

Boosting Hypnotic Response for Treating Anxiety: The Effect of Combining rTMS on the
left DLPFC with Hypnotherapy on Anxiety.

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Abstract

33.7% of the population will experience an anxiety disorder in their lifetime, according to large population surveys (Bandelow & Michaelis, 2015). Anxiety disorders are associated with immense health care costs and have a considerable adverse effect on daily life (Shin & Liberzon, 2010). Accepted anxiety treatments, such as psychotherapy and medication, can be time consuming and expensive, and often people do not respond to them. Hypnosis, which has been used to treat anxiety symptoms for centuries, is regularly overlooked despite having been shown to help reduce anxiety symptoms either as a stand-alone therapy or in conjunction with other therapies (Daitch, 2014; Hammond, 2010; Holdevici & Crăciun, 2013; Lotfifar, Karami, Daramadi, & Fathi, 2013).

Dienes and Hutton (2013), conducted a study into understanding hypnosis meta-cognitively using cold control theory of hypnosis. They hypothesised that disrupting the left DLPFC would increase hypnotic response, and a 6% increase in hypnotic susceptibility provided evidence to support their theory. The current research builds on these findings to consider if rTMS can increase the effectiveness of hypnotherapy for anxiety. The main result substantially supported the hypothesis, $P = .000$, $\eta^2 = .56$.

With positive results in decreasing anxiety, the lack of side-effects, ease of application and the possibility of reduced costs, this innovative intervention provides a plausible alternative to the accepted methods of treating anxiety.

Keywords: anxiety; rTMS; hypnosis; hypno-susceptibility; cold control theory.

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“Research is what I’m doing when I don’t know what I’m doing”

Wernher von Braun

Boosting Hypnotic Response for Treatment of Anxiety: The Effect of Combining rTMS on the left DLPFC with Hypnotherapy on Anxiety.

“Anxiety is a highly disabling pathological condition, involving cognitive, emotional, and physiological disturbances” (Gutiérrez-García & Contreras, 2013).

In 2013, there were 8.2 million cases of anxiety disorder in the UK, (Fineberg et al., 2013) and the National Wellbeing survey of people aged 16 and over found the average percentage of all respondents feeling anxious or depressed was 19%. This percentage was higher for females (21.5%) than for males (14.8%) (Evans, Macrory, & Randall, 2015). Anxiety disorders are associated with immense cost to the NHS and the economy; in 2013, these costs were estimated to be £9.8 billion (Fineberg et al., 2013).

Anxiety, it could be argued, is a normal emotion or negative mood state. It occurs when there is a potentially dangerous or uncertain event about to happen, or that is perceived to be about to happen. In 2014, General Anxiety Disorder (GAD) was one of the most common types of anxiety diagnosed in the UK population, at 5.9% (Edwards et al., 2016). People with GAD can have intense, disproportionate and constant fears about daily life. These emotions produce many physiological symptoms, such as sleep disturbances, muscle tension and difficulty concentrating, all which have a considerable adverse effect on their daily lives (Fineberg et al., 2013; Shin & Liberzon, 2010).

The current treatments for anxiety disorders take the forms of medication, psychological treatments such as ‘talking therapies’ (which are types of psychotherapy, such as psychodynamic and Cognitive Behavioural Therapies (NICE, 2014)) and additional, alternative health approaches such as relaxation, meditation and exercise, all of which have been variously recommended to help alleviate the symptoms of anxiety. Although the above interventions are effective, a considerable amount of people find that these accepted treatments do not work for them (Vennwald, Diemer, & Zwanzger, 2013). The number of

psychotherapy sessions needed can range from five to twenty, and costs can be between £40 and over £100 (in private treatment) (NHS, 2015). These statistics and research show how widespread and debilitating this condition is in society, and because many people do not respond to the recognised treatments, an alternative, safe and cost effective intervention is needed to fill the gap.

Hypnosis has been used to treat anxiety symptoms for centuries, but is not usually offered as a treatment option by health care practitioners, as the National Health Service cites paucity of research. A systematic review of fourteen random controlled trials (RCTs) found that due to poor methodological quality, hypnosis was not recognised as being effective for the treatment of anxiety (Coelho, Canter, & Ernst, 2008). Therefore, quality RCT's are needed to demonstrate its efficacy. However, this could prove problematic, as the field of consciousness is still quite new, and methods to test it are still in their infancy. Nonetheless, there is mounting scientific evidence that suggests that hypnosis is a powerful top-down process that can aid in the clinical process of therapy (Lynn, Kirsch, Barabasz, Carden~a, & Patterson, 2000; Lynn & Kirsch, 2006; Oakley & Halligan, 2009; Spiegel, 2013).

Hypnosis has been shown to help reduce anxiety symptoms either as a stand-alone therapy, or in conjunction with other therapies such as CBT (Nishith, Barabasz, Barabasz, & Warner, 1999; Baker, Ainsworth, Torgerson, & Torgerson, 2009; Snow et al., 2012). According to the National Council for Hypnotherapy, people normally have around six sessions for help with anxiety (NCH, n.d.).

It is thought that several brain regions are involved with hypnosis. Rainville, Hofbauer, Bushnell, Duncan, & Price, (2002) indicated that the anterior cingulate cortex, thalamus (responsible for attention, cortical arousal and self-regulation) and the brainstem (involved with sleep /wakefulness and attention) are all implicated in hypnosis. According to Spiegel, (2013) the dorsal anterior cingulate cortex and DLPFC (which controls attention and

conflict resolution - executive function) are involved with the top-down adjustment of perception during hypnosis, and with moving in and out of different mental states.

According to the General Hypnotherapy Register (GHR) “Hypnosis is a state of mind...” and hypnotherapy is when “...a professional utilises the resultant state of mind to encourage beneficial change to occur...” (GHR, n.d.).

There are several theories of hypnosis, however this research focuses on the Dienes and Perner (2007) cold control theory. It in turn is based on Rosenthal's, (1986) Higher Order Thought (HOT) theory of consciousness, which involves three levels: a first order thought, which makes us aware of the world, for example, ‘the chair is next to me’). A second order thought, which makes us aware of having the first order thought; ‘I see that the chair is red’. A third order thought, which makes us introspectively aware; ‘I am aware that I’m seeing that the chair is red’. Therefore, we are only conscious of our mental state of mind, when we think we are in that state. HOTs only occur at level two and three. Cold control theory puts forward that hypnosis forms inaccurate or absent HOTs thus, a hypnotic response is one that is intending to execute the suggestions of motor or cognitive deed, but being deprived of the intention to do so (Dienes & Perner, 2007).

Lau and Passingham, (2006) and Rounis, Maniscalco, Rothwell, Passingham, and Lau, (2010) during their studies on vision, potentially identified the left dorsolateral prefrontal cortex (DLPFC) as a region involved in creating accurate HOTs, an ‘area of metacognition’ if you will. The DLPFC is involved with executive functions, an umbrella term that encompasses the higher-order cognitive processes, such as attention, planning inhibition, working memory, decision making, flexibility and problem solving. A top-down process, that incorporates all the above functions, is emotional regulation. This is the ability to effectively deal with and respond to an emotional experience (Hughes, 2013; Najdowski, Persicke, & Kung, 2014; Peña-Gómez, Vidal-Piñeiro, Clemente, Pascual-Leone, & Bartrés-

Faz, 2011). It was from this premise, that Dienes and Hutton, (2013), using cold control theory of hypnosis, conducted a study into understanding hypnosis metacognitively. As the left DLPFC is feasibly where accurate HOTs are created, low frequency repetitive transcranial magnetic stimulation (rTMS) was used to disrupt the left DLPFC, which they hypothesised should make it harder to create accurate HOTs, therefore, easier to experience and respond to hypnotic suggestions. The rTMS protocol used was 1Hz for 5 minutes at 90% of the participants resting motor threshold. They found evidence to support their theory, with a 6% increase in hypnotic susceptibility.

There have been many robust studies using TMS as a treatment for depression with positive results (Gaynes et al., 2014), however few attempts have been made to explore low frequency rTMS as a treatment for anxiety. Bystritsky et al., (2008) was the first such study in which fMRI was used to locate the ‘anxiety area’ during a gambling / decision making task and it was found that the right DLPFC was this area. Six sessions of 1Hz rTMS at 90% intensity were given, and this study showed a decrease in anxiety, but the study was a small open trial, which can lead to better results. Diefenbach et al., (2016) also used the right DLPFC based on the Bystritsky et al., (2008) study. This was a RCT which consisted of thirty sessions of 1Hz rTMS for 15 minutes at 90% intensity. It showed a decrease in anxiety, however, participants could use stable pharmacotherapy throughout the trial, which may have influenced the overall decrease in anxiety, and the intense treatment schedule is quite arduous and time consuming. The final study only had one participant and he suffered from substance abuse, co-morbid anxiety and depressive symptoms. Anxiety did decrease; however, the participant knew what the objective of the treatment was, which could have skewed the results (Hone-Blanchet, Mondino, & Fecteau, 2017).

These studies which have looked at using rTMS for anxiety, have in the most part had poor methodologies or have had a lengthy intervention, which isn’t conducive to adherence to

a treatment regime. There are no reported studies that have used the results from Dienes and Hutton's (2013) research (on increasing hypno-susceptibility using rTMS on the left DLPFC to combine with hypnotherapy) as a treatment for anxiety.

Current study

Hypnosis provokes a decrease in the prefrontal cortex function. This has been a long-standing conclusion in hypnosis research for quite a while (Brammer et al., 2012; Farvolden & Woody, 2004; Jamieson & Sheehan, 2004). This concept corroborates the findings by Dienes and Hutton, (2013) whose study found that inhibiting the left DLPFC through rTMS stimulation assisted the process of being hypnotised. The present study will use cold control theory of hypnosis as the foundation for an innovative treatment for anxiety, thus making several unique contributions to the literature and guiding the four main research questions that were examined in the present study. The purpose of this study was to explicate the effect of low frequency rTMS to the left DLPFC, in conjunction with hypnosis, to make hypnotherapy a more effective alternative treatment for anxiety, which is concise, has an ease of application, a lack of adverse side effects, and is cost-effective. Anxiety is an important area of research, as anxiety disorders are prevalent and both the mental and monetary costs attached to them are high.

For the purposes of this paper, the term hypnotherapy will be used to mean that the altered state of awareness (hypnosis) has been achieved by the participant, which is then followed by the hypnotherapist giving beneficial hypnotic suggestions.

The first aim of this study was exploratory in nature. This study, based on cold control theory, predicted that there would be a significant decrease in anxiety after the left DLPFC was stimulated in conjunction with hypnotherapy. This was viewed as exploratory because there is very little research examining both rTMS with hypnosis as a treatment

method at all, and specifically as a treatment for anxiety. A secondary assumption was tested, that the short-term (within session) effects would mirror the long-term effects.

The second aim of the study was to examine the relationship between the order of site stimulation (left DLPFC v vertex) and the decrease in GAD-7 scores (an anxiety questionnaire designed by Spitzer, Kroenke, Williams, & Löwe, (2006).) A significant positive predication was made that the order of site of stimulation would influence the decreasing GAD-7 scores, due to the possible carry-over effects from the stimulation of the left DLPFC.

The third aim of the study was to explore if the depth of hypnotic state (trance) would assist in decreasing anxiety. This was based on previous research (Dienes & Hutton, 2013) that disrupting the left DLPFC would increase hypnotic susceptibility, thus a deeper trance (hypnotic state) would be achieved. The hypothesis that a deeper hypnotic trance would enhance the responsiveness to hypnotic suggestions regarding decreasing anxiety was investigated.

The fourth aim was to explore a prediction of cold control theory that a person cannot do anything under hypnosis that they wouldn't normally do. The only difference is that under hypnosis, the act would feel involuntary (i.e. automatic. Thus, executive control without awareness.) Therefore, a hypnotic suggestion of moving a dial up and down during the left DLPFC stimulation session, would score highly on the automatic scale compared to the vertex session.

Method

Participants

11 participants were recruited from both the public and psychology students who attend the University of Sussex, by means of posters, the psychology-subject-pool and social media. The participants (8 females, 3 males) ranged in age from 20 to 52 years ($M = 26.9$ years, $SD = 5.4$ years). They were entered into a prize draw to win £25 in Amazon vouchers. Informed written consent was obtained from all participants.

Inclusion

Over 18 years old. Have scored 5 or above out of 21 on the GAD-7 anxiety test. (Based on Spitzer, Kroenke, Williams, & Löwe, 2006)). Able to provide informed consent. English as their first language.

Exclusion

Diagnosed with clinical anxiety. Current or previous psychiatric or neurological illness. Taking psychoactive medication. Metal implants e.g. cardiac pacemaker, hair pins. History of epilepsy or fits, migraine or any history of brain damage. Pregnancy. Tinnitus. Participants were given an rTMS pre-screening questionnaire (see Appendix B) taken from Keel, Smith, and Wassermann, (2001).

Ethical Issues

All participants were given an identification code unique to them, so that anonymity could be maintained at all times. All data was kept secure in accordance with the Data Protection Act and written informed consent was obtained (see Appendix D). All participants were given a participant information sheet (see Appendix C) explaining the study, what was required of them, any risks, the advantages and disadvantages of taking part, how their information would be used, stored and be kept confidential and that they could withdraw at any time. A debrief was given to each person at the end of the study and any questions were

answered. A list of organisations that could offer further information or help regarding anxiety were provided. Ethics approval was received from the University of Sussex Cross-Schools Research Ethics Committee Ref: ER/SB738/1 (see Appendix H).

Design

The experiment had one main within-subjects factor: site of stimulation (left Dorsolateral Prefrontal Cortex (DLPFC) vs Vertex). Both groups had hypnotherapy. The hypnotherapist was blind to which site was stimulated, to minimise experimenter effects. The study was conducted as a randomised, within-subject cross-over design, where each participant had both sites stimulated but on different days.

Materials and Apparatus

Participants filled in the Generalised Anxiety Disorder 7 (GAD-7) questionnaire, which was administered online and recreated by the author (see Appendix A). A response booklet was completed after undergoing the hypnotisability test, SWASH (Sussex Waterloo Hypnotisability Scale) a University of Sussex adapted version of the Waterloo-Stanford Group Scale of hypnotisability, Form C (see Appendix G).

Generalised Anxiety Disorder 7 (GAD-7) is a self-reported questionnaire for screening and measuring of anxiety which is scored out of a possible 21 points (Spitzer et al., 2006). It has seven questions, which measure the severity of general anxiety according to a specified answer, with allotted points ranging from 0-3. It asks, “In the last 2 weeks, how often have you been bothered by any of the following problems?” For example: “Feeling nervous, anxious or on edge?” Participants choose their response from: not at all, several days, more than half the days or nearly every day. Participants filled in the GAD-7 anxiety test online one week before their first session, one week after their first session and one week

after their second session. This questionnaire was selected to screen for general anxiety as it is an effective, brief and efficient self-administered screening tool (Swinson, 2006). Dear et al.'s, (2011) study found GAD-7 had an internal consistency of Cronbach's α coefficients 0.79 – 0.91 with 195 participants. However, in this study with 11 participants the GAD-7 had an internal consistency of Cronbach's α coefficients 0.13 at the first time point of completing GAD-7, 0.69 at the second time point and 0.73 for final time point.

After the second session, participants were screened for hypnotisability using SWASH which was chosen for its robust scale and test-re-test reliability. This consisted of a shortened induction and the delivery of 10 suggestions taken from the WSGC scale. The dream and age regression suggestions were excluded to avert participants having distressing memories or thoughts (Cardeña & Terhune, 2009) and the test was delivered individually rather than in a group. Participants filled in a response booklet with their objective ratings. Each suggestion scored 1 if the suggestion would have been observed or 0, if it would not. For example: “Would you estimate that an onlooker would have observed that hand lowered at least six inches (before the time you were told to let your hand down deliberately)? Circle one: A. My hand had lowered at least six inches by then. B. My hand had lowered less than six inches by then”. Participants were classed as highly hypnotisable if they scored 8 or above from a possible 10, medium hypnotisable participants scored between 3 and 7 and low hypnotisable participants scored 2 or below (see supplementary material for hypnosis scripts and response booklet and scoring procedures). Unlike the WSGC; C, the SWASH response booklet additionally asked for their subjective ratings for the 10 suggestions, for example: “On a scale from 0 to 5, how strongly did you feel your hand becoming heavy, where 0 means you felt your arm was no more heavy than normal and 5 means you felt your arm becoming as heavy as if you had a heavy object in your hand, pulling it down?” Circle one: 0 1 2 3 4 5. This was requested for their degree of hypnotic response.

A picture of a Dial (see Figure 1) was shown to the participants and informed that the Dial was to represent their level of anxiety during the experiment. They were told that 0 represented not being anxious at all to 10 representing the most anxious they could imagine. Participants were informed that during hypnosis, hypnotic suggestions would be given to allow the Dial to move up and down, which would produce an associated change in their anxiety level.

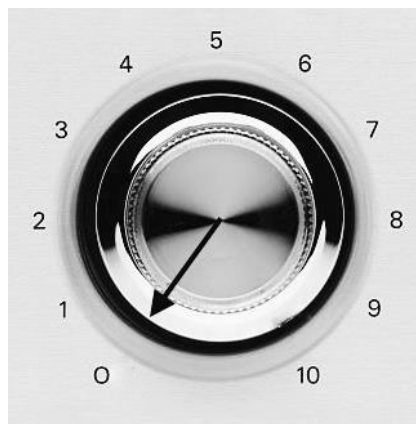


Figure 1. Picture of Dial used to represent anxiety level.

rTMS was applied to the vertex or left DLPFC. The vertex was the active stimulation control site, found at the intersection point of the tragus to tragus line and the nasion to inion line. The left DLPFC was located based on the F3 position of the International 10–20 system, (see Figure 2) using the modification described by Beam et al (2009) as it is a good alternative to an expensive MRI guided rTMS (Mir-Moghtadaei et al., 2015). This was used in conjunction with visor2TMST navigation software and a Magstim Rapid² magnetic stimulation unit with a figure-of-8-shaped coil. This type of coil provides a focused stimulation. These criteria were based on existing experiments that have used rTMS to stimulate these areas (e.g., Wagner, Rihs, Mosimann, Fisch, & Schlaepfer, 2006; Dienes & Hutton, 2013; Mir-Moghtadaei et al., 2015).

BA9 BA8 BA42 Location System		
Will Beam & Jeff Borckardt		
Web Interface Developed 6/7/2010		
(F3) Distance along circumference from midline (X):	(F3) Distance from vertex (Y):	(BA43) Distance from vertex through tragus (Z):
6.57 cm	9.35 cm Adjusted*: 9.70 cm	12.02 cm

BA9 BA8 BA43 Location System	
Will Beam & Jeff Borckardt	
Web Interface Developed 6/7/2010	
1. Tragus to Tragus (CM):	<input type="text" value="36"/>
2. Nasion to Inion (CM):	<input type="text" value="35"/>
3. Circumference (CM):	<input type="text" value="57"/>
	<input type="button" value="Calculate"/>

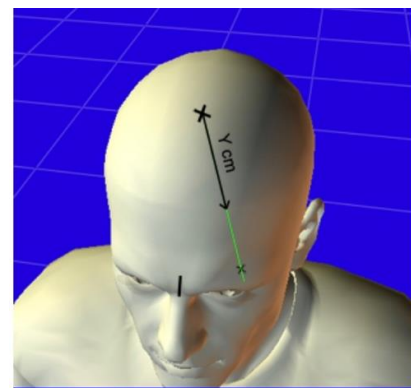
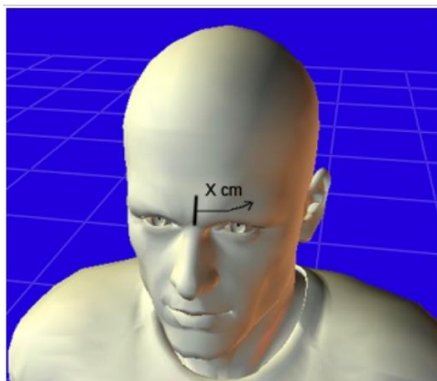


Figure 2. Screen shots of the F3 Locator programme. *Top Left)* The user enters the distances acquired from each person. *Top Right)* The programme produces two figures that are used to find F3. *Bottom Row)* Diagrams to show how to use the measurements to locate left DLPFC (F3). Adapted from Beam, W., Borckardt, J., Reeves, S.T., George, (2009).

To find the safe dose of rTMS for each participant, their resting motor threshold was established by producing a visible twitch in the left hand following a single pulse of stimulation at 1Hz. 85% of this intensity percentage was applied in the experiment (Herbsman et al., 2010).

Procedure

The experiment was adapted from Dienes & Hutton, (2013), which explored how applying rTMS to left DLPFC increases hypnotic suggestibility. Participants were randomly allocated (The TMS operator blind picked from a bag containing 12 pieces of paper, six with DLPFC and six with vertex written on them) to receive either rTMS to the left DLPFC at the first visit, ($N = 5$), followed by stimulation to the vertex (control site) or vice versa ($N = 6$). Participants were shown a picture of a Dial, with numbers around it. Participants were informed that the Dial was to represent their level of anxiety during the experiment. They were told that 0 represented not being anxious at all to 10 representing the most anxious they could imagine. Their anxiety level based on the Dial was requested at this point and noted.

Each participant received 5 minutes of low frequency (1Hz) rTMS, 300 pulses at a stimulation intensity of 85% of their motor threshold (Wassermann, 1998) to either the vertex or left DLPFC. The coil was held within 5mm of the site of stimulation by the TMS operator using visor2TMST navigation coil targeting software. The participant was asked to think about the Dial and their anxiety level based on the Dial was requested at this point and noted. The hypnotherapist was blind to the site being stimulated and so entered the room after the stimulation. In the 5-minute window of residual cortical disruption that followed, the hypnotic induction and deepeners were given (for the exact hypnosis script, see Appendix E). The participant was asked “on a scale of 0 to 10, 0 being no feeling of being in a trance, 10 being in the deepest trance possible, what number applies to you?” They were told, “from now on, when you hear the words “now you are in a deep trance”, you will re-enter into a deep trance. They were asked to think about the Dial and their anxiety level based on the Dial was requested at this point and noted. The wake-up procedure was given.

The hypnotherapist left the room, and the participant had another 5 minutes of low frequency (1Hz) rTMS. The hypnotherapist re-entered the room and asked the participant to

think about the Dial and give the number on the Dial that represented their anxiety level. In the 5-minute window of residual cortical disruption that followed, the participant was re-hypnotised by giving a few calming and relaxing suggestions and saying, "now you are in a deep relaxing hypnotic trance". Hypnotic calming, relaxing and ego-strengthening suggestions were given (exact hypnosis script see Appendix E). Their anxiety level based on the Dial was requested at this point and noted. A hypnotic suggestion was given for the Dial to be turned up as high as the participant would allow it to go, and the corresponding anxiety Dial ratings were recorded. The participant was asked, "on a scale of 0 to 10, 0 being not automatic at all (completely controlled by you), 10 being totally automatic (it happened by itself), how automatically did your anxiety change when you moved the pointer?" The hypnotic suggestion to move the Dial was adapted from Derbyshire, Whalley, and Oakley, (2009). The hypnotic suggestions were given to turn the Dial down as low as possible and Dial ratings again were recorded. The participant was asked, "on a scale of 0 to 10, 0 being not automatic at all (completely controlled by you), 10 being totally automatic (it happened by itself), how automatically did your anxiety change when you moved the pointer"? The wake-up protocol took place and their anxiety rating was taken for the last time based on the Dial.

After session one, there was a week's break and then participant filled in the GAD-7 questionnaire online, using their participant code for identification purposes. One week after this, the participant returned to have the opposite site stimulated, though they were not told of the site change-over. There then followed the two-week wash-out period (that is the period during the experiment where no intervention was given, to help with the potential issue of carry-over of the effects of the previous intervention - to the following session).

The second session followed the same format as first, excepting only the change of site of stimulation and that finding the participants' intensity percentage was not needed, as

this was already recorded. One week after the final session, they filled in the GAD-7 questionnaire online, using their participant code for identification purposes. After the second session, participants were screened for hypnotisability using SWASH.

Results

The results section will address the hypotheses based on the cold control theory of hypnosis (Dienes & Perner, 2007), that disrupting the left DLPFC with (1Hz) of rTMS, will increase hypno-susceptibility, due to a decrease in awareness of intention (Dienes & Hutton, 2013). The following results will address the secondary questions stemming from the main hypothesis: hypnotherapy for anxiety will be more effective long term when used in conjunction with low frequency rTMS on the left DLPFC than with a control site. Probability values referring to significance tests will be reported exactly.

To conduct this research, participants were randomly assigned to have either the vertex or left DLPFC to be stimulated first in conjunction with hypnotherapy. The vertex group had slightly more participants (6 v 5). The primary outcome measure for anxiety was the GAD-7 questionnaire. According to (Spitzer et al., 2006) participants were classed as having Severe anxiety if they scored 15 and above, Moderate anxiety 10 or above and Mild anxiety of 5 or below. Participants filled in the GAD-7 questionnaire 1 week before intervention ($M = 7.73$, $SD = 1.85$), 1 week after left DLPFC session ($M = 4.18$, $SD = 2.27$) and 1 week after vertex session ($M = 7.36$, $SD = 2.7$).

To test the above hypothesis, a one-way repeated measures ANOVA was conducted to compare scores on the GAD-7 questionnaire at the following time points: prior to any intervention; 1 week after left DLPFC stimulation and 1 week after vertex. There was a statistically significant difference between the three GAD-7 scores: $F(2, 20) = 12.50$, $P = .000$, $\eta^2 = .56$, see Figure 3. The results show that the time at which GAD-7 scores were taken significantly affected those GAD-7 scores. Bonferroni post-hoc tests revealed a

significant difference between the GAD-7 scores prior to any intervention and 1 week after left DLPFC stimulation, 95% CI [1.48, 5.61], $p = .002$ and also between GAD-7 scores taken 1 week after left DLPFC stimulation and 1 week after vertex, 95% CI [-5.50, -.86], $p = .008$. There was no significant difference between the GAD-7 scores prior to any intervention and 1 week after vertex was stimulated. The data indicated that it was after having the left DLPFC stimulated that the GAD-7 scores decreased.

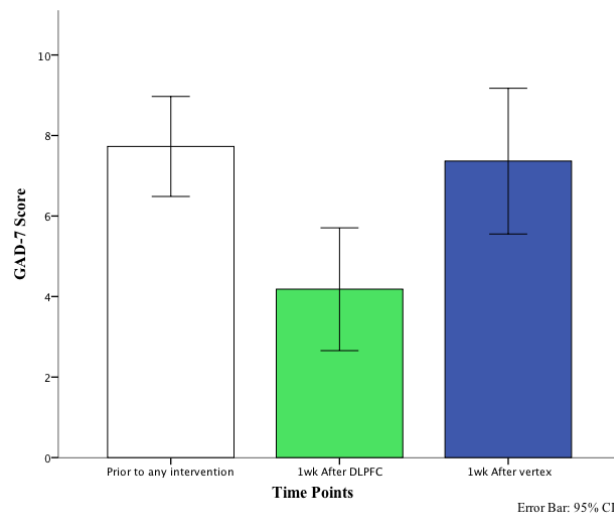


Figure 3. GAD-7 scores taken at different time points. GAD-7 scores taken 1 week after stimulation of the left DLPFC had the largest effect on decreasing GAD-7 scores.

It was hypothesised that the order in which the site of stimulation occurred would have an impact on decreasing GAD-7 scores (vertex then left DLPFC or vice versa). To test this, a Mann-Whitney U test (due to data not approximating a normal distribution, even after transformations) revealed no significant difference in the vertex first group ($Mdn = -4.00$, $N = 6$) and left DLPFC first group ($Mdn = -1.00$, $N = 5$), $U = 6.50$, $z = -1.56$, $p = .12$, $r = -.4$. The results show that the order of site of stimulation did not influence a decrease in GAD-7 scores. Although the results showed that the data was non-normal even after log transformations, it was decided to use the original data to observe any intervention as ANOVA is quite robust to violations of normality (see Appendix F for 2x2 mixed ANOVA

results). There was no interaction between site of stimulation and which site of stimulation occurred first (see Figure 4.)

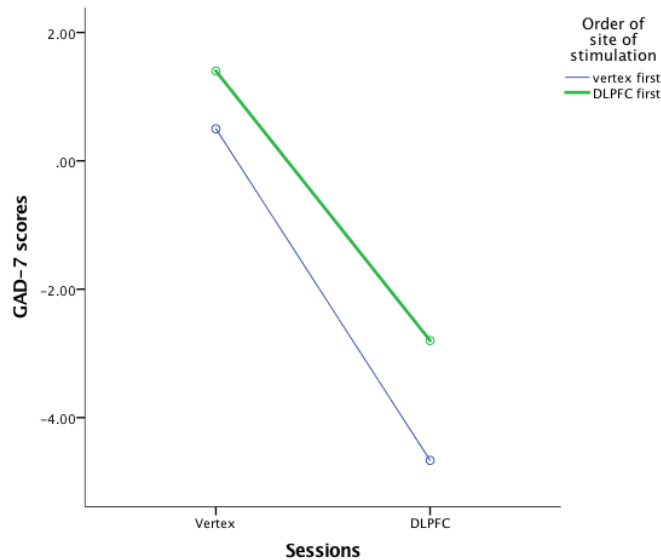


Figure 4. Interaction Graph. No interaction between which site was stimulated first and the site of stimulation sessions.

Following on from the main hypothesis, it was assumed that short term effects (in session) would mirror the long-term (weeks), so that anxiety scores would decrease more during the left DLPFC than the vertex session. To test this, anxiety scores were taken five times during the session, based on a dial rating of 0 -10, rather than the GAD-7 questionnaire, as the Dial is a quick and efficient way to attain an anxiety measure during the rTMS and hypnotherapy session.

A two-way repeated measures ANOVA was conducted to compare anxiety scores (based on a Dial rating of 0-10) during the vertex session and the left DLPFC session. The variables tested were the site of stimulation (vertex vs left DLPFC) and time points throughout session (initial, after 1st stimulation, 1st hypnotherapy, 2nd stimulation and 2nd

hypnotherapy). There was no statistically significant main effect on anxiety scores due to site of stimulation; $F(1,10) = .48, p = .505, \eta^2 = .05, 95\% \text{ CI } [1.30, -0.62]$. Therefore, the data supports the null hypothesis rather than the theory. There was a statistically significant effect on anxiety scores due to different time points during the session; $F(4,40) = 60.55, p = .000, \eta^2 = .86$. To explore this, post hoc Bonferroni tests indicated that there was no significant difference found between the time periods of initial and 1st stimulation, $p = .06, 95\% \text{ CI } [-0.02, 1.10]$ and time periods of 1st hypnotherapy and 2nd hypnotherapy, $p = 1.0, 95\% \text{ CI } [-0.97, 1.24]$, however, there was a significant difference found between all the other time points ($p < .05$). The results indicate that hypnotherapy is the biggest driver to decreasing anxiety scores. The site of stimulation x time points interaction was non-significant with a Greenhouse-Geisser correction $F(1.55,16.39) = 1.55, p = .12, \eta^2 = .14$. Figure 5 highlights that anxiety scores decrease regardless of site of stimulation.

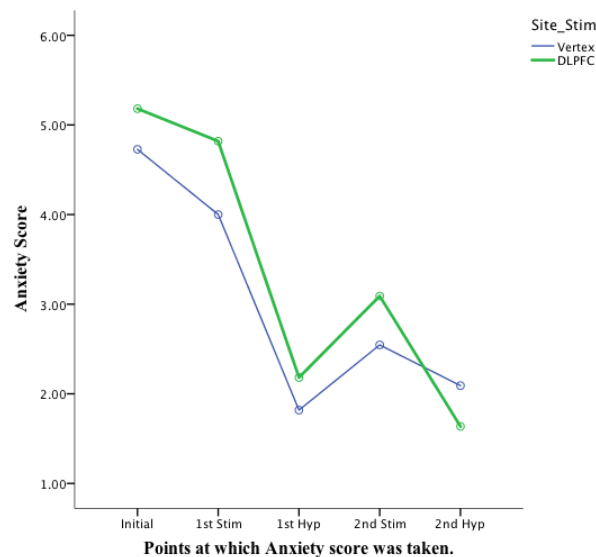


Figure 5. Anxiety Score throughout the session. The site of stimulation did not make a difference to decreasing anxiety in the short term.

Having shown that undergoing rTMS to the left DLPFC increases hypno-susceptibility, it was hypothesised that hypnosis in the left DLPFC sessions would create a deeper trance (hypnotic state), which in turn would assist in decreasing anxiety scores. To test this theory, a Wilcoxon Signed Ranks Test was conducted (due to scores not approximating a normal distribution) to evaluate if the vertex or the left DLPFC session produced a deeper trance (see Figure 6). The depth of trance after receiving rTMS to the vertex ($Mdn = 8$, $N = 6$) was not significantly different when applied to the left DLPFC ($Mdn = 7.50$, $N = 5$), $T = 5.00$, $p = 1.00$. $r = 0$, 95% CI $[-.42, .42]$. Therefore, the data supports the null hypothesis over the theory.

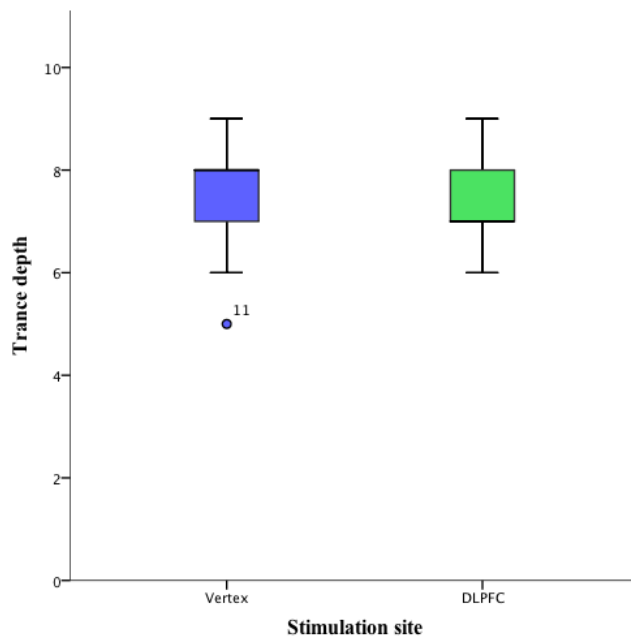


Figure 6. Depth of trance for both sites of stimulation, showing no statistically difference.

A prediction of this cold control theory is that a person cannot do anything under hypnosis that they wouldn't normally do. The only difference is, that under hypnosis it would feel involuntary, i.e. automatic. To test this, the automatic score each participant gave for how their anxiety changed when they moved the dial during both sessions was studied and a paired-samples t-test was conducted, (see Figure 7). Bayesian analysis was used to

assess the sensitivity of the data, as a non-significant result can still be interpreted. A correction was needed for the analysis as there were less than 30 participants. So, an increase to the SE was needed $SE \cdot (1 + 20/(df \cdot df))$, before the calculation could be done using the Bayes calculator (Dienes, 2008). A half normal was used as Dienes and Hutton (2013) got a difference of 0.3 rating units on their 0-5 scale; therefore, it was expected that a 0.6 difference would occur as this scale is out of 10. A β of 3 or above indicates support for the theory and a β of below 1/3 shows support for the null, a β of approximately 1, indicates the experiment is not sensitive, so suspend judgement (Dienes, 2008; 2014). There was no significant difference in automatic score between vertex ($M = 5.54, SD = 1.69$) and DLPFC ($M = 6.00, SD = 1.52$), $t(10) = .66, p = .52, r = .20, B_{H[0, 0.6]} = 1.07, 95\% CI [-1.07, 1.98]$. However, the trend is going in the right direction for the theory and the Bayes result indicates suspend judgement.

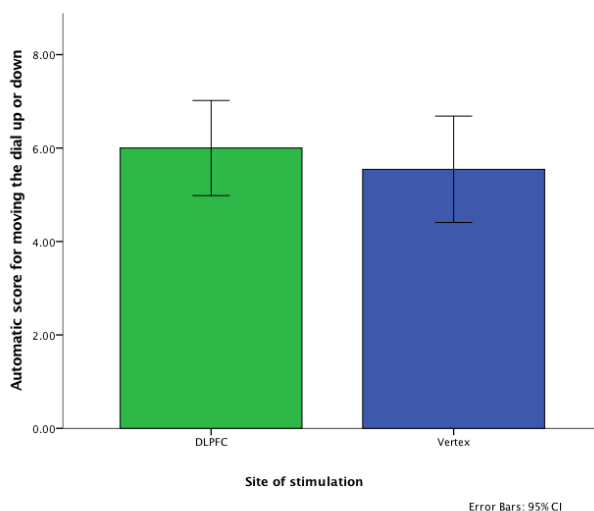


Figure 7. Automatic score for hypnotic suggestions of moving the dial up or down.

It was hypothesised that the participants' raw (without rTMS) hypnotic susceptibility score would influence the overall decrease in GAD-7 scores as the more susceptible to hypnosis a person is, the bigger the decrease would be. Participants filled in the SWASH

response booklet to obtain a hypnotisability score (objective). Participants were classed as highly susceptible if they scored 8 or above from a possible 10 on the objective scale, ($N = 0$), medium hypnotisable participants scored between 3 and 7 ($N = 10$) and low susceptible participants scored 2 or below, ($N = 1$). Objective hypnotic susceptibility score for the group ($M = 5.09$, $SD = 1.58$) and participants' degree of hypnotic response (subjective) was also obtained, this was out of a possible 5, ($M = 2.11$, $SD = .56$). To test this hypothesis a Pearson's coefficient was conducted. It was found that the correlation between the overall decrease in GAD-7 score and SWASH objective score was not statistically significant, $r(9) = -.33$, $p = .316$. Therefore, there was no relationship between a person's hypnotisability score and the decrease in their GAD-7 anxiety scores.

A Pearson's coefficient was conducted between the objective and subjective SWASH scores. There was a strong, positive, statistically significant relationship between SWASH objective and subjective scores $r(9) = .86$, $p = .001$, (see Figure 8). Hypnotic susceptibility score (objective) was related to how the participants scored their degree of hypnotic response (subjective) which would be intuitively expected.

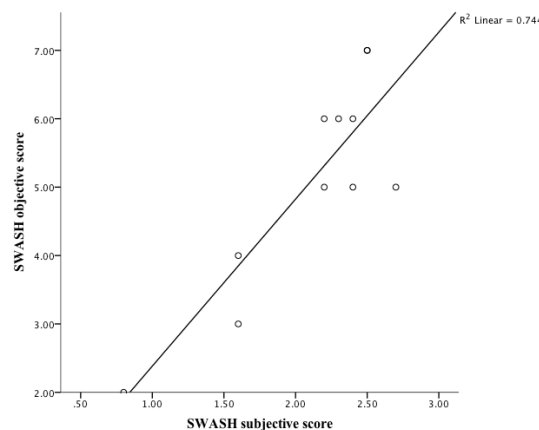


Figure 8. Correlation between SWASH objective and subjective scores.

Discussion

The present study predicted that disrupting the left DLPFC with rTMS would increase the effectiveness of hypnotherapy for anxiety. The results substantially support the hypothesis, in that participants who had rTMS on the left DLPFC and hypnotherapy, reported considerably less anxiety over time. These results are consistent with cold control theory of hypnosis, that hypnosis forms inaccurate HOT's (Dienes & Perner, 2007) and so, disrupting the region thought to be involved with creating HOTs will boost hypnotic response (Dienes & Hutton, 2013). The effect seen lends support to previous findings in the literature that inhibiting the left DLPFC would enhance hypnotic response (Brammer et al, 2012; Farvolden & Woody, 2004; Jamieson & Sheehan, 2004; Wagstaff, Cole, & Brunas-Wagstaff, 2007). Further tests carried out found that the two-week wash-out period had the desired effect (i.e. that no residual effects of the previous intervention affected the present), which indicates that this research did not have carry-over bias. Exploring these results indicated that it was not the order of site of stimulation that made the difference, but that the left DLPFC was stimulated in conjunction with hypnotherapy that had the effect of decreasing anxiety over time.

Contrary to expectation, there was no evidence found to support the assumption that the short-term reduction of anxiety would be mirrored in the long-term effects. Further examination of the results found that hypnotherapy, rather than the site of stimulation, was the biggest driver in decreasing anxiety scores within the session. Importantly, the decrease in anxiety in the vertex group was not maintained a week later, whereas the DLPFCs group's reduction was sustained or the reduction was increased.

These findings demonstrate that hypnotherapy alone is a powerful and effective therapy in the short-term, but when combined with stimulation to the left DLPFC, the effectiveness is increased to include long-term effects. Importantly, this reinforces the main

hypothesis of this study and alludes to a possible reduction in overall treatment time and therefore in cost of treatment.

What was surprising, is that stimulating the left DLPFC rather than the control site (vertex) did not create a deeper hypnotic trance (the function of which is to enhance responsiveness to suggestions), which is contrary to cold control theory. A possible explanation is that even though stimulating the left DLPFC did not produce any adverse side effects, it can be slightly uncomfortable compared to having the vertex stimulated. This could then affect how relaxed the participant was going into hypnosis. Therefore, it could be argued that the depth of trance achieved during the left DLPFC session was artificially understated. However, it maybe that there truly is no link between hypnotic depth and site of stimulation.

A prediction of cold control theory (Dienes & Perner, 2007) was that a hypnotic suggestion would feel automatic (i.e. involuntary) as opposed to voluntary, during a non-hypnotic state. When looking at the automatic scores during hypnosis, the results were disappointing and did not reach significance. However, closer inspection of the results using Bayes analysis, showed that the results were insensitive and thus judgment was suspended. Nevertheless, it was noted that the results were going in the right direction in support for cold control theory (consistent with the findings of Dienes & Hutton, 2013).

The final hypothesis of the current study was that a participants' hypnotic susceptibility score would influence the overall decrease in GAD-7 scores, as the assumption that the more a participant is susceptible to hypnosis, the bigger the effect on decreasing GAD-7 scores. Notably, there was no evidence found to support this theory. This apparent lack of correlation can plausibly be explained by looking at the methodology of both the hypnotic susceptibility scoring system and the GAD-7 scores. The first is a test followed by a response booklet that the participant must fill in whilst under several time restraints, which can make the participant feel under pressure. Moreover, participants frequently want to do

well in a test but also want to do well for the experimenter giving the test (Nichols & Maner, 2008). Furthermore, is not a therapeutic intervention and thus the participant knows it is unlikely to give them any benefit. Whereas, the rTMS and hypnotherapy interventions' aim is to decrease anxiety and so the participant will have more of a 'buy in' when undertaking it. Additionally, when they fill in the online GAD-7 questionnaire, they are possibly alone, relaxed, and in the comfort of their own home, which could possibly explain the effect it had on the scores the participant gave.

Some study limitations merit comment. The sample size was small, which is evidence of the difficulty of recruiting participants within the time frame who met both the inclusion and exclusion requirements. Statistical significance may have been reached with a larger sample size when looking at automaticity during hypnotic suggestions, as indicated by the Bayes analysis. Unfortunately, it was not possible to investigate if rTMS alone on the left DLPFC would have decreased GAD-7 anxiety scores, due to time constraints and availability of the lab. Given that my findings are based on a non-clinical group, caution is required when interpreting the results to use with a those who have a clinical diagnosis of anxiety.

Further studies should target clinical groups, using an experimental design that encompasses a larger sample group, replicating this protocol but having three groups: a group who would receive rTMS on the left DLPFC with no hypnosis, and then rTMS on the vertex with no hypnosis; a group who would receive two sessions of stimulation to the left DLPFC and hypnotherapy, and a third group who would have two sessions of rTMS on the vertex, with hypnotherapy. There should be extra follow-ups on GAD-7 scores at one and three months. Such a line of research may make it possible to ascertain if the intervention of rTMS on the left DLPFC aids the process of hypnotherapy in treating anxiety in a clinical sample, or if the decreases seen can simply be attributed to the effect of rTMS. A good indication of the number of sessions needed would be known, due to the extra follow-up results with

GAD-7 scores. If the results emulate this research in making hypnotherapy more effective, the number of sessions required to manage anxiety should be less than the normally recommended number of six.

In conclusion, the present study is important in two ways: it lends further credence to cold control theory of hypnosis, and it is of direct practical relevance to treating anxiety, by providing an innovative intervention which has positive results in decreasing anxiety, with lack of side-effects, ease of application and possibly a decrease in costs compared to the currently accepted treatments.

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