

Oxytocin impedes the effect of the word blindness post-hypnotic suggestion on Stroop task performance

Benjamin A. Parris,¹ Zoltan Dienes,² Sarah Bate,¹ and Stace Gothard¹

¹Psychology Research Centre, School of Design, Engineering and Computing, University of Bournemouth, UK, BH12 5BB, and ²School of Psychology and Sackler Centre for Consciousness Science, University of Sussex, UK, BN1 9QH.

The ability to enhance sensitivity to relevant (post)hypnotic suggestions has implications for creating clinically informed analogues of psychological and neuropsychological conditions and for the use of hypnotic interventions in psychological and medical conditions. The aim of this study was to test the effect of oxytocin inhalation on a post-hypnotic suggestion that previously has been shown to improve the selectivity of attention in the Stroop task. In a double-blind placebo-controlled between-subjects study, medium hypnotizable individuals performed the Stroop task under normal conditions and when they had been given a post-hypnotic suggestion that they would perceive words as meaningless symbols. In line with previous research, Stroop interference was substantially reduced by the suggestion in the placebo condition. However, contrary to expectations, oxytocin impeded the effect of the word blindness suggestion on performance. The results are explained in terms of the requirement for the re-implementation of the word blindness suggestion on a trial-by-trial basis and the need to sustain activation of the suggestion between trials. The findings contrast with a recent study showing a beneficial effect of oxytocin on sensitivity to (post)hypnotic suggestions but are consistent with findings showing a detrimental effect of oxytocin on memory processes.

Keywords: oxytocin; suggestion; hypnosis; stroop; memory

INTRODUCTION

The neuropeptide oxytocin is thought to be important for learning, memory and behavioural regulation in humans and non-humans and plays an important role in social affiliation. Central oxytocin receptors are found throughout the brain in many structures important for information processing, memory and emotion/reward including the hippocampus, amygdala, striatum, hypothalamus, nucleus accumbens and midbrain (Gimpl and Fahrenholz, 2001). In terms of its role in social affiliation, oxytocin administration has been shown to enhance trust as well as increase attention to social stimuli (Kosfeld *et al.*, 2005; Bartz and Hollander, 2006).

Oxytocin's role in increasing social affiliation has recently been investigated in the hypnotic context in which the relationship between the hypnotist and subject is pivotal (Sheehan and McConkey, 1982). Bryant *et al.* (2012) wanted to explore whether hypnotizability could be increased given the implications such a finding would have for hypnotic interventions for psychological and medical conditions. After an initial screening session establishing participants as low hypnotizable individuals (LHIs), Bryant *et al.* had participants inhale either oxytocin or a placebo and then re-screened them in a randomized, double-blind, between-subjects experiment, and compared their hypnotizability score with the previous screening session. Bryant *et al.* showed that for the participants that inhaled oxytocin, susceptibility to hypnotic suggestions increased significantly. Indeed, some of their participants (42%) went from scoring as LHIs to scoring as medium hypnotizable individuals (MHIs), although none went from LHIs to highly hypnotizable individuals (HHIs). Interestingly, only cognitive suggestions (e.g. swatting a hallucinated mosquito, hallucinating a taste, anosmia to ammonia, post-hypnotic amnesia) benefitted from oxytocin inhalation. No effects of oxytocin were detected for motor (moving hands apart) nor challenge (difficulty bending extended arm, difficulty lifting arm) suggestions. Nevertheless, the

finding of an effect on the more difficult suggestions is important, especially given the predominance of these suggestions in clinical settings. The authors interpreted their effects by suggesting that oxytocin leads to greater motivation to initiate appropriate cognitive strategies to respond to the suggestions as a result of increased attention to the hypnotist's social cues. In this study, we aimed to test the effect of oxytocin on a post-hypnotic suggestion whose remarkable effect has implications for creating clinically informed analogues of psychological and neuropsychological conditions (Oakley and Halligan, 2011).

Raz *et al.* (2002) showed that the Stroop effect (Stroop, 1935), one of the most robust effects in cognitive psychological research, can be virtually eliminated following a post-hypnotic suggestion. The Stroop task requires participants to identify the colour of the font in which a word is presented, while ignoring the meaning of the word itself. When the written word is incongruent with the ink colour (*red* written in blue), the time it takes to identify the colour is increased relative to neutral stimuli (i.e. when the word is not colour-related, e.g. *top* written in red). When the word is congruent with the colour (*red* in red), colour identification time is reduced compared with neutral stimuli. The effect of word congruency on colour classification times is known as the Stroop effect. The Stroop effect has been referred to as the 'gold standard' of attentional processes and has long been held as strong evidence for the obligatory nature of word processing (MacLeod, 1992). However, a post-hypnotic suggestion describing the word dimension of the Stroop stimulus as being made up of 'meaningless symbols' and 'characters of a foreign language' (to be referred to as the *word blindness suggestion*) resulted in the virtual elimination of not only Stroop interference (Incongruent-Neutral Stroop trials) but also Stroop facilitation (Neutral-Congruent trials) in the reaction time (RT) data, and Stroop effects typically observed in error data. The authors argued that their results were inconsistent with the notion that the processes of visual word recognition are obligatory and that the post-hypnotic suggestion works via a top-down mechanism that modifies the processing of input words through a means not voluntarily available.

As noted above, the effect of the word blindness suggestion highlights the potential of (post)hypnotic suggestions in exploring the

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Correspondence should be addressed to Benjamin A. Parris, Department of Psychology, School of Design, Engineering, and Computing, University of Bournemouth, Poole House, Talbot Campus, Poole BH12 5BB, UK. E-mail: bparris@bournemouth.ac.uk

cognitive and biological substrates underlying normal and impaired psychological functions (see Oakley and Halligan, 2009; Oakley and Halligan, 2011). For example, Raz *et al.* have shown that the word blindness post-hypnotic suggestion reduces activity in visual processing areas of the brain and areas known to be involved in conflict processing (Raz *et al.*, 2005), indicating that the word blindness suggestion might actually disable word reading, inducing a form of alexia that could be studied in the same way as any neuropsychological impairment [Oakley and Halligan, 2011; although see Augustinova and Ferrand (2012) for a contrasting viewpoint]. Indeed so remarkable is the effect of the word blindness suggestion on Stroop task performance that it stands as a marker in the literature for the potency of (post)hypnotic suggestions and provides an objective measure (one that does not rely on self-reporting) of the effect of a suggestion on performance.

In the original study, the word blindness suggestion effect was observed in highly hypnotizable individuals (henceforth HHIs) only and was remarkable in its all-encompassing effect on indices of Stroop task performance. In numerous subsequent studies, Raz *et al.* have shown that the suggestion effect on interference is replicable, although the effect on facilitation less so (Raz *et al.*, 2003, 2007; Raz and Campbell, 2011) and that the effect is observable in LHIs indicating a greater utility for (post)hypnotic suggestions in research and in psychological and medical interventions, since HHIs represent only a small proportion of the population (Raz and Campbell, 2011). However, the effect of the suggestion was much reduced in LHIs, being about half that observed in HHIs. Here, we explore the influence of oxytocin on the word blindness post-hypnotic suggestion in MHIs. Showing an enhanced effect of oxytocin inhalation on this particular suggestion would be of use not only in psychological and medical interventions but also for gaining a better understanding of the cognitive and biological substrates underlying normal and impaired psychological functions.

Other authors have also shown an effect on the word blindness suggestion on Stroop task performance. In a recent study, Parris *et al.* (2012) have shown that the effect of the word blindness suggestion is more likely when response–stimulus interval (RSI) is short (500 ms) compared with the interval used by Raz *et al.* (3500 ms). The implication here is that the suggestion is re-implemented on every trial. When time between re-implementations is too long, activation of the suggestion cannot be sustained. Hence, the ability to sustain the representation of the suggestion in memory is key to the successful application of the suggestion. In this study, we utilized the short RSI only to increase the likelihood of observing an effect on performance in both conditions. It was expected that there would be a word blindness suggestion effect in the placebo condition and that this effect would be enhanced by the inhalation of oxytocin. However, to foreshadow the results, despite the use of the shorter RSI, the reduction in interference observed in the placebo condition was not observed after oxytocin inhalation.

METHODS AND MATERIALS

Participants

Totally 137 students from the University of Bournemouth were screened for suggestibility using the Waterloo–Stanford Group Scale of Hypnotic Susceptibility, Form C (WSGC) (Bowers, 1993). The scale gives possible ratings from 0 to 12. However, we did not include the age regression suggestion, which means that the maximum possible score was 11. Participants were excluded from the experiment if they did not score in the medium suggestible range (4–7) on this scale and if they were pregnant, on medication, had a history of significant medical or psychiatric illness, had a history of substance abuse or had epilepsy.

The selected 36 proficient English speakers who took part in the study had an average age of 19.94 years (*s.d.* = 1.56). These participants were randomly assigned to one of the groups that would receive either the oxytocin or placebo nasal sprays. Neither the participants nor the hypnotist/experimenter were aware of group allocation at the time of testing. The two groups were matched for age: oxytocin [average age: 19.8 years (*s.d.* = 1.09)] and placebo [average age: 20.1 years (*s.d.* = 1.95)]; gender: 13 females and 5 males in both groups and hypnotizability: both groups scored an average of 5.2 on the Waterloo–Stanford Group Scale with *s.d.* 0.94 (oxytocin) and 0.88 (placebo: $P > 0.9$). Participants were paid £12 for their participation. Participants were asked to abstain from food and drink other than water for 2 h before the experiment, and from alcohol, smoking and caffeine for 24 h before the experiment.

Ethical considerations: The Ethics Committee at Bournemouth University approved the study and the research was carried out in line with institutional guidelines and regulations. All participants were informed about the risks of oxytocin inhalation prior to taking part and provided written consent. All participants were adult-age university students and therefore capable of giving informed consent.

Design

The experimental design was a mixed factorial model with Word Type (Incongruent, Neutral, Congruent) and Post-hypnotic Suggestion (Absent, Present) as the within-subjects factors and Inhalation condition (Oxytocin, Placebo) as a randomized, placebo-controlled, double-blind, between-subjects experimental factor.

Materials

Stroop task

The version of the Stroop task was identical to that used by Raz *et al.* apart from the time between trials. The present experiment utilized a response–stimulus interval of 500 ms because it has been shown that effects of the word blindness post-hypnotic suggestion are more likely at this interval (Parris *et al.*, 2012). The incongruent stimuli consisted of the words RED, BLUE, YELLOW or GREEN presented equally often in any of the three non-matching colours (e.g. The word RED was presented in blue, yellow or green). The congruent stimuli consisted of the words RED, BLUE, YELLOW or GREEN presented in red, blue yellow and green, respectively. The neutral stimuli were matched to the colour word stimuli for word length and frequency and consisted of the words LOT, SHIP, KNIFE and FLOWER presented in any one of the four colours. All characters were displayed in upper-case font against a white background, and the stimuli subtended visual angles of 0.5° vertically, and 1.3–1.9° horizontally (depending on word length). Red, blue, yellow and green colour patches were placed on the 'V', 'B', 'N' and 'M' keys, respectively, and participants were asked to use the index and middle fingers from each hand to respond.

Multidimensional mood questionnaire

Affect was measured throughout the experiment using the Multidimensional Mood Questionnaire (MMQ; Steyer *et al.*, 1994), to assess the possible mood-altering effects of oxytocin, and to control for non-specific effects of attention and wakefulness (the MMQ is composed of three sub-scales: good-bad, awake-tired and calm-nervous). Each participant was required to complete the MMQ at three intervals across the experiment: immediately following inhalation, after the 45 min resting period and at the end of the experiment.

Nasal sprays

Participants were given a single intranasal dose of 24IU oxytocin (Syntocinon Spray, Novartis; three puffs per nostril, each with 4IU oxytocin) or placebo spray. The placebo spray contained exactly the same ingredients as the experimental spray with the exception of the oxytocin and was prepared by an independent pharmaceutical company. The 24IU dose was selected to match that of Bryant *et al.* (2012).

Procedure

On arrival participants were told that a hypnotic induction and post-hypnotic suggestion would be administered at a certain point during the experiment. They were asked to sign a consent form and given 36 practice trials on the Stroop task. They were then asked to inhale either oxytocin or placebo depending on condition; neither the participant nor the experimenter knew which. Following inhalation, participants completed the MMQ for the first time and then sat quietly for 45 min, the length of time it is believed to take for central oxytocin levels to plateau (Born *et al.*, 2002). At the end of the 45 min period, participants were asked to complete the MMQ for the second time. The order in which the Suggestion Absent and Suggestion Present conditions were delivered was counterbalanced. Regardless of order of suggestion delivery, participants completed two blocks of 144 trials on the Stroop task in both the Suggestion Absent and Suggestion Present conditions (there was no main effect of block in this experiment, nor was the influence of any other variable modified by block, $P_s > 0.05$). Each 144 trial block consisted of 48 congruent, 48 neutral and 48 incongruent trials, which were intermixed and presented in random order. The first trial of each block began with a fixation cross at the centre of the screen that remained on screen for the duration of the response–stimulus interval (500 ms). The stimulus remained onscreen until response. After each response, visual feedback was present stating whether their previous response was ‘CORRECT’ or ‘INCORRECT’. The feedback was presented in black ink for 100 ms and was replaced by a fixation cross for the remainder of the response–stimulus interval. In the Suggestion Absent condition, participants were asked to respond as quickly and accurately as possible to the colour of the stimulus while ignoring the meaning of the presented word. In the Suggestion Present condition, the participants were given a standard induction (taken from the Waterloo–Stanford scale) followed by the following suggestion taken from Raz *et al.* (2002):

Very soon you will be playing the computer game. When I clap my hands, meaningless symbols will appear in the middle of the screen. They will feel like characters of a foreign language that you do not know, and you will not attempt to attribute any meaning to them. This gibberish will be printed in one of 4 ink colours: red, blue, green or yellow. Although you will only be able to attend to the symbols’ ink color, you will look straight at the scrambled signs and crisply see all of them. Your job is to quickly and accurately depress the key that corresponds to the ink colour shown. You will find that you can play this game easily and effortlessly.

After completion of either the Suggestion Absent or Suggestion Present conditions, participants were given a 10 min break. They then completed the remaining Suggestion condition, at the end of which they completed the MMQ for the third and final time. Twenty-four hours after test completion, the experimenter enquired about any adverse side effects during or since testing; none were reported.

RESULTS

As per previous studies utilizing the word blindness suggestion, RTs that were 3 s.d. either above or below the mean were excluded from the

analysis, which resulted in 1.7% of the trials being removed from the analysis. 4.6% of the data were counted as errors and were removed from the analysis of RTs.

The data were entered into a 2 (Suggestion: Present, Absent) \times 3 (Word Type: Incongruent, Neutral, Congruent) \times 2 (Inhalation: Oxytocin, Placebo) mixed model ANOVA with inhalation as a between-subjects factor. The results revealed no main effect of Suggestion, $F(1, 34) = 0.024$, $P > 0.8$, no main effect of inhalation $F(1, 34) = 1.683$, $P = 0.203$, but a main effect of Word Type, $F(2, 68) = 83.245$, $P < 0.001$. None of the two-way interactions were significant: Suggestion \times Word Type, $F(2, 68) = 0.839$, $P > 0.4$; Suggestion \times Inhalation, $F(1, 34) = 3.566$, $P = 0.068$; Word Type \times Inhalation, $F(2, 68) = 0.238$, $P > 0.7$. Finally, there was a significant three-way interaction where $F(2, 68) = 3.287$, $P = 0.043$ [see Table 1 for mean RTs (and their standard deviations) in each condition and interference and facilitation effects in each condition].

The three-way interaction was non-orthogonally decomposed into two $2 \times 2 \times 2$ interactions to investigate the effects of the experimental manipulations on Stroop interference and Stroop facilitation effects separately. A 2 (Suggestion: Present, Absent) \times 2 (Word Type: Incongruent, Neutral) \times 2 (Inhalation: Oxytocin, Placebo) ANOVA indicated a significant three-way interaction where $F(1, 34) = 5.444$, $P = 0.026$.

To test for the expected effect of suggestion on interference in the placebo condition, the data were submitted into a Suggestion and Word Type interaction analysis which revealed a significant interaction $F(1, 17) = 4.088$, $P = 0.029$ (one-tailed). Critically, there was no such interaction in the Oxytocin condition where $F(1, 17) = 1.481$, $P = 0.240$. This non-significant two-way interaction is consistent with either evidence for no reduction of the interference effect or simply with the absence of evidence for a reduction. To determine whether there was evidence for no effect of the suggestion, we used a Bayes factor (Dienes, 2008, 2011), where we contrasted the theory that the suggestion had some effect with the null hypothesis that the suggestion had no effect. We modelled the predictions of the theory of some effect with a uniform between 0 and 35 ms, i.e. any effect was as plausible as any other in the full range (35 ms is the size of the effect in the Placebo condition, rounded up, so defines the largest amount by which the suggestion could reduce the effect). The Bayes factor was 0.26, indicating there is evidence supporting the null hypothesis (0.33 and below being the cut off for strong evidence for the null). That is, there is evidence that the suggestion had no effect in the oxytocin condition. This is the key, surprising finding of this study: oxytocin impedes the effect of the word blindness suggestion on Stroop task performance.

In contrast to the Stroop interference data, the 2 (Suggestion: Present, Absent) \times 2 (Word Type: Neutral, Congruent) \times 2 (Inhalation: Oxytocin, Placebo) ANOVA did not reveal a significant three-way interaction $F < 1$.

ERROR ANALYSIS

The number of errors participants committed was entered into a 2 (Suggestion: Present, Absent) \times 3 (Word Type: Incongruent, Neutral, Congruent) \times 2 (Inhalation: Oxytocin, Placebo) mixed model ANOVA with inhalation as a between-subjects factor. Analysis revealed a main effect of Word Type, $F(2, 68) = 4.918$, $P < 0.01$, but for all other effects, $P > 0.1$.

ANALYSIS OF THE MMQ

Results at the three time points revealed that while there were mood changes over time ($F(4, 136) = 3.456$, $P = 0.010$), we did not detect an interaction with inhalation condition, $F(4, 136) = 1.139$, $P = 0.341$).

Table 1 Mean RTs (milliseconds) and % errors (with standard deviations in brackets), and magnitudes of interference (incongruent-neutral) and facilitation (neutral-congruent) as a function of condition

	Oxytocin		Placebo	
	Suggestion present	Suggestion absent	Suggestion present	Suggestion absent
Reaction times (ms)				
Incongruent	786 (72)	760 (49)	722 (94)	766 (88)
Neutral	735 (87)	727 (54)	704 (68)	714 (65)
Congruent	716 (68)	698 (52)	678 (55)	686 (61)
Interference	50**	33**	18	52**
Facilitation	20*	29**	26*	27*
Errors (%)				
Incongruent	3.9 (4.6)	4.6 (3.3)	5.2 (4.3)	8.2 (8.8)
Neutral	4.1 (2.4)	3.2 (3.7)	4.7 (3.6)	6 (5.2)
Congruent	3.1 (2.7)	4 (2.7)	4.1 (3.7)	4.3 (3.6)
Interference	-0.2	1.4	0.5	2.2
Facilitation	1	-0.8	0.6	1.7*

* $P < 0.05$; ** $P < 0.001$.

Further, the critical three-way interaction in the RT data with valence, wakefulness and nervousness from the third time point (the point when oxytocin was most likely to be affecting performance) entered simultaneously as covariates was significant, $F(1, 62) = 3.263$, $P = 0.045$ indicating that mood did not mediate the effect of oxytocin on performance.

DISCUSSION

The aim of the present experiment was to test the effect of oxytocin inhalation on the word blindness post-hypnotic suggestion because of the implications this effect has for creating clinically informed analogues of relevant psychological and neuropsychological conditions (Oakley and Halligan, 2011). As expected, Stroop interference was substantially reduced by the suggestion in the placebo condition. Contrary to expectations, however, oxytocin impeded the effect of the word blindness suggestion on performance; there was no effect of the suggestion when participants inhaled oxytocin. No effects of mood were detected. Indeed Stroop interference was numerically larger when the suggestion was present compared with when it was absent in this condition. Contrary to predictions from a recent study (Bryant *et al.*, 2012), oxytocin does not always increase susceptibility to hypnotic suggestions. The present results show a decreased sensitivity to a post-hypnotic suggestion, indicating a detrimental effect of oxytocin on performance.

Although oxytocin has generally been thought to exert situation-invariant effects on behaviour, the effects of oxytocin are often moderated by contextual factors including task difficulty and in-group/out-group membership [see Bartz *et al.* (2011) for a review]. Moreover, although most of the reported effects of oxytocin are positive/beneficial, a sizeable minority has shown that oxytocin can have a detrimental effect. For example, cooperation has been shown to decrease in a well-known economic game when the other player was unknown (Declerck *et al.*, 2010) or was a member of a social out-group (De Dreu *et al.*, 2011).

The present detrimental effect of oxytocin on a cognitive suggestion indicates that the efficacy of oxytocin on suggestions is moderated by contextual factors. A key difference between the word blindness suggestion and the suggestions presented by Bryant *et al.* is the need for re-implementation of the word blindness suggestion on each new trial (Parris *et al.*, 2012). Bryant *et al.* had their participants respond to each

suggestion only once. Parris *et al.* showed that the word blindness suggestion has to be re-implemented on every trial; it does not remain active from the starting cue until the end cue. Furthermore, it was shown that if the time between each successive trial is too long, activation of the suggestion dissipates to such an extent that it no longer affects performance. It is therefore possible that oxytocin interferes with the successive re-implementation of the suggestion and/or the sustaining of the suggestion between trials. Previous research has shown that oxytocin can impair some forms of memory, and cued recall in particular (Heinrichs *et al.*, 2004; see also Herzmann *et al.*, 2012) suggesting that oxytocin impedes either the initial activation of the suggestion in response to the given cue or the sustaining of the suggestion between trials, even at the shorter RSI.

Consistent with this, a further notable difference between this study and that of Bryant *et al.* is that, although they included a post-hypnotic suggestion in their study (post-hypnotic amnesia), the majority of the cognitive suggestions on which they observed an effect were hypnotic suggestions—suggestions given and responded to when under hypnosis. Bryant *et al.* did not report the effect of the suggestion on each individual cognitive suggestion, nor did they intimate that one was more or less affected than others. It is possible therefore that oxytocin confers benefits on hypnotic suggestions, but not post-hypnotic suggestions, which require processes of memory to link the suggestion to a given cue. Thus, oxytocin's effect on cued recall (Heinrichs *et al.*, 2004) could account for the observed impeding effect of oxytocin on post-hypnotic word blindness suggestion. Although the exact mechanisms behind this impeding effect of oxytocin on cognition is not known, Herzmann *et al.* (2012) posited that oxytocin's effect on memory is likely to be the result of a detrimental effect of oxytocin on the hippocampus and the amygdala to which oxytocin is assumed to bind, reducing activity and consequently processing in these areas.

Individual differences might also play a role in producing detrimental effects. For example, Ellenbogen *et al.* (2012) found that oxytocin impeded the ability to ignore task-irrelevant facial expressions of sadness in students with depressive symptoms, but observed no effect on those scoring low on measures of depression. It is therefore possible that oxytocin only enhances sensitivity to suggestions in low hypnotizable individuals such as those in the study by Bryant *et al.* However, it would be a surprising finding showing that individual differences predict qualitative and not just quantitative differences.

In conclusion, we have shown that inhalation of oxytocin impedes the effect of the word blindness suggestion on Stroop task performance. Although contrasting with a previous study investigating the influence of oxytocin on sensitivity to (post)hypnotic suggestions, the present findings are consistent with others showing a detrimental effect of oxytocin on performance. A future fMRI assay will reveal the differences in neural activations between the two conditions presented, perhaps elucidating the preventative mechanism impeding the word blindness suggestion. However, it is likely that the requirement for memorial processes in post-hypnotic suggestions, including the subsequent need to sustain activation of the suggestion in the present context, contributed to the effect observed. A key area for future research is in understanding when, what and why different types of memory are impaired by oxytocin inhalation and the implications for other factors under study.

Conflict of Interest

None declared.

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