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ORIGINAL INVESTIGATION

Enhancement of suggestibility and imaginative ability with nitrous oxide

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Abstract
Rationale Imaginative suggestibility, a trait closely related to hypnotic suggestibility, is modifiable under some circumstances. Nitrous oxide (laughing gas) is commonly used for sedation in dentistry and is reported to be more effective when combined with appropriate suggestions.
Objective The aim of this study was to determine whether nitrous oxide inhalation alters imaginative suggestibility and imagery vividness.
Methods Thirty participants were tested twice in a within-subjects design, once during inhalation of 25% nitrous oxide and once during inhalation of air plus oxygen. Before the study, participants' expectancies regarding the effects of nitrous oxide were assessed. Participants were blinded to drug administration. During each session, participants were verbally administered detailed measures of imagination and suggestibility: the Sheehan–Betts Quality of Mental Imagery scale and the Stanford Hypnotic Susceptibility Scale Form C, minus the hypnotic induction.
Results Imaginative suggestibility and imaginative ability (imagery vividness) were both elevated in the nitrous oxide condition. This effect was unrelated to participants' expectations regarding the effects of the drug.
Conclusions Nitrous oxide increased imaginative suggestibility and imaginative ability. Possible explanations of these findings are discussed with respect to the effects of *N*-methyl-*d*-aspartate antagonists and to other pharmacological effects upon suggestibility and imagination.

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Introduction

Nitrous oxide (laughing gas) inhalation is a form of conscious sedation and is an analgesic commonly used in dentistry and also in obstetrics. It has long been noted by dental practitioners that patients under nitrous oxide sedation are particularly suggestible and a number of investigators have noted the clinical advantages of using a hypnotic voice when administering nitrous oxide (Lippe 1944; Seladin 1947). Bingham (1964) describes a case of 'rapid hypnosis by using nitrous oxide' and Allen (1972) notes that during nitrous oxide sedation patients respond well to suggestions given in a quiet, hypnotic manner. Hilgard and Hilgard (1975) and Eysenck and Rees (1945) also informally note that sub-anaesthetic doses of nitrous oxide will heighten the hypnotic responsiveness of the patient. If there is a synergistic relationship between nitrous oxide inhalation and responsiveness to suggestions, then strategic use of appropriate suggestions for relaxation and analgesia should enhance the overall clinical effectiveness of nitrous oxide sedation procedures (Simons et al. 2007).

Suggestibility can also be assessed in the absence of hypnosis and is termed 'imaginative suggestibility' (Kirsch and Braffman 2001). Hypnotic inductions are commonly used to modestly increase suggestibility (Kirsch and Braffman 2001), and suggestibility can also be modified by either changing people's expectations (Vickery and Kirsch 1991), labeling a situation as hypnotic (Gandhi and Oakley 2005) or through training (Gorassini and Spanos 1989). There is disagreement, however, about the

magnitude to which suggestibility can be affected through training programs (e.g. Benham et al. 1998; Spanos 1986).

One study that has systematically examined the effect of nitrous oxide upon suggestibility involved 20 volunteers randomly divided into two groups (Barber et al. 1979). One group received nitrous oxide supplemented with oxygen and the other group received oxygen alone. In the nitrous oxide group, the dose was increased until a baseline level giving paraesthesia and generalised warmth was reached (20–40%). When signalled by the anaesthetist, both groups were read an identical list of suggestions involving analgesia in one leg, compulsive behaviour (picking up a pen) and amnesia. The group receiving nitrous oxide responded to more suggestions, and the authors report that this effect was unrelated to subsequently measured hypnotic susceptibility. Unfortunately, it is not clear whether nitrous oxide was administered throughout the test session, or just for the period prior to the suggestions, a detail that could particularly affect scores on the analgesia item. In addition, the use of a between-subjects design with a small N of hypnotically unselected participants increases the likelihood of any effects being due to uncontrolled pre-existing variations in responsiveness to suggestion.

The primary aim of the present study was to assess whether nitrous oxide sedation is associated with changes in suggestibility and imaginative ability, both measured in a within-subject design using standardised scales. Non-hypnotic imaginative suggestibility, rather than hypnotic suggestibility, was chosen in order to simplify the experimental procedure and to avoid any complications arising from participants' expectations regarding hypnosis. We formally assessed participants' beliefs about the effects of nitrous oxide in order to determine whether any increase in suggestibility was expectancy mediated.

Materials and methods

Participants

Participants in the study were 30 adults recruited from a dental surgery in Manchester, England. A notice requesting volunteers for a study of suggestibility and nitrous oxide was posted in the waiting room and the first 30 participants who volunteered and met the inclusion criteria were accepted. Inclusion criteria were that participants should be aged between 21 and 55 and not have any medical problem contraindicating the administration of nitrous oxide. Ethical approval was received from a University Research Ethics Committee. Thirty participants completed the study (ten males). Their average age was 40.06 (standard deviation (SD)=12.75).

Measures

All participants completed the Sheehan–Betts Quality of Mental Imagery Scale (QMI; Sheehan 1967) and the suggestions from the Stanford Hypnotic Susceptibility Scale Form C (SHSS:C; minus the hypnotic induction; Weitzenhoffer and Hilgard 1962). The QMI is a 35-item test assessing the vividness of different modalities of mental imagery (e.g. auditory, olfactory, tactile). It is a shortened version of Betts' (1909) original 150-item questionnaire. The scale was modified by the authors for verbal administration, but participants rated each item using the original seven-point scale (1 = as clear and vivid as the real thing; 7 = no image present at all, you only 'know' you are thinking of an object). Test–retest reliability for the Sheehan–Betts QMI has been found to be 0.75 for females and 0.72 for males after 2 weeks (Westcott and Rosenstock 1976). Factor analyses of the questionnaire items have revealed the presence of a large unitary factor corresponding to general vividness of imagery and modality specific factors (Sheehan 1967; Wagman and Stewart 1974; White et al. 1974).

The SHSS:C (Weitzenhoffer and Hilgard 1962) is a 12-item test, individually administered according to a standardised procedure. The researcher administering the scale objectively assesses participant's responses to each item. Suggestions on the test are progressively more difficult, enabling the researcher to terminate the test after the failure of three consecutive items. The SHSS:C was chosen for a number of reasons. Firstly, it contains proportionately more difficult items than other scales (Perry et al. 1992; Bertrand 1989), which is important to minimise any potential ceiling effects. Secondly, it contains a high proportion of cognitive items which we theorised might be less affected by lethargic feelings brought about by nitrous oxide sedation. As well as removing the hypnotic induction, we made a number of other modifications to the SHSS:C in order to increase its suitability for administering to participants inhaling nitrous oxide. For the age regression item, the American reference to school grades was omitted and replaced with the terms 'junior school' and 'infant school'. The anosmia to ammonia item was omitted to avoid having to remove nose mask used for administration of the nitrous oxide. A test of post-hypnotic suggestion modified from the Stanford Hypnotic Susceptibility Scale Form A (SHSS:A; Weitzenhoffer and Hilgard 1959) was added to replace the anosmia item. Post-hypnotic amnesia was assessed by joint criteria considering both initial amnesia and subsequent reversibility. Amnesia was scored as present only if the participants recalled both three or fewer critical items initially and two or more additional items following the reversal cue. The instructions for the reversibility test ask subjects to report *all* items they remember. These mod-

ifications have been used by other groups (Kihlstrom 2007). For the dream item (where participants are invited to have a dream), the word 'hypnosis' was replaced by 'relaxation'. The post-experimental interview was omitted after the first visit because it was thought that these questions might have affected the amnesia test for the second visit. However, after the second visit, these questions were included and the subject was asked to draw comparisons between the two visits.

Procedures

Participants made two visits to the dental surgery, with a gap of approximately 2 weeks. At the first visit, participants were given information about the study and provided informed consent. Participants were told that the study was an investigation of responses to imaginative suggestions, which would produce changes in sensation and perception. They were told that two sessions would be involved but that nitrous oxide would only be administered on one visit. Participants were explicitly told that the study was not a test of hypnosis.

Half of the participants received the nitrous oxide on the first visit and half on the second, randomised by a dental nurse who was blind to the study hypothesis. At the start of the first session, participants were asked whether they thought the administration of nitrous oxide would affect their suggestibility, which direction any effect might be in, and the extent of this expectation on a scale ranging from 0% to 100%. The mask was then fitted to the participant's nose and they were given instructions to breathe through the nose. Participants were made aware that breathing through the mouth would stop the gas from working. Nitrous oxide was delivered by a McKesson 882 continuous flow machine (McKesson Equipment Company, Chesterfield, UK). The nose mask was scented in order to disguise the sweet smell of the nitrous oxide. During the non-nitrous oxide visit, the mask was placed in position and the air intake valve left open, with oxygen still delivered at 3 L/min. This gave a mixture of oxygen diluted with air so that the subject could still feel and hear gas flowing through the mask. For the nitrous oxide session, the flow rate was increased slowly until 25% nitrous oxide was being delivered. The nitrous oxide and oxygen were always administered by the experimenter (GB).

At both sessions, the Sheehan–Betts Quality of Mental Imagery Scale (Sheehan 1967) and the suggestions from the Stanford Hypnotic Susceptibility Scale Form C (minus the hypnotic induction) (Weitzenhoffer and Hilgard 1962) were administered by the same experimenter (GB) who was not blind to the drug administration condition. For the QMI, participants were asked to close their eyes to listen to the description of each item and to imagine it as vividly as possible, then to open their eyes and rate the item using the scale. After the final item of the QMI, participants were asked to open their eyes and the investigator checked that they were feeling alright.

In the present investigation, the hypnotic induction that normally precedes the suggestions on the SHSS:C was omitted, making it a test of imaginative suggestibility (Kirsch and Braffman 2001). Administration of suggestions was conducted according to the manual. During the count down to normal alertness at the end of the SHSS:C, which was timed to last for 2 min, 100% oxygen was administered. This was to prevent diffusion hypoxia during emergence since the inhaled air (21% oxygen) is diluted by the rapid excretion of nitrous oxide, nitrogen being absorbed only slowly (Cass and Cass 1994).

The QMI was always delivered first because of the relative complexity of the SHSS:C. During the alerting phase of the final item of the SHSS:C, the delivery of nitrous oxide or oxygen was stopped and the participant was questioned about their memory for items in the test, followed by the SHSS:C post-experimental interview. Counterbalanced administration of the tests would have required restarting delivery of nitrous oxide after this alerting phase, and it was considered more feasible to deliver the tests in a single order with nitrous oxide delivery uninterrupted. At the end of the second session, participants were asked during which session they thought had received the nitrous oxide.

Results

Four patients dropped out after completing one session; they were replaced and their data were not used in the analysis. Imaginative ability measured by the Sheehan–Betts QMI was greater in the nitrous oxide condition (85.83, SD=37.63) than the oxygen alone condition (111.63, SD=37.77; lower scores on the QMI indicate higher imaginative ability). Imaginative suggestibility measured by the SHSS:C was greater in the nitrous oxide condition (7.33, SD=2.80) than the oxygen alone condition (6.16, SD=2.47).

To test for potential order effects, we included order of drug administrations as a factor in our analysis (group 1: first session = drug, second session = no drug; group 2: first session = no drug, second session = drug). Groups did not differ with respect to age ($t(28)=0.253$, $p=0.802$). A mixed-model analysis of variance with drug as a within-subjects factor (nitrous oxide vs. oxygen) and group as a between-subject factor was conducted for scores on the SHSS:C and the QMI. For scores on the SHSS:C, there was no main effect of group ($F(1,28)=0.483$, $p=0.493$) and no drug × group interaction ($F(1,28)=1.128$, $p=0.297$). For

scores on the Sheehan–Betts QMI, there was no main effect of group ($F(1,28)=2.075$, $p=0.161$) and no drug × group interaction ($F(1,28)=0.806$, $p=0.377$). For scores on the SHSS:C, there was a main effect of drug ($F(1,28)=11.418$, $p=0.002$, effect size (partial η^2)=0.290). For scores on the QMI, there was a main effect of drug ($F(1,28)=42.957$, $p<0.001$, effect size (partial η^2)=0.605).

To see whether nitrous oxide affected certain classes of suggestion more than others, response rates for each suggestion were assessed. The percentage pass rates for each are given in Table 1.

Participants' scores on the QMI were broken down by the modality of each item in order to assess whether any particular modality was more affected by the administration of nitrous oxide. Average scores per item are given in Fig. 1 (lower scores equate to higher imagery vividness). Items in all categories (visual, auditory, touch, movement, taste, smell, sensation) were significantly more vividly imagined in the nitrous oxide than in the oxygen condition (by modality, respectively: $t(4)=5.41$, $p=0.003$; $t(4)=15.5$, $p<0.001$; $t(4)=5.46$, $p=0.002$; $t(4)=6.35$, $p=0.001$; $t(4)=30.45$, $p<0.001$; $t(4)=4.18$, $p=0.007$; $t(4)=4.9$, $p=0.004$).

Only 11 participants (36.7%) correctly judged which session they had received nitrous oxide. A binomial test revealed that this proportion does not differ significantly from what would be expected by chance ($p=0.201$) and indicates that participants were unaware when they were being administered the nitrous oxide. In order to formally assess whether changes in suggestibility were affected or driven by participants' expectancy, we examined changes in suggestibility as a function of participants' expectations. Two participants expected the nitrous oxide to have no effect upon suggestibility, 19 did not know and nine participants expected the nitrous oxide to increase suggestibility. The participants who expected an increase were asked to estimate the size of the effect on a 100-mm visual analogue scale bounded by the terms 'no change' and 'large change'. The average magnitude of expected increase was 67.19 (standard deviation 11.27). The correlation between expected suggestibility change ('Don't know' responses assumed to have a magnitude of zero) and actual suggestibility change (difference in scores between the nitrous oxide and oxygen conditions) was small and non-significant ($r=0.039$, $p=0.838$ (two tailed)).

Change scores for imaginative suggestibility and imaginative ability (differences in scores between the nitrous oxide and oxygen conditions) were calculated by subtracting the oxygen score from the nitrous oxide score. These two change scores for each participant were then correlated to determine whether there was an association, revealing a significant relationship ($r=-0.511$, $p=0.004$ (two tailed)). Lower scores on the QMI indicate higher imaginative ability; thus, there exists a positive relationship between changes in imaginative ability and changes in imaginative suggestibility.

In the oxygen-alone condition, scores for imaginative ability and suggestibility were significantly correlated ($r=-0.312$, $p=0.0465$ (one-tailed)). However, in the nitrous oxide condition, the relationship was non-significant ($r=-0.194$, $p=0.152$ (one-tailed)).

Discussion

This investigation demonstrates, for the first time with a standardised test, that inhalation of 25% nitrous oxide produces objectively assessed increases in imaginative suggestibility. Nitrous oxide also increased imaginative

Table 1 Percentage pass rates and Z and p values (Wilcoxon-related samples) for items of the SHSS:C when participants were inhaling either nitrous oxide or oxygen

SHSS:C item	Item class	Percentage pass oxygen	Percentage pass N_20	Difference (N_20–oxygen)	Z	p (1-tailed)
Auditory hallucination	Cognitive (production)	6.6	3.3	-3.3	0.277	0.282
Moving hands apart	Motor (inhibition)	96.6	96.6	0	1	0.5
Post-hypnotic suggestion	Cognitive	30	33.3	3.3	0.333	0.3695
Hand lowering	Motor (production)	90	93.3	3.3	1	0.1585
Dream	Cognitive	56.6	63.3	6.7	0.577	0.282
Taste hallucination	Cognitive	43.3	50	6.7	0.707	0.24
Arm rigidity	Challenge	63.3	70	6.7	1.414	0.0785
Post-hypnotic amnesia	Cognitive	40	53.3	13.3	1.155	0.124
Negative visual hallucination	Cognitive (inhibition)	10	26.6	16.6	2.236	0.0125*
Age regression	Cognitive	56.6	73.3	16.7	2.236	0.0125*
Mosquito hallucination	Cognitive	63.3	80	16.7	1.89	0.0295*
Arm immobilisation	Motor (inhibition)	53.3	80	26.7	2.53	0.0055**

N_20 nitrous oxide
*$p < 0.05$, **$p < 0.01$

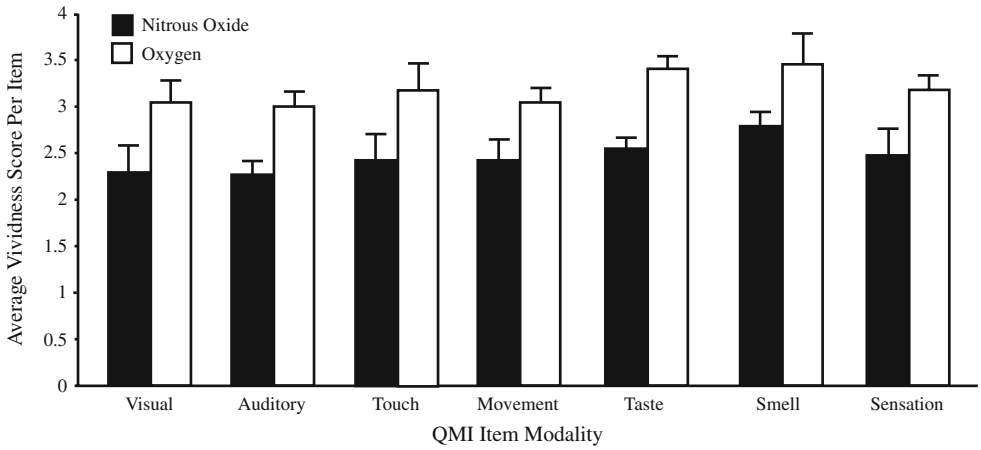

Fig. 1 Scores on the QMI broken down by modality and drug administration. Note: Lower scores indicate higher imaginative ability

ability, a change strongly correlated with the increase in suggestibility. The magnitude of the change in suggestibility induced by the inhalation of 25% nitrous oxide approached 10%. It is difficult to estimate a similar statistic for the imaginative ability scores because of the non-linear nature of the QMI scale, although with nitrous oxide inhalation average item ratings on the QMI improved from approximating 'moderately clear and vivid' towards 'very clear and comparable in vividness to the actual experience'.

Increases in imaginative ability under nitrous oxide sedation were not greater in any particular sensory type, indicating enhancement across the range of imaginative modalities. It is difficult to gauge the relative effects of nitrous oxide inhalation on different types of suggestion (motor, challenge, cognitive) because of the relative weighting of the SHSS:C towards cognitive items. The item demonstrating the single largest effect of nitrous oxide was the arm immobilisation (motor inhibition) item, although it is probable that this was due to participants feeling relaxed and heavy whilst inhaling the gas. Only one challenge item (arm rigidity) was included and demonstrated a modest increase. The nitrous oxide induced increase in suggestibility for cognitive items ranged from −3.3% for an auditory hallucination (friend's voice speaking) item to +16.7% for the mosquito hallucination and age regression items.

Previous studies have reported modest and uneven associations between imaginative ability and hypnotic suggestibility using a variety of measurement instruments (Sutcliffe et al. 1970; Crawford 1982; Glisky et al. 1995; for a review see de Groh 1989). The present study is novel in that it measures suggestibility in the absence of a hypnotic induction, yet the correlations found here are within the range found in previous studies, with a significant relationship demonstrated only in the non-drug condition.

Alterations in suggestibility are most commonly brought about by the induction of hypnosis (Kirsch and Braffman 2001) but have also been demonstrated via manipulations in expectancy (Vickery and Kirsch 1991), labelling a situation as 'hypnotic' (Gandhi and Oakley 2005) or undergoing a skills training programme (Gorassini and Spanos 1989). In order to assess whether the effects of inhaling nitrous oxide on suggestibility were due to an expectancy effect, we measured participants' expectancies at the start of the experiment. Only one third of participants expected the drug to increase suggestibility, with the majority answering that they did not know. Participants were not very accurate in identifying when nitrous oxide was being administered, with just over a third identifying in which condition they received the drug, further supporting our conclusion that expectancies did not mediate the observed effect. Lastly, we did not find expectancies to be related to the magnitude of changes in suggestibility. These results indicate the presence of a genuine drug effect upon suggestibility. Unlike other modifiers of suggestibility such as response expectancy (Kirsch 1985), the present effect seems to be independent of participant's expectations about the effect of the drug.

In the absence of an expectancy-mediated effect, it is interesting to speculate upon possible mechanisms by which nitrous oxide might mediate changes in suggestibility and imaginative ability. The strong correlation between changes in suggestibility and imaginative ability could indicate a drug effect upon a mechanism common to both of these changes. Nitrous oxide is one of the most widely used yet least well understood anaesthetic gasses (Franks and Lieb 1998) and until recently, relatively little was known about the mechanism of its action. Jevtovic-Todorovic et al (1998) found that nitrous oxide, like ketamine, acts as an antagonist at glutamatergic *N*-methyl-*d*-aspartate (NMDA) receptors, which are found throughout the brain but are densely located in the hippocampus and cerebral cortex (Morgan et al. 2004). NMDA receptor antagonists seem to preferentially block NMDA receptors on inhibitory GABAergic inter-neurons and thus increase

glutamatergic transmission via non-NMDA Glu receptors (such as α-amino-3-hydroxy-5-methyl-4-isoxazole propionate and kainite), which increases excitatory activity generally.

A brain-wide excitation might explain the present nitrous oxide induced increase in imagery vividness. The current consensus is that most of the neural processes that underlie like-modality perception are also used in imagery (Kosslyn et al. 2001), and a brain-wide excitation could explain the increases in vividness observed here across the full range of imagery modalities. Modality-appropriate sensory activation has also been observed in response to hypnotic suggestion (e.g. Szechtman et al. 1998; Kosslyn et al. 2000; Derbyshire et al. 2004), although the mechanism by which suggestions are experienced with an involuntary quality is thought to be the product of frontally mediated executive control systems (e.g. Brown and Oakley 2004; Dienes and Perner 2007). The suggestibility enhancement is more difficult to explain via a global excitation and it is useful to consider the effects of other drugs upon suggestibility.

Little research has investigated the effects of other drugs upon suggestibility in a controlled manner. Sjoberg and Hollister (1965) administered lysergic acid diethylamide (LSD), mescaline and psilocybin separately and in combination to participants and measured imaginative suggestibility before and after drug administration. Gibson et al (1977) measured the effect of benzodiazepine administration upon hypnotic suggestibility, and Kelly et al (1978) tested the effect of cannabis intoxication upon the imaginative suggestibility of participants initially scoring low to medium on a standardised scale. Details of these studies and the resulting changes in suggestibility are given in Table 2. The greatest changes in suggestibility, in order of decreasing size, are evident after administration of nitrous oxide, cannabis, LSD, mescaline, combination of [LSD+mescaline+psilocybin] and diazepam.

Sjoberg and Hollister cautiously interpreted the increases they observed for LSD, mescaline and psilocybin as a result of the withdrawal from active reality testing as a result of drug administration. Despite the advancement of cognitive models of response to suggestion (e.g. Brown and Oakley 2004; Dienes and Perner 2007), not enough is known about specific neuroanatomical correlates of such effects to allow prediction of physiological effects upon suggestion (Ott 2007). The fact that such a wide range of drugs with varying pharmacological properties have been demonstrated to affect suggestibility argues for a non-specific effect of drug upon suggestion: It is plausible that feeling sedated, dissociated, or in an altered state of consciousness with reality-testing impaired might lead participants to think they are less in control of their actions and cognitions, in turn leading to stronger endorsement of suggested effects

Table 2 Details of previous studies investigating pharmacological manipulation of suggestion

Study	Drug	Dose	Number	Suggestibility scale	Hypnotic induction?	No. items	Suggestibility		Suggestibility change	
							Non-drug	Drug	Absolute	Percentage
Sjoberg and Hollister (1965)	Mescaline	5 mg/kg	24	SSS:A/B[a]	No	17	3.33	5.5	2.16	12.7
	LSD-25	1.5 mcg/kg	24	SSS:A/B[a]	No	17	3.62	5.16	1.54	12.8
	Psilocybin	225 mcg/kg	24	SSS:A/B[a]	No	17	3.45	3.54	0.08	0.66
	Combination	1/3 of each of above	24	SSS:A/B[a]	No	17	3.33	4.75	1.41	11.75
Gibson et al (1977)	Diazepam	5 mg	34	SHSS:A/B[b]	Yes	12	4.44	4.55	0.11	0.91
	Placebo (nicotinic acid)	50 mg	37	SHSS:A/B[b]	Yes	12	5.24	5.29	0.05	0.41
Kelly et al (1978)	Cannabis	Until 'quite a bit high', average= 834 mg	17	HGSHS[c]	No	11	1.69	4.18	2.49	22.6
	Control (no drug)	NA	18	HGSHS[c]	No	11	2.5	2.56	0.06	0.54
Barber et al (1979)	Nitrous oxide	20–40%	20	Purpose built	No	5	1.5	3.3	1.8	36
	Nitrous oxide	20–40%	20	Purpose built (excluding analgesia)	No	4	1.3	2.4	1.1	27.5

SSS:A/B Stanford Suggestibility Scale Form A/B, *SHSS:A/B* Stanford Hypnotic Susceptibility Scale Form A/B, *HGSHS* Harvard Group Scale of Hypnotic Susceptibility

[a] Weitzenhoffer and Sjoberg (1961)

[b] Weitzenhoffer and Hilgard (1959)

[c] Shor and Orne (1962)

(c.f. Sjoberg and Hollister 1965). Hilgard (1986) describes the effect of a hypnotic induction (which increases suggestibility by similar amounts to the drug effects seen here) as a manipulation which impairs memory and reduces reality testing, meaning that response to the stimulation provided by the hypnotist takes precedence over planned or self-initiated action, resulting in the voice of the hypnotist becoming unusually persuasive (cf. Gorasini 2004). Future studies of the effects of drugs upon suggestibility should formally assess experiences of dissociation, relaxation, sedation and alterations in consciousness (Pekala and Kumar 2007).

Numerous studies have demonstrated powerful euphoric and dysphoric effects of nitrous oxide administration (for a review, see Walker and Zacny 2005) and it is therefore worth briefly considering the possibility of a mediating effect of emotion upon the present increases in imaginative ability and suggestibility. Holmes and Matthews (2005) briefly review the sparse literature on imagery and emotion and note that despite much theory and speculation, there is little empirical research. They found that instructions to imagine aversive events led to greater increases in reported anxiety than instructions to focus on the verbal meaning of the same descriptions. Whether anxiety or other emotional states led to increased vividness of imagery is currently unresolved, but future studies should closely assess the subjective effects of drug administration upon affect and look for interactions with imagery vividness.

There is an important caveat to the aforementioned results. The present study was single blind; although participants were unaware of whether they were receiving the drug, the experimenter who delivered the drug also administered the tests of imaginative ability and suggestibility. The QMI and SHSS:C were scripted and manualised; nevertheless, it is possible that the observed differences are due to some degree to demand characteristics and may not solely represent genuine drug effects (Orne 1962). Such a factor means that the present results should be considered preliminary and require confirmation by a double-blind study. The present results raise a number of other questions for future research. In this study, nitrous oxide concentration was fixed at 25%, low enough to avoid causing noticeable side effects, and fixed to avoid having the experimenter make a necessarily subjective judgment about how much effect the drug was having (as in Barber et al. 1979). Since drug concentration in the current study was fixed at a relatively low 25%, it will be important to determine whether there is a dose–response relationship between drug administration, suggestibility and imaginative ability. Additionally, we are concerned that the objective scoring criterion for each suggestibility item used in the present study may have masked more subtle effects in how strongly each suggestion was perceived and recommend the additional use of subjective assessment of response to suggestion. Similarly, a measure of imaginative ability using an interval linear scaling might be preferable to the ordinal responses required by the QMI, and a number of theoretically derived measures of imagery have recently been developed (McAvine and Robertson 2006–2007). Practically, since the objective of clinicians is to maximise responsiveness to suggestion, it will be interesting to see whether nitrous oxide administration plus a hypnotic induction would increase suggestibility additively. Finally, since nitrous oxide also has analgesic effects, it will be interesting to see how these interact with suggestions for analgesia since many clinicians informally report a synergistic effect between the two (Simons et al. 2007). Hypnosis in combination with conscious sedation has been shown to be clinically superior to conscious sedation plus alternative psychological approaches (Faymonville et al. 1997), and it will be important to test the analgesic properties of nitrous oxide alone and in combination with hypnotic suggestion.

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References

Allen WA (1972) Relative analgesia: an introductory note. Br Dent J 133:25–26

Barber J, Donaldson D, Ramras S, Allen GD (1979) The relationship between nitrous oxide conscious sedation and the hypnotic state. J Am Dent Assoc 99(4):624–626

Benham G, Bowers S, Nash M, Muenchen R (1998) Self-fulfilling prophecy and hypnotic response are not the same thing. J Pers Soc Psychol 75:1604–1613. doi:10.1037/0022-3514.75.6.1604

Bertrand LD (1989) The assessment and modification of hypnotic susceptibility. In: Spanos NP, Chaves JF (eds) Hypnosis: the cognitive–behavioral perspective. Prometheus Books, Buffalo (NY), pp 18–31

Betts GH (1909) The distribution and functions of mental imagery. Teachers College, Columbia University, New York

Bingham GD (1964) Rapid hypnosis by using nitrous oxide. Am J Clin Hypn 7:226–228

Brown RJ, Oakley DA (2004) An integrative cognitive theory of hypnosis and high hypnotisability. In: Heap M, Brown RJ, Oakley DA (eds) The highly hypnotizable person. Routledge, London, pp 152–186

Cass N, Cass L (1994) Pharmacology for anaesthetists. Churchill Livingstone, Edinburgh

Crawford HJ (1982) Hypnotizability, daydreaming styles, imagery vividness, and absorption: a multidimensional study. J Pers Soc Psychol 42:915–926

de Groh M (1989) Correlates of hypnotic susceptibility. In: Spanos NP, Chaves JF (eds) Hypnosis: the cognitive–behavioural perspective. Prometheus, Buffalo, NY, pp 32–63

Derbyshire SWG, Whalley MG, Stenger VA, Oakley DA (2004) Cerebral activation during hypnotically induced and imagined pain. Neuroimage 23:392–401. doi:10.1016/j.neuroimage.2004.04.033

Dienes Z, Perner J (2007) Executive control without conscious awareness: the cold control theory of hypnosis. In: Jamieson GA (ed) Hypnosis and conscious states. Oxford University Press, Oxford

Eysenck HJ, Rees WL (1945) States of heightened suggestibility: narcosis. J Ment Sci 91:301–310

Faymonville ME, Mambourg PH, Joris J, Vrijens B, Fissette J, Albert A, Lamy M (1997) Psychological approaches during conscious sedation. Hypnosis versus stress reducing strategies: a prospective randomized study. Pain 73:361–367. doi:10.1016/S0304-3959(97)00122-X

Franks NP, Lieb WR (1998) A serious target for laughing gas. Nat Med 4(4):383–384. doi:10.1038/nm0498-383

Gandhi B, Oakley DA (2005) Does 'hypnosis' by any other name smell as sweet? The efficacy of 'hypnotic' inductions depends on the label 'hypnosis'. Conscious Cogn 14:304–315. doi:10.1016/j.concog.2004.12.004

Gibson HB, Corcoran ME, Curran JD (1977) Hypnotic susceptibility and personality: the consequences of diazepam and the sex of the subjects. Br J Psychol 68:51–59

Glisky ML, Tataryn DJ, Kihlstrom JF (1995) Hypnotizability and mental imagery. Int J Clin Exp Hypn 43:34–54

Gorasini DR (2004) Enhancing hypotisability. In: Heap M, Brown RJ, Oakley DA (eds) The highly hypnotizable person. Routledge, London, pp 213–239

Gorassini DR, Spanos NP (1989) The Carleton Skill Training Programme for modifying hypnotic suggestibility: original version and variations. In: Kirsch I, Capafons A, Amigó S, Cardeña-Buelna E (eds) Clinical hypnosis and self-regulation therapy: a cognitive–behavioural perspective. American Psychological Association Books, Washington, DC, pp 141–77

Hilgard ER (1986) Divided consciousness: multiple controls in human thought and action (expanded edition). Wiley, New York

Hilgard ER, Hilgard JR (1975) Hypnosis in the relief of pain. Brunner/Mazel, Levittown, PA

Holmes EA, Matthews A (2005) Mental imagery and emotion: a special relationship? Emotion 5:489–497. doi:10.1037/1528-3542.5.4.489

Jevtovic-Todorovic V, Todorovic SM, Mennerick S, Powell S, Dikranian K, Benshoff N, Zorumski CF, Olney JW (1998) Nitrous oxide (laughing gas) is an NMDA antagonist, neuroprotectant and neurotoxin. Nat Med 4:460–463. doi:10.1038/nm0498-460

Kelly SF, Fisher S, Kelly RJ (1978) Effects of cannabis intoxication on primary suggestibility. Psychopharmacology 56:217–219

Kihlstrom JF (2007) Modified version of the SHSS:C. Retrieved September 30th, 2008, from http://socrates.berkeley.edu/~kihlstrm/PDFfiles/Hypnotizability/SHSSC%20Script.pdf

Kirsch I (1985) Response expectancy as a determinant of experience and behaviour. Am Psychol 40:1189–1202

Kirsch I, Braffman W (2001) Imaginative suggestibility and hypnotizability. Curr Dir Psychol Sci 10(2):57–61. doi:10.1111/1467-8721.00115

Kosslyn SM, Thompson WL, Constantini-Ferrando MF, Alpert NM, Speigel D (2000) Hypnotic visual illusion alters color processing in the brain. Am J Psychiatr 157:1279–1284. doi:10.1176/appi.ajp.157.8.1279

Kosslyn SM, Ganis G, Thompson WL (2001) Neural foundations of imagery. Nat Rev Neurosci 2:635–642

Lippe HT (1944) Nitrous oxide analgesia in cavity preparation. Temple Dental Review 14:7

McAvine LP, Robertson IH (2006-2007) Measuring visual imagery ability: a review. Imagin Cogn Pers 26:191–211. doi:10.2190/3515-8169-24J8-7157

Morgan CJA, Mofeez A, Brandner B, Bromley L, Curren HV (2004) Acute effects of ketamine on memory systems and psychotic symptoms in healthy volunteers. Neuropsychopharmacology 29:208–218. doi:10.1038/sj.npp.1300342

Orne MT (1962) On the social psychology of the psychological experiment: with particular reference to demand characteristics and their implications. Am Psychol 17(11):776–783

Ott U (2007) States of absorption: in search of neurobiological foundations. In: Jamieson GA (ed) Hypnosis and conscious states. Oxford University Press, Oxford

Pekala RJ, Kumar VK (2007) An empirical-phenomenological approach to quantifying consciousness and states of consciousness: with particular reference to understanding the nature of hypnosis. In: Jamieson GA (ed) Hypnosis and conscious states. Oxford University Press, Oxford

Perry C, Nadon R, Button J (1992) The measurement of hypnotic ability. In: Fromm E, Nash M (eds) Contemporary hypnosis research. Guilford, New York, pp 459–490

Seladin HM (1947) Practical anesthesia for dentistry and oral surgery. Lea & Febiger, Philadelphia

Sheehan PW (1967) A shortened form of Betts' questionnaire upon mental imagery. J Clin Psychol 23:386–389

Shor RE, Orne EC (1962) Harvard group scale of hypnotic susceptibility: Form A. Consulting Psychologists, Palo Alto, California

Simons D, Potter C, Temple G (2007) Hypnosis and communication in dental practice. Quintessence, London

Sjoberg BM, Hollister LE (1965) The effects of psychomimetic drugs on primary suggestibility. Psychopharmacology 8:251–262

Spanos NP (1986) Hypnosis and the modification of hypnotic susceptibility: a social psychological perspective. In: Naish P (ed) What is hypnosis? Open University Press, Philadelphia, pp 85–120

Sutcliffe JP, Perry CW, Sheehan PW (1970) Relation of some aspects of imagery and fantasy to hypnotic susceptibility. J Abnorm Psychology 76:279–287

Szechtman H, Woody E, Bowers K, Nahmias C (1998) Where the imaginal appears real: a positron emission tomography study of auditory hallucinations. Proc Natl Acad Sci USA 95:1956–1960. doi:10.1073/pnas.95.4.1956

Vickery AR, Kirsch I (1991) The effects of brief expectancy manipulations on hypnotic responsiveness. Contemp Hypn 8:167–171

Wagman R, Stewart CG (1974) Visual imagery and hypnotic susceptibility. Percept Mot Skills 38:815–822

Walker DJ, Zacny JP (2005) Subjective effects of nitrous oxide. In: Earlywine M (ed) Mind-altering drugs: the science of subjective experience. Oxford University Press, Oxford

Weitzenhoffer AM, Hilgard ER (1959) Stanford hypnotic susceptibility scale, Forms A and B. Consulting Psychologists, Palo Alto, CA

Weitzenhoffer AM, Hilgard ER (1962) Stanford hypnotic susceptibility scale, Form C. Consulting Psychologists, Palo Alto, CA

Weitzenhoffer AM, Sjoberg BM (1961) Suggestibility with and without 'induction of hypnosis'. J Nerv Ment Dis 132:204–220

Westcott TB, Rosenstock E (1976) Reliability of two measures of imagery. Percept Mot Skills 42:1037–1038

White K, Ashton R, Law H (1974) Factor analyses of the shortened form of Betts' Questionnaire Upon Mental Imagery. Aust J Psychol 26:183–190