.762>

45. Kirsch, I., & Lynn, S. J. (1999). Automaticity in clinical psychology. *American Psychologist*, 54(7), 504–515. <https://doi.org/10.1037/0003-066X.54.7.504>

46. Raz A. (2007). Hypnobo: perspectives on hypnosis and placebo. *The American Journal of Clinical Hypnosis*, 50(1), 29–36.

<https://doi.org/10.1080/00029157.2007.10401595>

47. Lifshitz, M., Sheiner, E. O., Olson, J. A., Thériault, R., & Raz, A. (2017). On Suggestibility and Placebo: A Follow-Up Study. *The American Journal of Clinical Hypnosis*, 59(4), 385–392. <https://doi.org/10.1080/00029157.2016.1225252>
48. Huber, M., Treutler, T., Martus, P., Kurzidim, A., Kreutz, R., Beige, J. (2013) Dialysis-Associated Hypertension Treated with Telmisartan – *DiaTel*: A Pilot, Placebo-Controlled, Cross-Over, Randomized Trial. *PLoS ONE* 8(11): e79322. <https://doi.org/10.1371/journal.pone.0079322>
49. Kihlstrom, J. F. (2008). The domain of hypnosis, revisited. In M. R. Nash & A. J. Barnier (Eds.), *The Oxford handbook of hypnosis: Theory, research, and practice* (pp. 21–52). Oxford University Press.
50. Parsons, R. D., Bergmann, S., Wiech, K., & Terhune, D. B. (2021). Direct Verbal Suggestibility as a Predictor of Placebo Hypoalgesia Responsiveness. *Psychosomatic Medicine*, 83(9), 1041–1049. <https://doi.org/10.1097/PSY.0000000000000977>
51. Krummenacher, P., Candia, V., Folkers, G., Schedlowski, M., & Schönbachler, G. (2010). Prefrontal cortex modulates placebo analgesia. *Pain*, 148(3), 368–374. <https://doi.org/10.1016/j.pain.2009.09.033>
52. Coltheart, M., Cox, R., Sowman, P., Morgan, H., Barnier, A., Langdon, R., et al. (2018). Belief, delusion, hypnosis, and the right dorsolateral prefrontal cortex: A transcranial magnetic stimulation study. *Cortex*, 101, 234–248.
53. Dienes, Z., & Hutton, S. (2013). Understanding hypnosis metacognitively: rTMS applied to left DLPFC increases hypnotic suggestibility. *Cortex*, 49(2), 386–392. <https://doi.org/10.1016/j.cortex.2012.07.009>
54. Benedetti, F. (2009). *Placebo effects: Understanding the mechanisms in health and disease*. Oxford University Press.

55. Amanzio, M., & Benedetti, F. (1999). Neuropharmacological dissection of placebo analgesia: expectation-activated opioid systems versus conditioning-activated specific subsystems. *The Journal of Neuroscience*, 19(1), 484–494.
<https://doi.org/10.1523/JNEUROSCI.19-01-00484.1999>
56. Eippert, F., Bingel, U., Schoell, E. D., Yacubian, J., Klinger, R., Lorenz, J., et al. (2009). Activation of the opioidergic descending pain control system underlies placebo analgesia. *Neuron*, 63(4), 533–543. <https://doi.org/10.1016/j.neuron.2009.07.014>
57. Stein, D. J., Ahokas, A., Albarran, C., Olivier, V., & Allgulander, C. (2012). Agomelatine prevents relapse in generalized anxiety disorder: a 6-month randomized, double-blind, placebo-controlled discontinuation study. *The Journal of Clinical Psychiatry*, 73(7), 1002–1008. <https://doi.org/10.4088/JCP.11m07493>
58. Wager, T. D., Rilling, J. K., Smith, E. E., Sokolik, A., Casey, K. L., Davidson, R. J., et al. (2004). Placebo-induced changes in fMRI in the anticipation and experience of pain. *Science (New York, N.Y.)*, 303(5661), 1162–1167.
<https://doi.org/10.1126/science.1093065>
59. Landry, M., Lifshitz, M., & Raz, A. (2017). Brain correlates of hypnosis: A systematic review and meta-analytic exploration. *Neuroscience and Biobehavioral Reviews*, 81(Pt A), 75–98. <https://doi.org/10.1016/j.neubiorev.2017.02.020>
60. Parris, B. A. (2017). The role of frontal executive functions in hypnosis and hypnotic suggestibility. *Psychology of Consciousness: Theory, Research, and Practice*, 4(2), 211–229. <https://doi.org/10.1037/cns0000106>
61. von Baeyer, C. L., Piira, T., Chambers, C. T., Trapanotto, M., & Zeltzer, L. K. (2005). Guidelines for the cold pressor task as an experimental pain stimulus for use with children. *The Journal of Pain*, 6(4), 218–227. <https://doi.org/10.1016/j.jpain.2005.01.349>

62. Duncan J. (2005). Frontal lobe function and general intelligence: why it matters. *Cortex*, 41(2), 215–217. [https://doi.org/10.1016/s0010-9452\(08\)70896-](https://doi.org/10.1016/s0010-9452(08)70896-)
63. Foley, P., Kong, Y., Dirvanskiene, R., Valdes-Hernandez, M., Bastiani, M., Murnane, J., et al. (2022). Coupling cognitive and brainstem dysfunction in multiple sclerosis-related chronic neuropathic limb pain. *Brain communications*, 4(3), fcac124. <https://doi.org/10.1093/braincomms/fcac124>
64. Mendonça, B. T. V., Machado, V., Silva, G. G., & Dias, N. M. (2024). Executive functions and functioning in women with fibromyalgia. Funções executivas e funcionalidade em mulheres com fibromialgia. *Arquivos de neuro-psiquiatria*, 82(9), 1–9. <https://doi.org/10.1055/s-0044-1790577>
65. Geers, A. L., Fowler, S. L., Wellman, J. A., Helfer, S. G., Close, S., & France, C. R. (2015). Prior experience with a pain stimulus as a predictor of placebo analgesia. *Journal of Behavioral Medicine*, 38(1), 136–142. <https://doi.org/10.1007/s10865-014-9586-1>
66. Washington, L. L., Gibson, S. J., & Helme, R. D. (2000). Age-related differences in the endogenous analgesic response to repeated cold water immersion in human volunteers. *Pain*, 89(1), 89–96. [https://doi.org/10.1016/S0304-3959\(00\)00352-3](https://doi.org/10.1016/S0304-3959(00)00352-3)
67. Mitchell, L. A., MacDonald, R. A. R., & Brodie, E. E. (2004). Temperature and the Cold Pressor Test. *The Journal of Pain*, 5(4), 233–238. <https://doi.org/10.1016/j.jpain.2004.03.004>
68. Finlay, K. A., & Anil, K. (2016). Passing the time when in pain: Investigating the role of musical valence. *Psychomusicology: Music, Mind, and Brain*, 26(1), 56–66. <https://doi.org/10.1037/pmu0000119>
69. Golden, C. J., and Freshwater, S. M. (2002). *The Stroop Color and Word Test: A Manual for Clinical and Experimental Uses*. Chicago, IL: Stoelting.

70. Weitzenhoffer, A.M. & Hilgard, E.R. (1962). Stanford Hypnotic Susceptibility Scale, Form C. Palo Alto, CA: Consulting Psychologists Press.
71. Montgomery, G., & Kirsch, I. (1996). Mechanisms of placebo pain reduction: An empirical investigation. *Psychological Science*, 7(3), 174-176. <https://doi.org/10.1111/j.1467-9280.1996.tb00352.x>
72. Casiglia, E., Schiavon, L., Tikhonoff, V., Haxhi Nasto, H., Azzi, M., Rempelou, P., et al. (2007). Hypnosis prevents the cardiovascular response to cold pressor test. *The American Journal of Clinical Hypnosis*, 49(4), 255–266. <https://doi.org/10.1080/00029157.2007.10524503>
73. Jeffreys, H. (1961) Theory of Probability. 3rd Edition, Clarendon Press, Oxford.
74. Lee, M. D., & Wagenmakers, E.-J. (2013). *Bayesian cognitive modeling: A practical course*. Cambridge University Press. <https://doi.org/10.1017/CBO9781139087759>
75. Blythe, J. S., Thomaidou, M. A., Peerdeman, K. J., van Laarhoven, A. I. M., van Schothorst, M. M. E., Veldhuijzen, D. S., et al. (2023). Placebo effects on cutaneous pain and itch: a systematic review and meta-analysis of experimental results and methodology. *Pain*, 164(6), 1181–1199. <https://doi.org/10.1097/j.pain.0000000000002820>
76. Camerone, E. M., Battista, S., Benedetti, F., Carlino, E., Sansone, L. G., Buzzatti, L., et al. (2022). The Temporal Modulation of Nocebo Hyperalgesia in a Model of Sustained Pain. *Frontiers in Psychiatry*, 13, 807138. <https://doi.org/10.3389/fpsyt.2022.807138>
77. Camerone, E. M., Wiech, K., Benedetti, F., Carlino, E., Job, M., Scafoglieri, A., et al. (2021). 'External timing' of placebo analgesia in an experimental model of sustained pain. *European Journal of Pain (London, England)*, 25(6), 1303–1315. <https://doi.org/10.1002/ejp.1752>

78. Vase, L., Petersen, G. L., Riley, J. L., 3rd, & Price, D. D. (2009). Factors contributing to large analgesic effects in placebo mechanism studies conducted between 2002 and 2007. *Pain*, 145(1-2), 36–44. <https://doi.org/10.1016/j.pain.2009.04.008>
79. Milling, L. S., Kirsch, I., Allen, G. J., & Reutenauer, E. L. (2005). The effects of hypnotic and nonhypnotic imaginative suggestion on pain. *Annals of Behavioral Medicine*, 29(2), 116–127. https://doi.org/10.1207/s15324796abm2902_6
80. Vase, L., Riley, J. L., 3rd, & Price, D. D. (2002). A comparison of placebo effects in clinical analgesic trials versus studies of placebo analgesia. *Pain*, 99(3), 443–452. [https://doi.org/10.1016/S0304-3959\(02\)00205-1](https://doi.org/10.1016/S0304-3959(02)00205-1)
81. Sharpe, L., Perry, N. K., Rogers, P., Dear, B. F., Nicholas, M. K., & Refshauge, K. (2010). A comparison of the effect of attention training and relaxation on responses to pain. *Pain*, 150(3), 469–476. <https://doi.org/10.1016/j.pain.2010.05.027>
82. Treister, R., Eisenberg, E., Demeter, N., & Pud, D. (2015). Alterations in pain response are partially reversed by methylphenidate (Ritalin) in adults with attention deficit hyperactivity disorder (ADHD). *Pain Practice*, 15(1), 4–11. <https://doi.org/10.1111/papr.12129>
83. Hayes, S. C., Levin, M. E., Plumb-Villardaga, J., Villatte, J. L., & Pistorello, J. (2013). Acceptance and commitment therapy and contextual behavioral science: examining the progress of a distinctive model of behavioral and cognitive therapy. *Behavior Therapy*, 44(2), 180–198. <https://doi.org/10.1016/j.beth.2009.08.002>
84. Keogh, E., Bond, F. W., Hanmer, R., & Tilston, J. (2005). Comparing acceptance- and control-based coping instructions on the cold-pressor pain experiences of healthy men and women. *European Journal of Pain*, 9(5), 591–598. <https://doi.org/10.1016/j.ejpain.2004.12.005>

85. Oosterman, J. M., Dijkerman, H. C., Kessels, R. P., & Scherder, E. J. (2010). A unique association between cognitive inhibition and pain sensitivity in healthy participants. *European Journal of Pain (London, England)*, 14(10), 1046–1050. <https://doi.org/10.1016/j.ejpain.2010.04.004>
86. Cipolotti, L, Healy, C, Chan, E, MacPherson, SE, White, M, Woollett, K, et al. (2015). The effect of age on cognitive performance of frontal patients. *Neuropsychologia*, 75, 233-241. <https://doi.org/10.1016/j.neuropsychologia.2015.06.011>
87. Graff-Guerrero, A., González-Olvera, J., Fresán, A., Gómez-Martín, D., Méndez-Núñez, J. C., & Pellicer, F. (2005). Repetitive transcranial magnetic stimulation of dorsolateral prefrontal cortex increases tolerance to human experimental pain. *Cognitive Brain Research*, 25(1), 153–160.
88. Ong, W. Y., Stohler, C. S., & Herr, D. R. (2019). Role of the Prefrontal Cortex in Pain Processing. *Molecular Neurobiology*, 56(2), 1137–1166. <https://doi.org/10.1007/s12035-018-1130-9>
89. Wiech, K., Ploner, M., & Tracey, I. (2008). Neurocognitive aspects of pain perception. *Trends in Cognitive Sciences*, 12(8), 306–313. <https://doi.org/10.1016/j.tics.2008.05.005>
90. Egorova, N., Yu, R., Kaur, N., Vangel, M., Gollub, R. L., Dougherty, D. D., et al. (2015). Neuromodulation of conditioned placebo/nocebo in heat pain: anodal vs cathodal transcranial direct current stimulation to the right dorsolateral prefrontal cortex. *Pain*, 156(7), 1342–1347. <https://doi.org/10.1097/j.pain.0000000000000163>
91. Lieberman, M. D., Jarcho, J. M., Berman, S., Naliboff, B. D., Suyenobu, B. Y., Mandelkern, M., et al. (2004). The neural correlates of placebo effects: a disruption account. *NeuroImage*, 22(1), 447–455. <https://doi.org/10.1016/j.neuroimage.2004.01.037>

92. Pariente, J., White, P., Frackowiak, R. S., & Lewith, G. (2005). Expectancy and belief modulate the neuronal substrates of pain treated by acupuncture. *NeuroImage*, 25(4), 1161–1167. <https://doi.org/10.1016/j.neuroimage.2005.01.016>
93. Wager, T. D., & Atlas, L. Y. (2015). The neuroscience of placebo effects: connecting context, learning and health. *Nature Reviews Neuroscience*, 16(7), 403–418. <https://doi.org/10.1038/nrn3976>
94. Tasso, A. F., Pérez, N. A., Moore, M., Griffio, R., & Nash, M. R. (2020). HYPNOTIC RESPONSIVENESS AND NONHYPNOTIC SUGGESTIBILITY: *DISPARATE, SIMILAR, OR THE SAME?* *The International Journal of Clinical and Experimental Hypnosis*, 68(1), 38–67. <https://doi.org/10.1080/00207144.2020.1685330>
95. Hilgard, E. R., MacDonald, H., Marshall, G., & Morgan, A. H. (1974). Anticipation of pain and of pain control under hypnosis: Heart rate and blood pressure responses in the cold pressor test. *Journal of Abnormal Psychology*, 83(5), 561–568. <https://doi.org/10.1037/h0036940>
96. Maurer, C., Santangelo, M., & Claiborn, C. D. (1993). The effects of direct versus indirect hypnotic suggestion on pain in a cold pressor task. *The International Journal of Clinical and Experimental Hypnosis*, 41(4), 305–316. <https://doi.org/10.1080/00207149308414560>
97. Sharav, Y., & Tal, M. (2004). Focused analgesia and generalized relaxation produce differential hypnotic analgesia in response to ascending stimulus intensity. *International Journal of Psychophysiology*, 52(2), 187–196. <https://doi.org/10.1016/j.ijpsycho.2003.10.001>
98. Tenenbaum, S. J., Kurtz, R. M., & Bienias, J. L. (1990). Hypnotic susceptibility and experimental pain reduction. *American Journal of Clinical Hypnosis*, 33(1), 40–49. <https://doi.org/10.1080/00029157.1990.10402899>

99. Kiecolt-Glaser, J. K., Graham, J. E., Malarkey, W. B., Porter, K., Lemeshow, S., & Glaser, R. (2008). Olfactory influences on mood and autonomic, endocrine, and immune function. *Psychoneuroendocrinology*, 33(3), 328–339.
<https://doi.org/10.1016/j.psyneuen.2007.11.015>
100. De Craen A J M, Roos P J, de Vries A L, Kleijnen J. (1996). Effect of colour of drugs: systematic review of perceived effect of drugs and of their effectiveness. *British Medical Journal*, 313 :1624 doi:10.1136/bmj.313.7072.1624
101. Fillingim, R. B., & Maixner, W. (1995). Gender differences in the responses to noxious stimuli. *Pain Forum*, 4, 209-221.
102. Riley, J. L., 3rd, Robinson, M. E., Wise, E. A., Myers, C. D., & Fillingim, R. B. (1998). Sex differences in the perception of noxious experimental stimuli: a meta-analysis. *Pain*, 74(2-3), 181–187. [https://doi.org/10.1016/s0304-3959\(97\)00199-1](https://doi.org/10.1016/s0304-3959(97)00199-1)
103. Kamody, R. C., Woltja, E., Bugeja, A. D., Jackson, S., & Helfer, S. G. (2011). The Placebo Effect and the Relation Between Blood Pressure and Pain Sensitivity. *Psi Chi Journal of Undergraduate Research*, 16(4), 175-179.
104. Aslaksen, P. M., Myrbakk, I. N., Høifødt, R. S., & Flaten, M. A. (2007). The effect of experimenter gender on autonomic and subjective responses to pain stimuli. *Pain*, 129(3), 260–268. <https://doi.org/10.1016/j.pain.2006.10.011>
105. Gijsbers, K., & Nicholson, F. (2005). Experimental pain thresholds influenced by sex of experimenter. *Perceptual and motor skills*, 101(3), 803–807.
<https://doi.org/10.2466/pms.101.3.803-807>
106. Freeman, R., Barabasz, A., Barabasz, M., & Warner, D. (2000). Hypnosis and distraction differ in their effects on cold pressor pain. *American Journal of Clinical Hypnosis*, 43(2), 137–148. <https://doi.org/10.1080/00029157.2000.10404266>

Figure Captions

Figure 1. Box plots showing the distribution of pain threshold and pain tolerance times (in seconds) in the Hypnotic analgesia (A), Placebo analgesia (B) and Control (C) conditions.

Figure 1.



