Inhibition of retrieval in hypnotic amnesia

Citation for published version:

Digital Object Identifier (DOI):
10.1093/nc/nix005

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published In:
Neuroscience of Consciousness

Publisher Rights Statement:
This article has been accepted for publication in Neuroscience of Consciousness ©: 2017, Graham A. Jamieson Marios D. Kittenis Ruxandra I. Tivadar Ian D. Evans. Published by Oxford University Press. All rights reserved.

General rights
Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.
Inhibition of retrieval in hypnotic amnesia: dissociation by upper-alpha gating

Graham A. Jamieson1,*, Marios D. Kittenis2, Ruxandra I. Tivadar3 and Ian D. Evans4

1School of Behavioural, Cognitive and Social Sciences, Psychology Lane, University of New England, Armidale, NSW 2351, Australia; 2School of Philosophy Psychology and Language Sciences, University of Edinburgh, 7 George Square, Edinburgh, EH8 9JZ, UK; 3Department of Radiology and Clinical Neurosciences, University Hospital Center and University of Lausanne, Rue du Bugnon 46, Lausanne, 1011, Switzerland; 4School of Psychology, Building 32, University of Wollongong, NSW 2522, Australia

*Correspondence address. School of Behavioural, Cognitive and Social Sciences, University of New England, Armidale, NSW 2351, Australia. Tel: +61 2 6773 4279; E-mail: gjamieso@une.edu.au

Abstract

Hypnotic amnesia is a functional dissociation from awareness during which information from specific neural processes is unavailable to consciousness. We test the proposal that changes in topographic patterns of cortical oscillations in upper-alpha (10–12 Hz) band selectively inhibit the recall of memories during hypnotic amnesia by blocking availability of locally processed information at specific points in retrieval. Participants were prescreened for high or low hypnotic susceptibility. Following hypnotic induction, participants were presented with a series of 60 face stimuli and were required to identify affective expressions. Participants received a suggestion for amnesia for these faces. They were then presented with a set of 30 old and 30 new faces and identified each as old or new. Amnesia suggestion was lifted and recall tested using the remaining 30 old faces and another 30 new faces. Exact Low Resolution Brain Electromagnetic Tomography source analyses are reported for 64 channel event-related electroencephalogram recorded from highs showing reversible amnesia to old faces. For high-susceptible participants, the amnesia suggestion significantly increased old faces wrongly identified while for low-susceptible participants amnesia suggestion increased the new faces wrongly identified. There were no differences between high- and low-susceptible participants following reversal of the suggestion. For previously seen faces which were wrongly identified, compared to new faces correctly identified, (late) evoked upper-alpha is significantly higher in right BA7 in a region implicated in top-down executive control to assist recall of visual information. Lagged nonlinear connectivity between cortical sources in upper-alpha in the same condition showed significantly increased connectivity between right BA34 (parahippocampal gyrus) and right BAs 7, 20 and 22. Integration between these regions is essential for recall of recent faces. During amnesia, spatial and temporal coordination of upper-alpha appears to suppress integrated functioning of these regions (hence recall). These patterns were absent after reversal of amnesia suggestion.

Key words: alpha inhibition; functional connectivity; face recognition; hypnosis; amnesia; dissociation
Introduction

A wide variety of hypnotic phenomena can be reliably induced in responsive individuals using standardized procedures which permit them to be studied under laboratory conditions (Hilgard, 1965, 1977). While hypnosis research is now established as a legitimate and fertile field for cognitive neuroscience investigation (Oakley and Halligan, 2013), a comprehensive understanding of hypnotic phenomena remains elusive and little theoretical consensus has been reached regarding their nature. This study seeks to test a specific model of hypnosis and of the neurophysiological mechanisms by which high-susceptible individuals are able to maintain experiences suggested to them without being overridden by salient contradictory aspects of inner or outer reality.

The core feature of this theory may be described as a change in the relationship between mental processes which normally operate together, so that one is no longer under the influence of another. This psychological process was termed dissociation by Pierre Janet (Van der Hart and Horst, 1989) and identified by him as underlying not only hypnotic responses but also a range of hysterical symptoms that Freud had sought to explain with his competing psychodynamic theory of repression. Hilgard (1977) later reformulated Janet’s dissociation process as a cognitive psychological theory in which experience corresponds to representations at the highest level of a hierarchically nested system of control governing the operation of numerous specific lower level psychological processors (cf. Jack and Shallice, 2001). Dissociation was conceptualized by Hilgard as a temporary split in the unity of control at this highest level resulting in parallel streams of executive control (and thus, on this account, awareness) each with limited access to the inputs, outputs and internal states of the other.

Bowers and co-workers then developed the first fully cognitive neuropsychological account of dissociation in hypnosis which they called ‘dissociated control’. Their account was based upon the Norman and Shallice (1986) model of executive control as a (pre)frontal system of top-down attention which selectively activates otherwise automatic, and more posterior, brain processes guided by conscious goals and performance feedback (Bowers, 1990, 1992; Woody and Bowers, 1994). In this theory, hypnotic dissociation arises from the disruption of regulation by this top-down control system, leaving posterior processing mechanisms to operate unconsciously (unsupervised) and nonvolitionally (automatically), both recognized hallmarks of the classic hypnotic suggestion effect (Weitzenhoffer, 1980). Gruzelsier and Warren (1993) presented evidence from neuropsychological testing that cognitive skills selectively impaired by left frontal cortical lesions are transiently impaired for more highly susceptible participants during a hypnotic condition providing early initial support for this view.

Dissociation theories of hypnosis continue to interact with advances in the neuroscience of cognitive control. Functional imaging studies have fractionated the operation of the executive control system in classic executive function tasks (such as the Stroop paradigm) into separate monitoring and control components (MacDonald et al., 2000). Egner et al. (2005) employed a similar Stroop response conflict paradigm in conjunction with fMRI, to show that hypnosis leads to increased conflict monitoring activity in the anterior cingulate cortex in those with high (but not low) hypnotic susceptibility. At the same time, they found no effect for hypnosis or hypnotic susceptibility on the activity of task set or goal representations in left lateral prefrontal cortex. They further employed electroencephalogram (EEG) measures of gamma band coherence to assess functional connectivity changes between these cortical regions and found a decrease in such connectivity (coordinated activity), once again in the high-susceptible participants during hypnosis. Together, functional magnetic resonance imaging (fMRI) and EEG results were interpreted as indicating a state of functional dissociation following a hypnotic induction in the form of a failure to integrate information between monitoring and control components of the frontal executive system, but only in those with high hypnotic susceptibility. In this condition, top-down control processes (for example the goals of hypnotic suggestions) selectively activate lower-level response processes, but do so relatively free from the disruption of negative feedback from external and internal monitoring systems.

What is common to all recent forms of dissociation theory is that they operate in hierarchically organized networks of functionally specialized and reciprocally connected neural processes. Dissociation in these networks is functional, in that either the specialized processing activity of specific neural regions is disrupted, or the flow of psychologically salient information to or from these regions is disrupted, temporarily altering the functioning of the entire network. Ultimately both forms of dissociation, loss of local functional activity and loss of functional connectivity, are so closely intertwined that whenever one occurs in a currently functioning network the other will follow. What all forms of dissociation theory lack is a common neurobiological mechanism that can implement the different specific dissociations that would be required to support the content of diverse hypnotic suggestions.

Broad-band cortical alpha activity is closely associated with reduced functional processing activity in the sensory cortex when sense input is withdrawn; e.g. closing the eyes leads to synchronized (increased amplitude) alpha activity in the visual cortex (Pfurtscheller, 2003). However, increased alpha activity is also widely reported in many perceptual and cognitive paradigms, with many reviews converging to suggest a specific functional role for alpha in support of current cognitive tasks, by active inhibition of information processing in regions which may compete or interfere with task requirements (Jensen et al., 2014).

Of particular relevance to the present study, Klimesch et al. (2007) (see Klimesch, 1999 for a review) have identified increased activity in the upper-alpha band (10–12 Hz) observed across a range of memory tasks as facilitating performance in correct retrieval of information from semantic memory. Klimesch et al. (2007) extend these observations to argue that the cognitive role of increased alpha activity is to inhibit access to memory representations which compete with current task demands at critical stages of information processing. Recent studies add support to this interpretation; e.g. Buschman et al. (2012) found that alpha activity in prefrontal cortex of monkeys undertaking a rule-based stimulus–response task was positively associated with the inhibition of incorrect competing rules. On this account, temporal and spatial changes in alpha activity direct the flow of information processing in task-related networks by actively inhibiting the processing of specific types of information in specialized cortical areas at critical time points.

Whereas locally synchronized alpha activity suppresses action potentials at the peak of each wave, this suppression is released during the wave trough (Jensen and Mazaheri, 2010) producing pulses of inhibition in efferent cortical connections from that region synchronized to the phase of the local alpha
(in this case upper-alpha) rhythm. It is expected that this local alpha synchronization (amplitude) will drive entrainment in the timing (phase) of the alpha rhythm throughout the functional network with which it is currently engaged. In a reciprocally connected network, with short (relative to the alpha cycle) but differing transmission times, the resulting phase synchronization will be time-lagged but nonlinear (Pascual-Marqui, 2007a; Brown, 2009). While local amplitude increases in event-related upper-alpha implement inhibition of specialized processing regions, this is expected to be accompanied by increases in lagged nonlinear connectivity (upper-alpha phase synchronization) between regions in the same functional network, thereby inhibiting active information processing in the network as a whole. The functional effects of inhibitory control through (upper) alpha amplitude and phase synchronization fit closely with the descriptions of information processing dynamics found in dissociation theories of hypnosis. We theorize that both these interrelated neurophysiological mechanisms are the means by which high-susceptible people temporarily inhibit the operation of specific cognitive processes and the availability or influence of specific forms of information explicitly required by ‘dissociative’ hypnotic suggestions (Terhune et al., 2011).

The hypnotic amnesia suggestion is a paradigm case of dissociation; it is a difficult hypnotic hallucination requiring a high level of hypnotic susceptibility for success (Hilgard, 1965). The hypnotist suggests that memories of events occurring during the hypnotic session cannot be recalled until a specific command is given. The phenomenon of hypnotic amnesia is reliably, safely and reversibly produced under laboratory conditions in prescreened high-susceptible individuals by simple direct amnesia suggestion. In his cognitive formulation of ‘neo-dissociation’ theory, Hilgard (1977) termed the functional barriers to the flow of information between monitoring and control functions within the central executive as ‘amnestic barriers’, in effect implying that the mechanism of hypnotic amnesia was the fundamental mechanism in all forms of hypnotic dissociation. Therefore, this study focuses on hypnotic amnesia as a paradigm case in which to test the theory of functional inhibition by upper-alpha as the mechanism of hypnotic dissociation.

Suggested hypnotic amnesia has also been proposed as an experimental model of functional or psychogenic amnesia. Both phenomena involve retrieval failures which have no overt physiological basis, but appear to be related to changes in executive functions such as attention monitoring and control (Mendelsohn et al., 2008). Psychogenic amnesia and other functional syndromes are clinically classed as dissociative disorders and described as being ‘characterized by transient or chronic alterations in consciousness, memory, perception, identity or emotion’ (Staniloiu et al., 2012). Fugue states, multiple personality, somatizing and conversion disorders, spirit possession and mediumship all share in common dissociations in the conscious access of information and processes upon which the normal identity of the person is based. Therefore, understanding the neurophysiological basis of hypnotic amnesia may also provide a basis for understanding how memory mechanisms are altered in a broad range of dissociative psychological conditions.

Current standardized tests of hypnotic amnesia require participants to engage in free recall of the suggestions presented earlier in the hypnotic session. However, this form of hypnotic amnesia suggestion is not well suited to the requirements of EEG recording paradigms and the analysis of functionally specified event-related changes in electro-cortical activity, or even the behavioural analysis of specific types of responses. Therefore, a more controlled, event-related recognition paradigm, permitting the creation of epochs around precise stimulus and response events with a correspondingly specific form of hypnotic amnesia suggestion is required as a test case for the current theory. For this purpose, an adaptation of the Old–New recognition memory paradigm (see Squire et al., 2007) in which participants must identify specific stimuli as either old (recognized as previously presented) or new (unrecognized), is employed using face stimuli in conjunction with a simple suggestion for amnesia for the faces presented earlier in the hypnosis session. Face recognition has itself been the subject of intensive investigation using EEG and brain imaging paradigms and is known to have clearly delineated and well-mapped functional neural networks (Gobbini and Haxby, 2007). Specifically, it is hypothesized that in high-susceptible participants given a hypnotic amnesia suggestion for recently viewed faces, evoked upper-alpha will suppress processing at cortical sources required for face recognition on those trials where amnesia suggestion successfully blocks recognition (compared to functionally equivalent trials in which amnesia suggestion is ineffective). Similarly, upper-alpha lagged nonlinear functional connectivity between key nodes of the face recognition network will be significantly greater in the same comparisons. While it is expected that the regions showing these patterns of response will be identifiable with nodes within face recognition network results in the established literature, neither the precise regions nor the time window of these effects is specified a priori. If this theory of hypnotic dissociation is correct, then these patterns will not be found in the equivalent trials, either in the same high-susceptible participants when amnesia suggestion is cancelled, or in low-susceptible participants (who are unable to respond to hypnotic suggestions) during suggested amnesia.

Materials and Methods

Participants

Approximately 700 English speakers were first assessed for their hypnotic susceptibility using the Harvard Group Scale of Hypnotic Susceptibility, Form A (HGSHS-A) (Shor and Orne, 1962); this was administered after public lectures on hypnosis research presented by the authors at various academic institutions in Edinburgh, to those attendees who volunteered to take part. A total of 82 of these volunteers who scored either >9 (high susceptibility), or ≤3 (low susceptibility) in that scale were then tested again in individual sessions using the ‘Stanford Hypnotic Susceptibility Scale, Form C’ (SHSS:C) (Weitzenhoffer and Hilgard, 1962). In all, 41 individuals who scored >9 or ≤3 in both scales were then invited to take part in the experiment, and 24 of these accepted the invitation and participated in the study (n = 24; 15 high-susceptible; 15 female; mean age: 27.2 years; age range: 18–65 years) [note that while participants are not informed of their susceptibility level it will be apparent to most, following screening, that they are relatively responsive or unresponsive to the suggestions being administered. Differences in self-perception of response to hypnotic suggestion are likely between the high- and low-susceptible experimental groups. For an experimental evaluation of effect of response expectancies on response to suggestion see Benham et al. (2006)]. The study received ethical approval from the Psychology Research Ethics Committee of Edinburgh University (ref. 140–1213/7).
participants gave their written informed consent and were paid £15 for their participation.

**Apparatus and materials**

Experimental sessions were conducted in the Cognitive Neuroscience Suite laboratories of Edinburgh University in an electrically shielded and dimly lit room, using a ‘BioSemi’ (BioSemi Inc., Amsterdam, The Netherlands) 64-channel EEG system and headcap with pin-type active electrodes arranged in the 10/20 system. For a detailed description of the referencing and grounding conventions used by the BioSemi system, see www.biosemi.com/faq/cms&drl.htm. BioSemi maintains an output impedance of less than 1 Ohm on all active electrodes. The recording was referenced online to the average of left and right mastoid and offline to common average reference. The EEG signal was sampled at 512 Hz and recorded through a 0.16–100 Hz bandpass filter. Electrooculogram (EOG) was recorded via BioSemi flat-type active electrodes, placed on the orbis ocularis muscle above and below the left eye and on the left and right outer canthi, approximately 1 cm lateral to either eye.

The face recognition memory task was presented using a computer running ‘Inquisit’, a command-driven software platform for the implementation of cognitive and psychophysiological experimental paradigms (Millisecond Software, USA). Inquisit has been independently tested for timing accuracy using a system developed for assessing experimentation software, and the relative difference between the timing data given by Inquisit and this system never exceeded 1.84 ms (Clercq et al., 2003). A command script written for this software controlled the presentation of stimuli, recorded behavioural task performance (accuracy and reaction times), and delivered associated signals to the BioSemi amplifier (TTL logic) to mark the time and type of stimulus and response events in the EEG records.

Two unique sets of 60 faces (i.e. 120 different faces) obtained from the University of Stirling Psychological Image Collection (http://pics.psych.stir.ac.uk) were used as stimuli. The faces were black and white photographs (approximately 5 cm wide by 6.5 cm high) of the head and shoulders of men and women, with either a neutral, happy or sad emotional expression (20 faces with each expression in each set), facing directly towards the participant. Each set consisted of 30 men and 30 women. The faces were presented at the centre of a computer screen situated approximately 1.5 m from the participant with the centre of the screen at eye level.

**Procedure**

After electrode placement, participants were taken to the experimental room and seated in front of a desk with a computer screen and mouse; a neck pillow was used to increase participant comfort. The experimental procedure was described and participants were given an opportunity to practice example trials of the memory tasks they would later perform (Acquisition and Recognition Tasks, described below), and to ask any questions regarding the procedure and experiment. When the participant was settled and ready to begin, 2 min of eyes-closed, resting EEG was first recorded as a sample of spontaneous brain activity before the hypnotic induction. A 15-min, guided-relaxation-based hypnotic induction procedure was verbally administered (see Supplementary Material 1 for this script).

Immediately following the hypnotic induction, 2 min of (eyes closed) resting EEG was recorded (during-hypnosis sample), and participants were then instructed to complete the Acquisition task in the computerized memory paradigm. In this task, 60 faces (the memory acquisition set) are sequentially presented in a randomized order for a 1-s duration, and after each presentation participants are asked to indicate with a mouse button press whether each face shows a neutral or an emotional (sad/happy) expression. Responses were recorded but not used in the analysis; this affective recognition task was designed to engage attention and encourage deeper cognitive processing, in order to facilitate memory encoding of the presented faces.

In each of the two subsequent recognition memory tests, 60 faces were presented: 30 of the faces shown during the acquisition stage, randomly interspersed with 30 faces never presented before. Participants were asked to indicate with a mouse button press whether they had seen each face before (Old), or whether it was shown for the first time (New). In each trial, a fixation cross was presented in the centre of the screen (for 500 ms) before each face stimulus was presented (for 1000 ms); this was followed by a blank screen (for 300 ms) and then the words ‘Old’ and ‘New’, each presented either on the left- or right-hand side of the screen. Participants were asked to press either the left or right button on the mouse according to which side of the screen the correct response appeared. The placement of ‘Old’ and ‘New’ choices on the left or right side was randomized between trials to prevent anticipatory responses and to maintain attentional engagement with the task (and the number of ‘Old–New’ and ‘New–Old’ presentations was counterbalanced within tasks).

After participant responses (Old or New selection), an inter-trial interval (blank screen) followed for a randomized duration (1000–1500 ms) before the next trial began (Fig. 1).

After the memory acquisition task was completed, participants were given a hypnotic suggestion to experience amnesia for the faces they had just seen (adapted from the SHSS:C post-hypnotic amnesia item; see Supplementary material 2a for details), and were then asked to perform the first recognition task (hypnotic amnesia condition). After this task was completed, hypnotic amnesia was cancelled with a further suggestion (see Supplementary material 2b) and participants were asked to perform the second recognition task (no amnesia condition). After both recognition tests had been completed, the hypnotic induction was reversed and terminated and a further 2 min of eyes-closed resting EEG (post-hypnosis) was sampled. Recording was then terminated; participants were debriefed and thanked for their participation.

**EEG data analysis**

Data processing was conducted using MATLAB r2011a (The Mathworks Inc., 2011) and IBM SPSS Statistics v21 (IBM Corporation, 2012). EEG data were re-referenced offline to a common average, then subjected to a second-order Butterworth bandpass filter set to 0.5–48 Hz. Epochs were extracted relative to the onset of face stimuli (t = 0), from −250 ms pre-stimulus to 1250 ms post-stimulus onset, and baseline adjusted using the pre-stimulus interval. Eye movement artefacts were removed using independent components analysis via Fully Automated Statistical Thresholding for EEG artifact Rejection (FASTER) (Nolan et al., 2010). Epochs were visually inspected for any remaining artefacts, and any contaminated epochs were removed.

A bandpass filter of 10–12 Hz was applied to the dataset to extract upper-alpha activity. Epochs were averaged in groups using a combination of the following factors: presence or absence of amnesia suggestion, whether the face was new or old,
and whether the recognition response was accurate or inaccurate. The processed data was then analysed using eLORETA (exact Low Resolution Brain Electromagnetic Tomography) (Pascual-Marqui, 2007b) to identify sources of upper-alpha activity. Based on the scalp-recorded electric potential distribution, the eLORETA software (publicly available at http://www.uzh.ch/keyinst/loreta.htm) was used to compute the cortical three-dimensional distribution of current source density (CSD). The eLORETA method is a discrete, three-dimensional distributed, linear, weighted minimum norm inverse solution. The specific weights used in eLORETA endow the tomography with the property of exact localization to test point sources, yielding images of current density with exact localization, albeit with low spatial resolution (i.e. neighbouring neuronal sources will be highly correlated). The method is described in detail in Pascual-Marqui (2009) and Pascual-Marqui et al. (2011). For each connectivity analysis, regions of interest (ROI) were identified using the peaks in the maximum voxel statistic plot of the preceding eLORETA analysis (see Supplementary material 3); then any voxel with at least four rhythmic peaks was considered a region of interest (these sources were considered separately for each connectivity analysis discussed in the results). This resulted in six ROIs being entered into the connectivity analysis for the hypnotic amnesia condition and eight ROIs for the amnesia lifted condition; significant connectivity results are presented below.

Results

Data inclusion

From the 24 participants who completed the study, the first 5 to be tested were excluded from further analyses due to a problem with the recording of event markers, and one additional participant was excluded due to the high level of artefact in their EEG recording. Data from the 18 remaining participants (7 low- and 11 high-susceptible) were included in subsequent analyses.

Behavioral results

Response accuracy

A mixed design analysis of variance (ANOVA) was carried out on incorrect responses to the Old–New Face recognition task using AMNESIA (Present versus Lifted) and FACE (Old versus New) as within-subject factors, and GROUP (High versus Low Hypnotic Susceptibility) as a between-subjects factor. Response accuracy was analysed for 8 low- and 11 high-susceptible participants. A highly significant interaction effect was observed between all three factors; F(1,16) = 19.050, P < 0.001, η² = 0.544.

A significant two-way interaction effect was also found for GROUP by FACE, F(1, 16) = 9.424, P < 0.007, η² = 0.371. No other significant main effects or interaction effects were observed for Old–New response accuracy. The three-way interaction is the focus of interpretation (Keppel and Wickens, 2004). Mean accuracy (incorrect responses) with 95% confidence intervals for all conditions in this three-way interaction are presented in Fig. 2. It is apparent when comparing the high- and low-susceptible groups, that errors in recognizing old faces and errors in recognizing new faces are significantly differentiated in the presence of amnesia suggestion, but not following the lifting of the amnesia suggestion. However, the direction of the difference between the Old and the New face errors during amnesia suggestion is reversed for the high- and low-susceptible groups, respectively.

Reaction time

Two high-susceptible participants produced no errors in identifying new faces in the amnesia condition; one low- and one high-susceptible participant produced no errors in recognizing old faces in the amnesia condition, therefore their data is excluded from the reaction time analyses reported here. This left six low- and eight high-susceptible participants available for the reaction time analysis below. Reaction time was analyzed using a mixed design ANOVA with AMNESIA (Present versus Lifted), FACE (Old versus New) and ACCURACY (Correct versus Incorrect) as within-subject factors and GROUP (High versus Low Hypnotic Susceptibility) as the between-subjects factor.

There was a significant main effect for ACCURACY; F(1, 12) = 7.630, P < 0.017, η² = 0.389 with incorrect responses \( M = \)
1160 ms, \( \text{SEM} = 39 \) being slower than correct responses (\( \text{M} = 1128 \text{ ms, SEM} = 49 \)). However, this must be interpreted in light of a highly significant three-way interaction between FACE, ACCURACY and GROUP; \( F(1, 12) = 24.936, P < 0.001, \eta^2 = 0.675 \). This interaction is presented in Fig. 3, where it can be seen that the high-susceptible group responds significantly slower on New face errors (than New face correct), while the low-susceptible group responds significantly slower on Old face errors (than Old face correct).

A marginal four-way interaction was also present \( F (1, 12) = 4.587, P < 0.053, \eta^2 = 0.277 \) but this is not interpreted here due to failure to reach significance. No other significant main effects or interaction effects were observed for reaction time.

eLORETA

Amnesia present: evoked upper-alpha

In order to identify cortical sources of evoked upper-alpha activity specific to successful responses to suggested amnesia (i.e. failure to recognize Old faces), eLORETA was used to compare the evoked 10–12 Hz activity in high-susceptible participants in the Amnesia condition when Old face stimuli were followed by an incorrect (i.e. ‘New’) response, to activity in the same participants and condition when New face stimuli were followed by a correct (i.e. ‘New’) response. In both cases, participants report having the same experience, i.e. the face stimuli are perceived as novel and unfamiliar, although in the first case it represents a recognition failure while in the second case this is a correct judgement. The behavioural responses of two high-susceptible participants failed to show a successful amnesia suggestion effect (i.e. their recognition accuracy for Old faces was high and was unchanged between testing during amnesia suggestion and after the cancellation of amnesia), therefore they were excluded from the EEG source analysis results presented below. These are based on the nine high-susceptible participants whose face recognition accuracy results show a successful effect of the amnesia suggestion.

As there was no hypothesis concerning when effects were expected to occur, all time points in the epoch from stimulus onset to +1000 ms post-stimulus onset were analysed; a maximally conservative approach with corrections for multiple testing tightly constraining the probability of obtaining significant results. Under these stringent conditions a random permutation test with 5000 iterations (Nichols and Holmes, 2002) identified a significant increase in evoked upper-alpha in epochs related to Old face stimuli followed by incorrect responses (i.e. recognition failures) at 908 ms post-stimulus onset. This comparison reached significance at a single voxel in right BA7 (Superior Parietal Lobule, MNI: 15, –60, 65; \( F = 2.78, P = 0.026 \); see Fig. 4).

Amnesia present: lagged nonlinear connectivity

A lagged nonlinear connectivity analysis (Pascual-Marqui, 2007a) for the upper-alpha band was undertaken for the time segment –300 ms to +300 ms around the time point of peak statistical difference between Old faces identified as new and New faces identified as new in the previous analysis (that is 608–1208 ms...
This analysis was conducted on the nine high-susceptible participants whose behavioural responses demonstrated effects of the suggested amnesia for faces. See Supplementary material 3 and Methods section above for details of ROI selection process. Those ROI with significantly increased lagged nonlinear upper-alpha connectivity for this comparison in amnesia present were:

- **BA7**: MNI 45, 60, 50 (right superior parietal lobule)
- **BA20**: MNI 40, 35, 20 (right fusiform gyrus)
- **BA22**: MNI 55, 35, 5 (right middle temporal gyrus)
- **BA34**: MNI 20, 10, 20 (right parahippocampal gyrus)

Lagged nonlinear connectivity for each pair of ROI was estimated as the average of that obtained between all pairs of voxels within a 10 mm radius of each ROI coordinate. Statistical comparisons of these connectivity estimates were made between Old face stimuli followed by incorrect ‘new’ responses, and New face stimuli followed by correct ‘new’ responses, using the same random permutation method as above to determine significance while correcting for multiple comparisons. Those connections with significantly increased lagged nonlinear upper-alpha connectivity are shown in red in Fig. 5. There were no significant decreases in this connectivity measure.

### Amnesia lifted: evoked upper-alpha

In order to determine whether the cortical source differences in inhibitory evoked upper-alpha activity identified above in high-susceptible participants during suggested amnesia are truly specific to the functional demands of these responses, the same analysis steps were repeated for these participants with event-related epochs of the same stimulus types obtained during the second recognition test they underwent after the cancellation of the amnesia suggestion.

A significant increase in evoked upper-alpha activity was found in Old face stimuli followed by a new (incorrect) response compared to New face stimuli followed by a new (correct) response at 674 ms post-stimulus onset. This comparison was observed to reach significance at a single voxel in left BA9 (Sub-gyral Frontal Lobe, MNI: −25, 30, 35, F = 3.27, P = 0.048; see Fig. 6). As expected, these results for ostensible instances of forgetting stimuli from the same set of recent faces do not follow, even in broad outline, those obtained for ostensible instances of forgetting during the suggested hypnotic amnesia response.

### Amnesia lifted: lagged nonlinear connectivity

A similar lagged nonlinear connectivity analysis to that reported for the amnesia present condition was also conducted for the high-susceptible participants after the amnesia suggestion was cancelled. ROI and time period for analysis were selected in the same fashion, but in this instance were based on the evoked upper-alpha results reported above for Amnesia Lifted. In this case, the analysis was conducted using the time period from 373 to 973 ms post stimulus. Those ROI with significantly increased lagged nonlinear upper-alpha connectivity for this comparison in amnesia lifted were:

- **BA3**: MNI 55, 25, 40 (right postcentral gyrus)
- **BA6**: MNI 45, 50, 50 (right precentral gyrus)
- **BA9**: MNI −25, 30, 35 (left sub-gyral frontal lobe)
- **BA13**: MNI 35, 100 (right insula)
- **BA18**: MNI 20, 70, 15 (right cuneus)
- **BA19**: MNI −40, 80, 5 (left middle occipital gyrus)

---

Figure 4. Peak voxel difference for evoked upper-\(\alpha\) (Old Face wrong versus New Face correct) in responsive high-susceptible participants during hypnotic amnesia suggestion.

Figure 5. Upper-\(\alpha\) lagged nonlinear connectivity increases (Old Face wrong versus New Face correct) in responsive high-susceptible during hypnotic amnesia suggestion. Only significant connections are shown.
Lagged nonlinear connectivity for each pair of ROI was estimated as the average between all pairs of voxels within a 10 mm radius of each ROI coordinate. Statistical comparisons of these connectivity estimates were again made between Old face stimuli followed by incorrect ‘new’ responses and New face stimuli followed by correct ‘new’ responses, using a non-parametric random permutation test with 5000 iterations. Connections with significantly increased lagged nonlinear upper-alpha connectivity are shown in red in Fig. 7. There were no significant decreases.

Just as for cortical sources temporarily inhibited by evoked upper-alpha activity, the patterns of information exchange inhibited in functional neural networks (indicated by lagged nonlinear upper-alpha connectivity) are completely distinct in retrieval failures during suggested hypnotic amnesia from those found following cancellation of the amnesia suggestion.

**Discussion**

Behavioural results for face recognition accuracy demonstrate that the experimental paradigm elicits failures in the recognition of recently presented face stimuli in the high hypnotically susceptible participants, responding to a hypnotic amnesia suggestion to forget these stimuli. Most importantly, retrieval of these stimuli is restored after the cancellation of the amnesia suggestion to a level indistinguishable from that of a group of non-hypnotically susceptible participants. The present paradigm therefore appears to elicit a classic hypnotic amnesia response to a select class of personally salient stimuli, human faces, the recognition of which has been extensively studied in the cognitive neuroscience literature.

**Evaluation of behavioural results**

Analysis of reaction times in relation to accuracy shows that overall correct responses are significantly faster than incorrect responses, suggesting extended processing prior to incorrect responses but certainly indicating the absence of a speed/accuracy trade-off underlying incorrect responses in this paradigm. Closer scrutiny showed that this effect was stronger for old faces in the low-susceptible group and for new faces in the high-susceptible group. While the absence of a speed/accuracy trade-off is maintained, this interaction effect requires explanation. This is consistent with the greater motivational salience of errors to old faces in the low-susceptible group and of errors to new stimuli in the high-susceptible group.

This interpretation is also consistent with aspects of the significant three-way interaction between susceptibility-group, amnesia suggestion and Old–New face stimuli in the accuracy data in the current study. Looking at Fig. 2 for errors to Old faces, inspection of the 95% confidence intervals reveals that following amnesia suggestion, the high-susceptible group show significantly more retrieval failures (congruent with the amnesia suggestion) than the low-susceptible group, and that following cancellation of suggestion both groups respond with an almost identical error rate. While the error rate of the high-susceptible group decreases following cancellation of amnesia suggestion, the error rate of the low-susceptible group increases. The hypnotic amnesia suggestion, therefore, affects
the recollection of old faces in the high-susceptible and the low-susceptible groups in different ways. Consider the corresponding accuracy results for the New face stimuli in Fig. 2; a similar pattern is repeated but with the positions of the high- and low-susceptible groups reversed with respect to the number of errors. Not only does the amnesia suggestion have a different effect on the frequency of errors in the low- and high-susceptible groups, but the direction of these effects are reversed for the Old faces and the New faces, respectively.

The effects of this amnesia suggestion on failures to recognize old faces in the Old–New paradigm is very similar to the pattern of memory retrieval failures observed in the free recall hypnotic amnesia suggestions found in standard hypnotic susceptibility scales. This response is present only in the high-susceptible group and is reversed by cancellation of the suggestion. It is not found in all high-susceptible individuals however; two of the high-susceptible group did not show this response (and so were excluded from the eLORETA analysis). When present the extent and content of positive hypnotic responses varies between individuals and within the same participant.

Along with this classic form of the hypnotic amnesia effect, the current paradigm also elicits a shift in response sets to new and old faces, but in a diametrically differing way in the high- and low-susceptible groups. In the high-susceptible group, accurate recall of old faces increases following cancellation of amnesia, while in the low-susceptible group it decreases (indicating that amnesia suggestion enhances recall in the low-susceptible group, just as it impairs recall in the high-susceptible group). In parallel with this, errors in correctly identifying new faces decline in the low-susceptible group following the cancellation of amnesia suggestion, while increasing in the high-susceptible group.

Increases in reaction time to errors may point to different response sets, to old and new faces, in the high and low groups. In the highs, this difference appears in response to new faces but not to old faces, which is consistent with a truncation of processes related to error avoidance (in this case retrieval failure). In the lows, this pattern is reversed, consistent with a response set which directs processing to avoid retrieval failures rather than false recollections.

While this and other studies focus on the mechanisms underlying the distinctive successful responses of susceptible individuals to specific forms of hypnotic suggestion, the present behavioural results underscore the existence of underlying counter responses rather than the simple non-sensitivity of those in the extreme low-susceptible range of hypnotic susceptibility. Further study is required to identify the unique psychological and neurophysiological processes underlying these responses in low susceptibles and their wider functional significance in the lives of those individuals. We tentatively suggest motivation and expectancy factors tied to self-representations are likely to play a major role here.

Traditionally, extreme low-susceptible participants have been employed as a control group in hypnosis research on the presumption that they do not respond to hypnotic suggestions. Present results suggest that, at least in some cases, hypnotic suggestion elicits distinct counter suggestion processes in this group. As was the case in this study, future research must carefully consider the suitability of this group for that purpose. One alternative may be to employ lower, but not extreme low, responders for this role; excluding those who show difficulty responding to the standard ‘easy’ ideomotor suggestions in addition to excluding those who are able to respond to the more difficult motor inhibition suggestions or the very difficult positive or negative hallucination suggestions.

**Task related upper-alpha following amnesia suggestion**

This study predicted first that failure to recall recent experiences induced by hypnotic amnesia suggestions are due to the inhibition of processing at key nodes in the neural networks which represent and reactivate these experiences by increased upper-alpha activity in those regions at critical time points in the recollection process. Second, integration of the required information between key nodes of the relevant functional network was predicted to be prevented by increased synchronization in the upper-alpha band between these network nodes (effectively functional dissociation).

**Evoked upper-alpha source activity**

The first prediction was tested by comparing the amplitude of cortical source activity in evoked upper-alpha between event-related epochs when the hypnotic amnesia effect is expressed (that is, failures by high-susceptibles to recognize old faces during hypnotic amnesia suggestion), with the closely matched condition of the same participants (highs), correctly identifying a new face under the same instructions (hypnotic amnesia suggestion). In an analysis corrected for multiple comparisons across all voxels and all time points (Nichols and Holmes, 2002), this comparison was found to be significant at a peak voxel in right BA7, superior parietal lobule, but more specifically directly adjacent (see Fig. 4) the posterior region of the intraparietal sulcus.

The functional role of this region, the superior parietal lobule, has itself been the subject of many independent studies. It has been identified as playing a major role in the voluntary orientation of attention from one feature of the perceptual world to another. Evidence from neuroimaging and animal studies indicate that the superior parietal lobule, in the region of the posterior intraparietal sulcus mediates top-down control of attention to different perceptual objects (Ciaramelli et al., 2008). This same region is also consistently found to be activated during retrieval in functional imaging studies of episodic memory (Wagner et al., 2005); yet lesions to this region do not abolish episodic recall. In a wide-ranging review, Carbeza et al. (2008) argue that the superior parietal lobule plays a similar role in episodic recall to that in perceptual orientation, which is to provide top-down attention to support mnemonic (or perceptual) representations in order to facilitate current goal-directed processes. This model closely fits the current findings in which locally synchronized upper-alpha activity (interpreted here as functional inhibition), is evoked in this region in the context of a hypnotic amnesia suggestion, following a correct retrieval cue but prior to an incorrect retrieval decision.

**Upper-alpha network connectivity**

While this effect reaches a maximum and becomes statistically significant at 908 ms post-stimulus onset, rhythmic pulses of upper-alpha activity in this region appear and begin to build from at least 300 ms earlier in the epoch and extend at least another 300 ms until the end of the epoch. Descriptively, this activity appears as a temporal peak in a network of regions swept by a series of phase-lagged upper-alpha oscillations similar to the travelling alpha waves described by Nunez and Srinivasan (2006). These observations match directly our theoretical model that dynamic spatial patterns of upper-alpha oscillations are engaged by those with the requisite abilities (hypnotic susceptibility) to inhibit the operation of high-level cognitive processes, the output of which are incompatible with maintaining the
experience of specific hypnotic suggestions. This theoretical framework provides the basis for the novel method (see Supplementary material 3) adopted in this study, to select ROI (and corresponding time frames) for connectivity analysis to determine the functional networks in which processing of information conflicting with the suggested experience is being inhibited by synchronized upper-alpha band activity.

Of the regions entered into this lagged nonlinear connectivity analysis of the present hypnotic amnesia effect, significant increases in upper-alpha phase synchronization were found between a hub located in right parahippocampal gyrus (which plays an essential role in the reactivation of recently coactive cortical networks prior to memory consolidation [Wang and Morris, 2010]), and individual nodes in right superior parietal lobule (discussed above), right fusiform gyrus BA20 and right midtemporal gyrus BA22 respectively (see Fig. 5). Haxby and Gobbini (2011) distinguish between core and extended networks involved in processing face information with preferential activations in the right hemisphere. They identify recognition of familiar faces with (re-)activation of representations of personal information (such as emotional states) and associated episodic memories located in more anterior regions of the right temporal lobe. Although the right temporal regions which showed increased upper-alpha phase and synchronized with the right parahippocampal gyrus (medial temporal region) during failed retrieval of recent faces are associated with many other functional roles, they add consistently to our functional interpretation of these results as inhibition in the exchange of information between specialized processing regions required for the retrieval of recently viewed faces. Most importantly, this network of increased upper-alpha connectivity is not observed in the high-susceptible group during retrieval failures following the cancellation of the hypnotic amnesia suggestion.

**Task related upper-alpha following lifted amnesia suggestion**

In order to confirm that the upper-alpha findings related to retrieval failures in the highs during amnesia are not simply the neural correlates of ordinary forgetting, we undertook this same series of eLORETA source analyses, first in evoked upper-alpha and then in lagged-nonlinear upper-alpha connectivity, in the high-susceptible group performing the same Old-New recognition task (with a different set of stimuli) following the cancellation of the hypnotic amnesia suggestion. The same parameters and decision criteria were used at every step of this analysis.

For the comparison between unrecognized old faces and correctly identified new faces, significantly greater upper-alpha activity was found in a peak voxel in the sub-gyral region of left BA9 (see Fig. 6) at 674 ms post-stimulus onset. This is relatively late in the evoked stimulus processing sequence (but not as late as in hypnotic amnesia) suggesting inhibition of a high-level cognitive process. Left BA9 activity is closely associated with goal and task set representations required for the selection and control of current cognitive operations, including retrieval from episodic and working memory (Rugg and Henson, 2002; Owen et al., 2005). In this case (unlike hypnotic amnesia), relative inhibition of activity in this area is linked to failures in face memory retrieval, indicating that in the highs a different set of neurophysiological mechanisms is responsible for retrieval failures in hypnotic amnesia and following cancellation of the amnesia suggestion (while still in hypnosis). Connectivity analysis showed an extensive network of regions sharing phase synchronized upper-alpha activity, including the region of left BA9 identified above; however there was no overlap in nodes (and hence connections) between this functionally inhibited network and the corresponding network identified in the hypnotic amnesia condition (see Fig. 7).

**Dissociation of cognitive control in hypnosis**

It is instructive that the region of maximum increase in upper-alpha (functional inhibition) evoked by unrecognized (old) faces shifts from right BA7 (superior parietal lobule) during hypnotic amnesia response to left BA9 (sub-gyral frontal lobe) for the high group when the amnesia suggestion is cancelled, but while still in the hypnosis condition. Both of these regions are closely associated with top-down attentional control. Inhibition of executive control functions mediated by left frontal cortex are expected in the dissociated control model of hypnosis (Woody and Bowers, 1994; Farvolden and Woody, 2004) and were originally described by Gruzelier and Warren (1993) using classic neuropsychological testing methods. Egner et al. (2005) and Miltner and Weiss (2007) report evidence of a breakdown in gamma band connectivity (active information integration) between control regions within left frontal cortex and other monitoring and control regions within the frontal lobe. Jamieson and Woody (2007) proposed a general model in which breakdowns in the functional integration between different components of executive control networks account for core features in the phenomenology of the hypnotic condition. The increased phase synchrony in the inhibitory upper-alpha band between a left frontal executive control region and a diverse network of left and right hemisphere, anterior and posterior regions observed here during a memory task demanding cognitive control resources for effective execution, in a hypnotized high-susceptible group in the absence of a specific hypnotic suggestion may be a specific example of this general mechanism.

To test this idea, we undertook a post-hoc comparison of the same evoked upper-alpha source activity differences in the behaviourally equivalent non-amnesia Old–New face memory test of the low-susceptible group. Using the same analysis parameters, we found no significant source differences in evoked upper-alpha in failures to recall old faces in the low-susceptible group in this condition. While great caution is warranted in drawing inferences from a negative result, we would suggest that the localized upper-alpha activity in left BA9 and the associated phase synchronized network in the high- (but not low-) susceptible group during hypnosis, but in the absence of specific suggestion, is further evidence for the sort of alterations within and between high-level cognitive control mechanisms predicted by dissociation theories of hypnosis (Woody and Sadler, 2008).

**Conclusions**

Dissociation theories of hypnotic amnesia propose that the (reversible) failure to recall suggested types of (veridical) events shown by some high-susceptible individuals during hypnosis corresponds to the temporary unavailability of this information both to conscious experience and to the cognitive mechanisms which normally guide and facilitate retrieval of those types of memories. The present study proposed that gated inhibition of cortical information processing by the dynamic topographic expression of upper-alpha band activity is the neurophysiological mechanism by which functional dissociation is implemented in hypnotic amnesia. By constraining the hypnotic amnesia suggestion to face stimuli, and testing
memory with an Old–New recognition paradigm which presents stimuli time-locked to a dense array EEG recording, this study confirmed predictions that inability to recognize old faces in response to the amnesia suggestion, and only this condition, is linked to significant increases in evoked upper-alpha (hence functional inhibition) in a region which provides top-down control for precisely this form of recollection (right BA7 superior parietal lobule). In the same condition upper-alpha phase synchrony uniquely increased between this and other functionally specific regions required for the recollection of recent faces. Responses to hypnotic amnesia suggestion vary from person to person and over time within each person. Positive responses to hypnotic amnesia suggestion (for recent faces) were accompanied by phase synchronization in upper-alpha, indicating inhibition of information integration, between key nodes in a network of specialized processing regions critical for top-down control (right BA7), recent memory retrieval (right BA34) and specific face memory representations (right BA20 and BA22). This pattern of inhibition in processing activity in a functionally specialized region, and in the flow of information in a network which processes a form of knowledge restricted by a specific suggestion, is precisely that form of change in cognitive architecture posited by dissociation theories to implement responses to hypnotic suggestion. These changes temporarily restrict the availability of outputs from high-level cognitive processes to conscious representation or other cognitive control systems in order to sustain the suggested response (see Smith et al., 2013).

As predicted from the recently emerging understanding of the functional role of alpha oscillations (Klimesch, 2012) and in particular the role of the upper-alpha band (Bazanova and Vernon, 2014) in inhibiting competing processes during memory and cognitive processing, the proximal mechanism for dissociation in hypnotic amnesia, at least for recent faces, was found to be the inhibitory effect of specific evoked upper-alpha activity, and the phase synchronization of upper-alpha in associated functional networks on processing the type of information ‘restricted’ by the hypnotic suggestion. Rigorous double screening of participants for hypnotic susceptibility and further selection of high-susceptible participants who individually demonstrated the suggestion responses under investigation hypnotic face amnesia were important components of the present experimental paradigm. The high validity of the current findings has come at the cost of fewer participants and hence lower generalizability. If replicated in a larger sample these findings are of landmark importance for the understanding of the neurophysiological mechanism of dissociation as found in hypnosis, suggestion and placebo, non-organic (psychogenic) dissociative symptoms in a range of psychological conditions and in anthropological studies of trance and possession states. The specificity of the stimulus and suggestion type (faces) was an important strength of this study but also limits the generalizability of the results. It will be necessary to extend this methodological approach from faces to other stimulus types with well-specified functional neural processing networks, such as visual or auditory word stimuli, in order to establish the character of the dissociation response to specific forms of hypnotic amnesia suggestion.

Acknowledgements

This research was supported by a grant to M.D.K. and G.A.J. from the Bial Foundation (Bursary 222/12). Data will be made available on request to the corresponding author.

Conflict of interest: None declared.

References


Supplementary data

Supplementary data is available at Neuroscience of Consciousness Journal online.