

Towards a profile of the hypnotic state:
Continuing the search for a state marker



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ABSTRACT

It is widely disputed whether or not hypnosis, as distinct from responses to specific hypnotic suggestions, constitutes a discrete change in the operating state of the mind-brain system. If hypnotic responses require the on-set of such a background state, characteristic differences in the organization of neuronal activity should be visible between hypnotic and non-hypnotic conditions. This study sought to delineate a neuronal state ‘marker’ of hypnosis, thereby aiming to extend recent EEG findings of topographically specific increases in theta band functional connectivity and decreases in beta1 band connectivity in high compared to low susceptible subjects following a hypnotic induction (Jamieson & Burgess, 2014). Specifically, this study extends the findings from sensor space (electrodes) to source space (cortical voxels). For this, resting EEG with eyes closed was recorded before, during and after hypnosis in 8 low susceptible and 11 high susceptible participants. Spectral band power analysis was conducted on the data, yielding, as expected, no significant results. Current source density estimations and connectivity analyses were done using the Key Institute eLORETA software. Cortical source activity did not show any significant hypnosis-related differences. However, as expected, hypnosis-related increases in functional connectivity in the theta band were found within nodes of the executive control network, in the salience network and in the default mode network. Moreover, also as expected, hypnosis-related decreases in beta1 band functional connectivity was found, specifically within nodes of the dorsal attention network and the executive control network. There were also two unexpected hypnosis-related increases in beta1 connectivity within nodes of the dorsal attention network and the salience network. These results indicate that reported changes in the theta and beta1 band functional connectivity in hypnosis are linked with a reorganization within the operations of the major networks regulating the flow of conscious experience, thereby supporting an altered state account of the hypnotic condition.

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Introduction

1. Defining the subject matter. Researchers and clinicians who seek to understand hypnosis are confronted with a multidimensional problem. A full account of hypnosis will explore the trait of hypnotic susceptibility (i.e. the subject's responsiveness to hypnotic suggestions), the procedure of hypnotizing someone, and the product of the hypnotic induction procedure (Barnier & Nash, 2012).

Hypnotic susceptibility can be defined as "a cognitive trait allowing subjects to modulate perception, emotion and behavior, according to specific suggestions" (Carli, Cavallaro & Santarcangelo, 2007). The hypnotic procedure, includes a hypnotic induction and is used to encourage and evaluate responses to suggestions (Green, Barabasz, Barrett & Montgomery, 2005). Thereby, the hypnotized individual undergoes not only psychological changes, such as distortions in consciousness and volition, with increased suggestibility and reduced peripheral attention (Spiegel & Spiegel, 2004, p.19), but also phenomenological changes, such as changes in perception, volition, body image, meaning, affect and imagery (Pekala & Kumar, 2007; Kirsch, 2001), and neurodynamical changes, expressed through alterations in neural activity (Kihlstrom, 2013). While it is agreed that hypnosis brings about altered experiences (Kallio & Revonsuo, 2005), the question of whether a hypnotic state facilitates such experiences is one of the main issues in the current debate regarding hypnosis. It is these aspects of hypnosis, rather than specific types of hypnotic suggestion, that will form the focus of the present study.

2. Developments and Current Theories. In order to appreciate the current debate, it is necessary to remember that the issue of the state versus non-state explanations has been the center of scientific disputes ever since hypnosis was first adopted in western medicine (Fingelkurts, Fingelkurts, Kallio & Revonsuo, 2007b; Milling, 2009; Lipari et al, 2011). For 200 years, the views on the causal mechanism of these phenomena have ranged between "animal magnetism" on one end and imagination on the other (Kallio & Revonsuo, 2003). Braid's 'Neurypnology' (Braid, 1843) is one of the first attempts at defending the idea that the effects of hypnosis are not solely due to imagination and suggestion. Even nowadays, many studies focus on demonstrating differences between a hypnotic and a non-hypnotic suggestion or an imagined action (see e.g. Derbyshire, Whalley & Oakley, 2009; Milling, 2009; Müller, Bacht,

Schramm & Seitz, 2012; Huber, Lui & Porro, 2013; Hutchinson –Phillips, Jamieson & Gow, 2005).

As described by Lynn, Kirsch, Knox, Fassler and Lilienfeld (2002), during the 1960s and the 1970s, the altered state debate was acknowledged as the most ardent debate in the field. Although resolutions on this debate have been pronounced from time to time, the issue is far from settled (Lynn et al, 2002). Currently, there are various explanations for hypnotic phenomena. The two main views can be named as the ‘state’ approach and the ‘non-state’ approach. The ‘state’-approach represents the hypnotic state as a distinct/altered state of consciousness, which enables specific hypnotic experiences to be produced. On the contrary, the ‘non-state’-approach appeals to mundane, psychological mechanisms – such as relaxation and focused attention/disattention (Gruzelier, 2005) – or social-psychological mechanisms – such as implicit and explicit response expectations and compliance (Fingelkurts et al, 2007b; Milling, 2009; Gheorghiu & Mölz, 2008) – to explain hypnotic phenomena. Whereas the former view holds that it is the ability to move into another state of consciousness – an altered one – which needs to be explained, the latter views susceptibility as the only variable needing further exploration (Kallio & Revonsuo, 2003). However, researchers have also formulated alternative views. For example, the weak state view holds that ‘altered state’ only has a descriptive function rather than a causal one in hypnotic phenomena (Lynn et al, 2002). In addition, the epiphenomenal hypothesis agrees to changes in experience and in the neural organization, regarding these merely as epiphenomenal – they do not affect responsiveness to suggestions or performance on tasks (Mazzoni, Venneri, McGeown & Kirsch, 2013).

Although “more than half a century of behavioural research on the altered state issue resulted in a stalemate” (Mazzoni et al, 2013, p. 401), the emergence of neuroscience has revived research in hypnosis during the last three decades. Neuroscience has contributed to this debate by adding objective, reliable measures to the simple behavioural observations and subjective reports of hypnotized individuals. The main focus of investigation in the last decade was the search for a neurophysiological correlate of hypnosis – a ‘marker’ by which to identify the hypothesized ‘background’ state underlying the suggested hypnotic experiences (see e.g. Fingelkurts, Fingelkurts, Kallio & Revonsuo, 2007a). The idea behind this search was that if phenomenological changes corresponding to a discrete, altered state of consciousness (Tart, 1975, ch. 5) are produced following a hypnotic induction, these

should have discrete, identifiable neural correlates. Jamieson and Hasegawa (2002) use Tart's (1975) definition to develop the concept of discrete altered states of brain networks. Such brain states are present when the dominant patterns of functional connectivity between specific networks and their oscillatory dynamics have changed from a baseline state. Indeed, measures developed to assess such changes have helped demonstrate that the hypnotic state is characterized by a specific pattern of brain activity, with changing neural dynamics (e.g. Raz & Shapiro, 2002; Halligan & Oakley, 2013a; Hoeft et al, 2012).

Specifically, these changes present themselves in EEG, PET and fMRI recordings (see e.g. Halligan et al, 2013; Oakley & Halligan, 2013; Hinterberger, Schöner, Halsband, 2011; Maquet et al, 1999; Kihlstrom, 2013). For example, Rainville, Hofbauer, Bushnell, Duncan and Price (2002), have shown that hypnosis brings about changes in structures contributing to consciousness (see also Deeley et al, 2012; Rainville & Price, 2003). Using positron emission tomography (PET), Rainville and colleagues (2002) scanned ten participants during non-hypnotic and during hypnotic conditions (4 scans each). Their results show that hypnosis modulates activity in structures involved in self-regulation and in the regulation of consciousness states, such as the thalamus, the brainstem nuclei and the ACC (Rainville et al, 2002).

In addition, McGeown, Mazzoni, Venneri and Kirsch (2009) demonstrated that hypnosis modulates activity in the default mode network (DMN). The DMN represents a network of brain regions, which is active at rest, as compared to a goal-directed cognitive task or any external task whatsoever (see e.g. Chen, 2007), and supports intrinsic functional/communicational activity, thereby contributing to consciousness. In order to assess activity changes in the DMN, McGeown et al (2009) scanned 10 high susceptible and 7 low susceptible participants with an fMRI scanner. Specifically, individuals were scanned in resting periods and these scans were compared to conditions of passive (viewing a pattern or a complex colour) and active viewing (active modification of pattern: draining colour away, adding colour). The scans were performed with and without hypnotic induction. Results indicate a hypnosis-related decrease in activity in the anterior part of the DMN (prefrontal cortex) in highly susceptible participants after a hypnotic induction without simultaneous expected changes in other structures (see McGeown et al, 2009).

3. EEG findings. EEG recordings have demonstrated a variety of different changes following a hypnotic induction and different hypnotic suggestions. For example, following the study of De Pascalis, Marucci and Penna (1988), who found lower levels of 40-Hz (gamma) activity in both hemispheres during eyes-closed resting in hypnosis and in waking conditions in highly susceptibles, it was proposed that gamma-activity might provide a ‘marker’ of the hypnotic state. However, ten years later, De Pascalis, Ray, Tranquillo and D’Amico (1998) published another study, which compared resting conditions in waking and hypnosis with conditions of emotional recall (i.e. where the participants had to think about an emotional event; emotional here had three aspects: happiness, sadness and neutral relaxation). The results suggest higher theta1 (4-6 Hz) activity in left and right frontal and right posterior areas and lower alpha1 (8.25-10 Hz) over left and right frontal areas in highs in waking rest and hypnosis rest.

Recently, studies publishing EEG results continue the pattern of ambiguous findings. White, Ciorciari, Carbis and Liley (2009), for example, tested low and high susceptible volunteers with a virtual reality hypnotic (VRH) induction, administered via special goggles and headphones. They compared a baseline condition (resting, eyes-closed), with a hypnotic condition (following hypnotic induction, resting, eyes closed) and found higher beta coherence at baseline and a decrease from baseline to hypnosis in highly susceptibles, while the opposite relationship was observed for the low susceptible participants. Another study by Kirenskaya, Novototski-Vlasov and Zvonikov (2011) measured EEG during eyes closed resting conditions both before and during a hypnotic induction and found higher fronto-central-parietal theta spectral power and higher delta, theta and alpha3 (11.15-13 Hz) coherence in highly hypnotizable subjects, whereas lows exhibited higher beta2 (19-27 Hz) and gamma1 (27-40 Hz) spectral power and coherence.

Moreover, numerous other studies focusing on specific suggestions have found a variety of EEG patterns following hypnotic inductions. For example, two recent studies, which measured EEG during hypnotic arm levitation (Halsband, Müller, Hinterberger & Strickner, 2009, and Cardeña et al, 2012), also found slightly different patterns of activation. While Halsband et al (2009) report higher theta power in central areas, alpha power in occipital and parietal areas and gamma power in occipital and temporal cortex in highly susceptible participants), Cardeña et al (2012) found hypnosis-related increases in delta and theta activity in central-parietal regions

and beta and gamma in anterior regions in highly hypnotizable subjects. Lastly, a recent review of EEG studies on hypnosis (Vanhaudenhuyse, Laureys & Faymonville, 2013) concludes that there is evidence for the involvement of alpha, beta, theta and gamma frequency bands in hypnosis. However, the study concludes, the major problem is that results are not being replicated.

So why are there no consistent, reliable results? Well, there are various problems that may contribute to this issue. First of all, these studies present wide methodological differences (see e.g. Fingelkurts et al, 2007b) and differences in the selection of the subjects they study. For example, not all studies assess eyes-closed resting conditions. Some studies look at responses to specific suggestions (for example recall of an emotional event), thereby testing a specific psychological mechanism, and not whether there is a background state, which (perhaps) enables these specific responses. Furthermore, different measurement and analysis methods are employed (e.g. fMRI vs. EEG, power spectrum analysis vs. connectivity measures). Specifically, some methods of analysis are themselves flawed. For example, when analyzing spectral band power or amplitude, one assumes linearity (i.e. constant mean and variance) of the brain waves and stationarity, which means no stage transitions during the recording. Likewise, there are also problems with coherence analysis: it is sensitive to volume conduction (i.e. when the signal from a single source is detected at multiple electrode sites) and to type - I error (i.e. as there are multiple possibilities of combination of electrode channels, one must control for multiple comparisons). In addition, hypnosis consists of continuous state changes (Hinterberger et al, 2011), whereas EEG studies usually concentrate on timely distant 2-minute segments of the recordings (e.g. before and after a hypnotic induction). Moreover, specific states are arguably characterized by specific patterns of interaction between specific brain regions (Fingelkurts et al., 2007a; Fingelkurts, Fingelkurts & Neves, 2013a; Stam & Straaten, 2012), whereas spectral band power or amplitude expresses only localized brain activity at a surface (rather than 'deep') structure of brain organization (Jamieson & Burgess, 2014).

However, EEG has proven a good measure for profiling various states of consciousness, such as sleep, vegetative states and minimally conscious states etc. (Fingelkurts, Fingelkurts, Bagnato, Boccagni & Galati, 2012; 2013b). For example, Fingelkurts et al (2012) found that loss of consciousness changes cortical activity dramatically. Moreover, EEG allows for more direct measurement than for example

PET, fMRI or MEG. In addition, as stated above, states of consciousness are characterized by the joint simultaneous operation of many neuronal assemblies in the brain (Fingelkurts et al, 2013a). This synchrony or communication between different brain areas is best assessed with functional connectivity measures. This is why Stam and Straaten (2012) emphasize the necessity of combining electrophysiological measures with functional connectivity analysis. Hence, when considering studies that assess functional connectivity, the picture becomes more reliable: results consistently point to hypnosis-related changes in the integration of the frontal-parietal executive network, more specifically in the dorsolateral prefrontal cortex (DLPFC) and the dorsal anterior cingulate cortex (dACC) (see e.g. Egner, Jamieson & Gruzelier, 2005; Terhune, Cardeña & Lindgren, 2011; Hoeft et al, 2012; Huber, Lui, Duzzi, Pagnoni & Porro, 2014).

4. Functional Connectivity Findings. A recent study by Cardeña, Jönsson, Terhune, and Marcusson-Clavertz (2013) assessed ‘neutral’ hypnosis (i.e. resting eyes-closed periods following a hypnotic induction) with a global functional connectivity measure, Omega Complexity (Wackermann, 1995) and found reduced global functional connectivity in high susceptibles. Spectral band power analysis revealed greater beta2 (18.2-21 Hz), beta3 (21.5-30 Hz) and gamma power among highs. What is interesting about this study is that the researchers applied a neurophenomenological approach, where they correlated self-reports of participants experience with EEG activity. After extracting nine major dimensions from the self-reports (exceptional, imagery, negative, body, normal cognition, environmental, relaxation and forgetting), which were acquired during hypnosis, and after correlating these with EEG activity, they found effects of group (low, medium and high susceptibles score differently on imagery, body feelings, normal cognition and exceptional experiences) on these factors. Moreover, they found significant correlations between two dimensions on which highs score mostly (imagery and exceptional) and Omega Complexity, suggesting lower global functional connectivity in highs. These results are interesting, as they represent one of the first attempts to map subjective personal experience unto objective measurement of neural activity. Besides helping in the clarification of the functional roles of specific brain frequencies, they aid in understanding the subjective changes that hypnotic states are

associated with, thereby also giving more security and precision if functional conclusions are to be drawn.

Jamieson and Burgess (2014) report a sophisticated functional connectivity analysis in a study, where they recorded EEG from 23 participants. Following this, they applied a power spectrum analysis and a conventional coherence analysis with no significant results. Then, they measured functional connectivity with imaginary coherence – iCOH – which escapes the problems of volume conduction, and applied Partial Least Squares (Lobaugh, West & McIntosh, 2001), which escapes the problem of inflated type – I error to make comparisons between high and low susceptibles before and after a hypnotic induction, during periods of eyes-closed rest. Results show increased functional connectivity in the theta band around a central-parietal hub lying directly over the medial superior parietal lobe (precuneus) and decreased beta1 connectivity (13-19.9 Hz) around a fronto-central and occipital hub during hypnosis in high susceptible participants (see Figure 1). The authors conclude that the increase in theta activity around the precuneus suggests an implication of executive control networks through the reorganization of higher-level control processes, and the decrease in beta activity around the motor cortex and the supplementary motor area may contribute to the feeling of involuntariness over one’s actions experienced by the hypnotized individual (Jamieson & Burgess, 2014). They also indicate that these two findings might designate candidate neuropsychological markers of the hypnotic state.

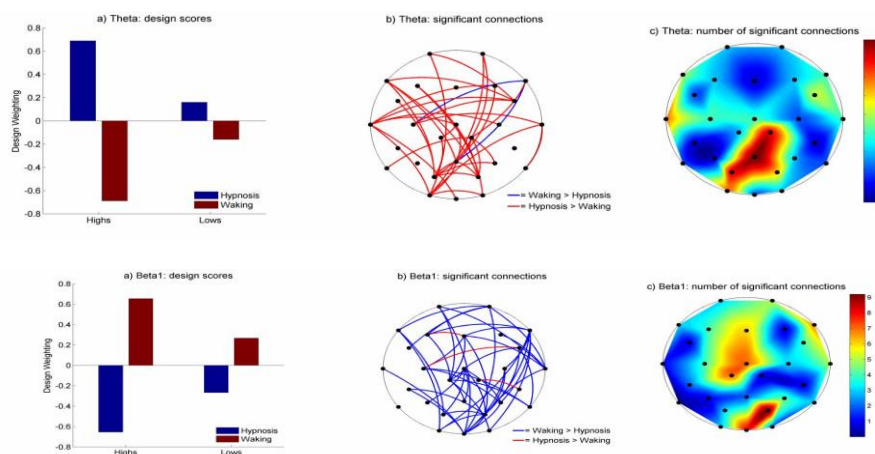


Figure 1. Results presented in Jamieson & Burgess (2014). Increased theta iCOH is visible in the representations above, decreased beta1 iCOH in those below.

5. Aims and Hypotheses. The first aim of this study is a robust quasi-replication of the findings presented by Jamieson and Burgess (2014), with conceptually parallel but operationally distinct procedures and analysis tools. Thereby, electrophysiological correlates of the hypnotic state will be explored, in order to narrow the search for a reliable hypnotic state ‘marker’ (i.e. a neurophysiological correlate that always accompanies the on-set of hypnotic states). The second aim is to build upon these results in order to identify the impact of the hypnotic induction on the organization of functional neural networks (see Raichle, 2011) regulating consciousness in the hypnotic state. Nevertheless, if a distinct hypnotic state exists, and is brought about by a hypnotic induction, then we should expect to find the neural correlates of this state to be directly related to hypnotic susceptibility and/or most evident in high (rather than low) susceptible participants. The phenomenological changes characteristically reported by high susceptibles in hypnosis should be reflected in changes in the organization of individuals’ brain connectivity

In order to establish these neural correlates, participants’ EEGs were recorded, for their known sensitivity in profiling different states of consciousness. Spectral band power analyses was computed using the Fast Fourier Transform (FFT) algorithm and the eLORETA software respectively, in order to confirm the spectral analysis findings presented by Jamieson & Burgess (2014) – who found no effects or interaction effects for scalp topography (sensor space) – and extend these into source space. Moreover, the possible interaction effects of gender were additionally considered. In addition, a replication of higher beta1 (13.5 -21 Hz) and lower theta (4.5 – 8) functional connectivity in high susceptible participants following a hypnotic induction was attempted. However, whereas Jamieson and Burgess (2014) focused on sensor space (scalp electrodes), the present study extends this analysis into source space (estimated activity at cortical grey matter voxels) using eLORETA connectivity analysis (see Canuet et al, 2011). Changes in functional connectivity between the major nodes of cortical networks (such as the dACC and the lateral PFC identified in previous studies) during hypnosis will be systematically explored in the theta and beta1 frequency bands, which are the focus of this study.

A quasi-replication of the design used by Jamieson & Burgess (2014), where participants had their EEG recorded before and after a hypnotic induction in an eyes-closed resting condition, was sought. However, in addition to Jamieson & Burgess (2014), a period of time after de-induction, in the same eyes-closed resting condition

was recorded. This was done in order to counterbalance the order of hypnotic and non-hypnotic testing and thereby control for order effects. Thus, comparisons of differences between pre-hypnosis and hypnosis and hypnosis and post-hypnosis were possible. Furthermore, the analysis only focused on the two-minute eyes-closed resting recordings (pre-, during, and post-hypnosis), in order to separate the effect of the hypnotic induction from the effect of specific suggestions. The reason behind this was to assess the neurophysiological correlates of the neutral hypnotic state. Likewise, in order to separate the effects generated by the presence of a hypnotic state from those produced by other aspects of the hypnotic induction, low susceptible participants were included (see Mazzoni et al, 2013). If other aspects of the induction, such as relaxation, produce the differences between pre-hypnosis and hypnosis, these changes should be visible in low susceptible participants as well.

Methods

Participants. 20 English-speaking participants (mean age: 28.7, SD = 12.7, 12 female) were recruited out of a pool of pre-screened participants to take part in this experiment, which received ethical approval from the Psychology Research Ethics Committee, School of Philosophy, Psychology and Language Sciences, the University of Edinburgh (ref. 140–1213/7). All of the participants gave informed consent and were paid £15 for their participation. The participants were pre-screened with both the Harvard Group Scale of Hypnotic Susceptibility, Form A (HGSHS:A) (Shor & Orne, 1962), and the Stanford Hypnotic Susceptibility Scale, Form C (SHSS:C) (Weitzenhoffer & Hilgard, 1962). Both these tests are of standard use for assessing hypnotic susceptibility. Specifically, the SHSS:C contains 12 items, which call for ideomotor responses, positive and negative hallucinations, anosmia, and posthypnotic amnesia. We excluded the posthypnotic suggestion, so that the highest score achieved was 12 points. Based on their results in the SHSS:C, participants who scored ≥ 8 were assigned to the highly susceptible group (highs) and participants who scored ≤ 4 were assigned to the low susceptible group (lows).

Apparatus. EEG was recorded in the EEG-ERP laboratory in the Dugald Stewart building of the University of Edinburgh on a BioSemi system (BioSemi Inc., Amsterdam, The Netherlands), in an electrically shielded and dimly lit room, via a

64-channel BioSemi electrode head-cap, with pin-type active electrodes placed according to the international 10-20 system. As Nolan, Whelan and Reilly (2010) note, the Biosemi system replaces the ground electrodes used in conventional systems with two separate electrodes: Common Mode Sense active electrode and Driven Right Leg passive electrode. These two electrodes form a feedback loop, which drives the average potential of the subject (the Common Mode voltage) as close as possible to the analogue-to-digital reference voltage in the AD-box (the analogue-to-digital reference can be considered the virtual ground of the amplifier). For a detailed description of the referencing and grounding conventions used by the Biosemi active electrode system, the interested reader is referred to the following website: <http://www.biosemi.com/faq/cms&drl.htm> (Nolan et al, 2010). Regarding electrode impedance, in active electrodes interference suppression is provided by impedance transformation directly on the electrode, which results in an output impedance of less than 1 Ohm. The recording was referenced online to the left and right mastoid and offline to a common average reference. Signal was sampled at a rate of 512 Hz and passed through a 0.16 Hz to 100 Hz bandpass filter. The 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.

Procedure. Hypnosis induction was administered verbally and personally to the participants (see Appendix for script; script was strictly followed in order to avoid problems of standardization). After preparation, the participant was taken in the experimental room, in which he was seated in front of a table with a computer screen on it. A neck pillow was used to increase the comfort of the participants. An explanation of the procedure followed, after which the baseline 2 minutes eyes-closed resting period was recorded. Then, the participant was asked to fill out the Phenomenology of Consciousness Inventory (PCI: Pekala, 1991), where it was emphasized that the focus of the questions would be the phenomenological experience during the baseline recording period. A relaxation exercise then followed, which lasted for about 15 minutes, in order to balance out environmental effects (i.e. sitting on an uncomfortable chair with an EEG-cap on). After this, a hypnotic induction (finishing with a countdown from 10 – 0) was administered. The next eyes-closed

resting period was recorded as soon as the induction finished, the participant only being instructed to rest with their eyes closed.

At this point, individuals were given independent instructions and suggestions for a computer-based face recognition and memory tasks. These tasks are not discussed further, as the results will not be reported here. Furthermore, these suggestions were only administered when the 2-minute recording after the hypnotic induction had been completed; therefore, it is dubitable that these suggestions have affected the data.

A dream suggestion was then administered, which was adapted from the SHSS:C. This suggestion was chosen in order to study specific facets of hypnotic phenomenology and was excluded from the current analysis. Following this, de-induction was completed and another two-minute resting eyes-closed period was recorded. In the end, the participant had to fill out another PCI, which concentrated on the dreaming experience. The analysis of the PCIs is also not included in this thesis.

To sum up the presentation of experimental conditions, two-minute periods of eyes-closed resting were recorded at baseline (pre-hypnosis), after the hypnotic induction (during-hypnosis) and at the end, after de-induction (post-hypnosis). In addition, we administered the PCI (Pekala, 1991) at baseline (before hypnosis; here, participants were asked to describe how they felt during the baseline resting period) and at the end (after hypnosis; here, participants were asked to rate their experience during the dream suggestion, irrespective of whether they had experienced a dream or not).

Analysis.

SPECTRAL ANALYSIS. Data was filtered (0.16 Hz - 100 Hz), artifact corrected and epoched in BrainVision analyser (Brain Products Inc.). Each 2-minute recording was divided into segments of 2000ms. Epochs with values exceeding the range -100 μ V to +100 μ V were excluded. Spectral band power was computed using the Fast Fourier Transform (FFT) algorithm. The FFT is a mathematical manipulation, which is commonly used in order to transform the signal from the time domain to the frequency domain. Squaring of the Fourier coefficients creates the power spectrum, which is a representation of the signal in terms of frequency vs. intensity (Fisch, 1999). The power spectrum was estimated in the 0.48-44.9 Hz frequency range. The frequency bands were defined following Jamieson & Burgess (2014): delta (0.1-3.9Hz), theta (4-7.9Hz) alpha (8-12.9Hz), beta1 (13-19.9Hz), beta2 (20-29.9Hz) and

gamma (30-45Hz). Given the exploratory nature of this part of the analysis, and given that eLORETA was later applied, the values were averaged over all electrodes and ANOVAs were performed on the natural logarithm of mean values with R (R Core Team, 2014; available at <http://www.R-project.org/>; the code is provided in the Appendix). The averaged spectral power values were log-transformed in order to meet distributional assumptions. In order to determine whether hypnosis as a state or hypnotic susceptibility as a trait modulate differences in EEG spectral power, we examined the data for any significant effects or interactions, especially ‘state’ (pre-hypnosis vs. hypnosis vs. post-hypnosis) and ‘trait’ (low vs. high susceptible) interactions.

FASTER. Fully automated statistical thresholding for EEG artifact rejection (FASTER) is an algorithm, which uses independent component analysis (ICA) to separate the EEG signal from artifacts (Nolan et al, 2010). FASTER is employed to clean the data from physiological (eye movements, eye blinks, muscle movements, skin potentials) and technical (electromagnetic interference, electrode pop off or drift, shifting electrodes and residual white noise) artifacts (Thomas, Jamieson & Cohen, 2014). In addition, the application also detects and removes bad channels or very noisy data sets, re-references to common average reference and extracts epochs. Z-score thresholds for artifact components were set at 2.5, except for EOG, where they were set at 2.0. These scores are the thresholds above which, if a component happens to fall, FASTER will consider it as artifact and remove it. FASTER runs within EEGLAB (Delorme & Makeig, 2004; <http://sccn.ucsd.edu/eeglab/>), using MATLAB 8.3 (2014a, <http://www.mathworks.com/>).

Each two-minute recording was divided into two-second epochs. Even though the recordings were done with eyes closed, each recording was also visually inspected for eye movements and muscle artifacts and any identified ‘noisy’ epochs were removed.

eLORETA.

Source localization. Based on the scalp-recorded electric potential distribution, the exact low-resolution brain electromagnetic tomography (eLORETA) software (publicly available software 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 (3D) 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. neighboring neuronal sources will be highly correlated). The description of the method together with the proof of its exact zero-error localization property, are described in Pascual-Marqui (2007b) and Pascual-Marqui (2009). It is also important to emphasize that eLORETA has no localization bias even in the presence of structured noise and is therefore an improvement over previously developed tomographies LORETA (Pascual-Marqui, Michel & Lehmann, 1994), and the standardized version sLORETA (Pascual-Marqui, 2002).

As described in Canuet et al (2011), differences in CSD between groups in each band are computed using voxel-by-voxel independent sample F-ratio tests, which are based on eLORETA log-transformed current density power. The CSD estimations made with eLORETA were computed using a realistic head model, where the three-dimensional solution space was restricted to cortical gray matter. As described in Thomas et al (2014), the intracerebral volume is partitioned in 6239 voxels of 5x5x5 mm³ spatial resolution. eLORETA statistical images represent the electric activity at each voxel in Montreal Neurological Institute (MNI) space as the exact magnitude of the estimated current density. Anatomical labels and Brodmann areas are reported using MNI space, with correction to Talairach space.

Connectivity Analysis. For our functional connectivity analysis, it was decided to focus within specific networks of the brain. Only the theta and beta1 frequency bands were used, given the interest in extending the results in Jamieson & Burgess (2014). After personal correspondence with G. Jamieson, it was decided that theta was to be defined as ranging between 4.5 and 8 Hz and beta1 as ranging from 13.5 to 21 Hz. To compute the regions of interest (ROIs), a method that uses all voxels within 20 mm of the centroid of the defined network nodes was chosen. These network nodes and corresponding MNI coordinates were taken from Raichle (2011) (see Fig. 2) for the executive control network, the dorsal attentional network, the salience network and the default mode network. These networks were selected, as previous research indicates an implication of these mechanisms in hypnosis (see e.g. McGeown et al, 2009) and in the generation of conscious experience (see e.g. Rainville et al, 2002;

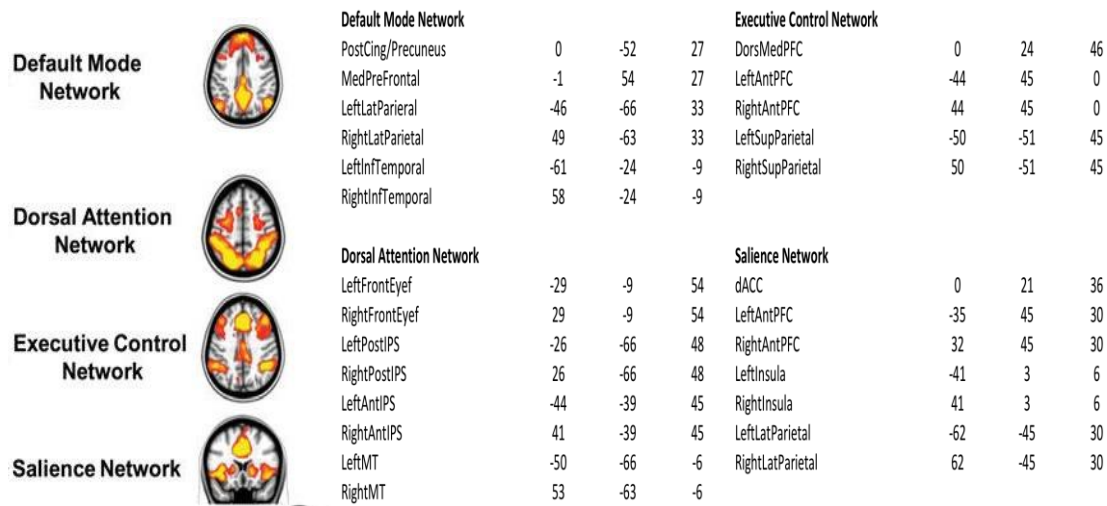


Figure 2. The picture on the left side is taken from Raichle (2011), and it is a visual representation of the networks which appear on the right side. On the right side, a table of all the used ROIs and their anatomical labels is given, including their corresponding networks.

Heine et al, 2012). As a measure of connectivity, the lagged linear connectivity measure (Pascual-Marqui, 2007a) implemented in the KEY Institute eLORETA software package was used. Lagged linear connectivity measures similarities of a time segment of a signal estimated at one location and a time segment of a similar signal from another location. Furthermore, for linear similarities, values of some aspect of the signal in the first time segment have to be directly proportional with values of the same aspect of a time segment at a different location. In addition, lagged connectivity measures reveal similarities between signals both across distance and at a time lag. As this excludes instantaneous functional connectivity, such measures escape the problem of volume conduction. Thereby, driving influences between one brain region and another are captured, unfortunately without resolving the direction of causality.

Differences in functional connectivity between experimental conditions were also assessed using regression analyses, where the independent variable was the hypnotic susceptibility of each participant. No other transformations were applied to the data. The resulting statistical images of functional connections showing significant differences between conditions related to hypnotic susceptibility were computed by statistical non-parametric mapping, applying 5000 permutations. The critical *r*-value resulting from these permutations is adjusted to control for type-I error.

Results

SPECTRAL BAND POWER. A series of mixed-design ANOVAs with factors ‘trait’ (low vs. high susceptibles) and gender (male vs. female) as between-subject measures and ‘state’ (pre-, during-, post-hypnosis) as within-subject measure were computed for scalp averaged power values in each of the six frequency bands defined above. After applying a Bonferroni statistical correction for repeated measures, no main effects were found. Moreover, a ‘state’ and ‘trait’ interaction was not found for any of the six frequency bands defined by Jamieson & Burgess (see above). There were two other significant interactions, however. In the delta frequency band, a significant interaction between trait and gender was found, $F(1, 53) = 9.76, p < 0.001$ (see Figure 3). The same applies for the theta frequency band, $F(1, 53) = 9.79, p < 0.001$ (see Figure 3). Examination of effect sizes revealed an $R^2 = .125$ for the delta frequency band, which means that 12.5% of the total variance in the scalp log-transformed averaged delta frequency band power was accounted for by this interaction. For the theta frequency band, the effect size was much smaller, $R^2 = .041$, which means that only 4% of the total variance in the log-transformed mean scalp power of this frequency band was accounted for by this interaction.

For post-hoc comparisons, Tukey’s Honest Significant Difference (HSD) test was chosen, as it has good power and control over type-I error (Fields, Miles & Field, 2012, p. 432), and does multiple comparisons in one single step. Tukey’s tests for the delta frequency band revealed a significant difference (at $p = 0.0004$) within the low susceptible group between males and females, whereas for the theta frequency band there were two significant differences – within the low susceptible group between males and females (at $p = 0.008$) and within the males between low and high susceptibles (at $p = 0.009$). Figure 3 displays the significant interaction effects. Thus, the analysis of the FFT power spectrum only revealed effects of an interaction between gender and ‘trait’ in the delta and theta frequency band. As expected, no main effects were found, nor were there significant interactions between ‘trait’ and ‘state’ in any frequency band. However, the scores are combined for illustrative purposes in figure A (see Appendix).

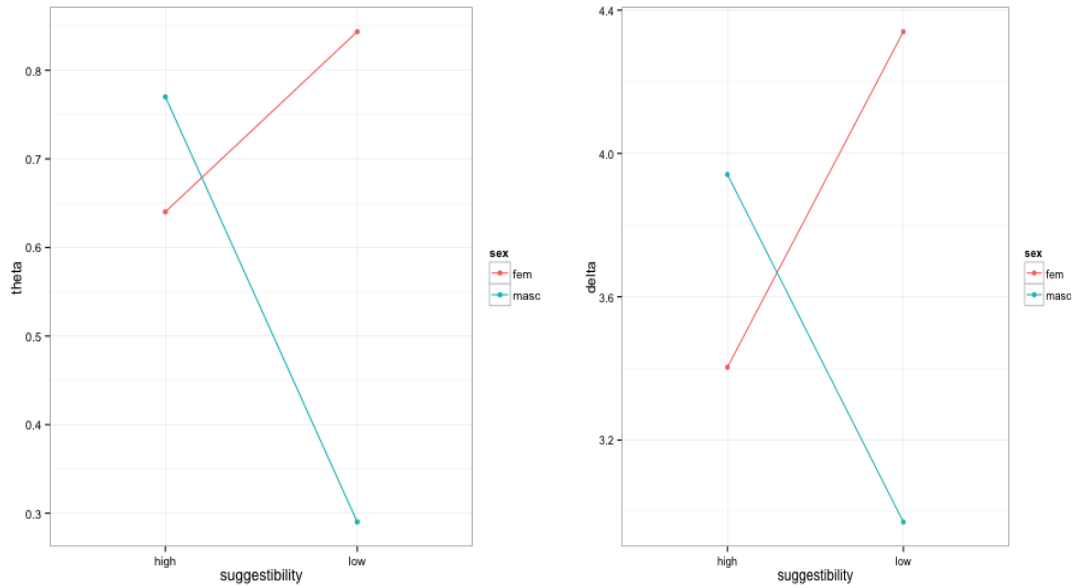


Figure 3. On the left hand side, the natural logarithm of scalp mean theta power is depicted by gender and susceptibility. On the right hand side, the same interaction between gender and susceptibility is shown for the natural logarithm of mean delta power. On both sides, the x-axis represents susceptibility (high vs. low), whereas the y-axis illustrates values of the natural logarithm of scalp mean theta (left) and delta (right) power. The blue lines represent males whereas the red lines represent females.

eLORETA.

Source localization. We conducted two regression analyses within eLORETA, to test for differences in CSD between high and low susceptibles, which are modulated by hypnotic susceptibility. All frequencies mentioned above were included (delta, theta, alpha, beta1, beta2 and gamma). As described above, the r -statistic was calculated voxel by voxel for each frequency band. Following the procedure implemented in the eLORETA package, we applied 5000 random permutations in order to compute the distribution of the maximum r -value for the full voxel set. The computed distribution establishes thresholds of significance of the r -statistic obtained at individual voxels, correcting error-rates due to multiple testing.

We conducted comparisons between the recordings taken before versus during hypnosis and (separately) during versus after hypnosis. Specifically, the first regression compared differences between before and during hypnosis, which are linearly related to hypnotic susceptibility. The second regression looked at differences between during and after hypnosis and their relationship to hypnotic susceptibility. As

predicted, neither the comparison before-during, nor the comparison during-after yielded any significant results.

Connectivity Analysis. Linear lagged functional connectivity (LLFC) (Pascual-Marqui, 2007a) was first calculated between ROIs with centroid coordinates defined by the major cortical nodes of the functional networks identified by Raichle (2011) in each experimental condition and for each individual in the theta and beta1 frequency bands respectively. Then hypnotic susceptibility was applied as a regressor to the changes in LLFC from before to during hypnosis and during to after hypnosis. The significance of the resulting r statistic was assessed with the standard nonparametric statistical method described above. This was done in order to identify those changes in functional connectivity specifically modulated by hypnotic susceptibility. As a parallel analysis, t -test statistics were calculated for differences in the strength of each functional connection between experimental conditions in low and high susceptible groups separately. Note that the significance reported for these t statistics is also evaluated by the same nonparametric statistical testing procedure described above.

Theta. Figure 4 displays the significant theta connectivity results. For theta, we found the predicted increase in LLFC related to hypnotic induction (depending on hypnotic susceptibility) to occur between key nodes of the default mode network (DMN), the salience network (SalN) and the executive control network (ECN). In the DMN, we found a significant increase in theta functional connectivity between the left and right lateral parietal cortex ($t = 3.17$, $p < 0.05$), when only comparing highs in the conditions before – during hypnosis. In addition, there was a significant decrease in theta connectivity between the left and right lateral parietal cortex in highs during – after hypnosis ($t = 3.69$, $p < 0.05$). In the SalN, a borderline significant increase in theta connectivity was found between the left anterior PFC and the right insula when testing differences before-during between highs and lows, modulated by hypnotic susceptibility (significant at $r = 0.54$; $r = 0.55$ for $p < 0.1$). The same trend, although not significant, was visible when highs as a group were compared across conditions before – during hypnosis). Moreover, there was a significant decrease in theta connectivity between the dACC and the left lateral parietal cortex when comparing highs during – after hypnosis ($t = 3.95$, $p < 0.01$), and a decrease between the left anterior PFC and the dACC for the same group and condition ($t = 3.26$, $p < 0.05$).

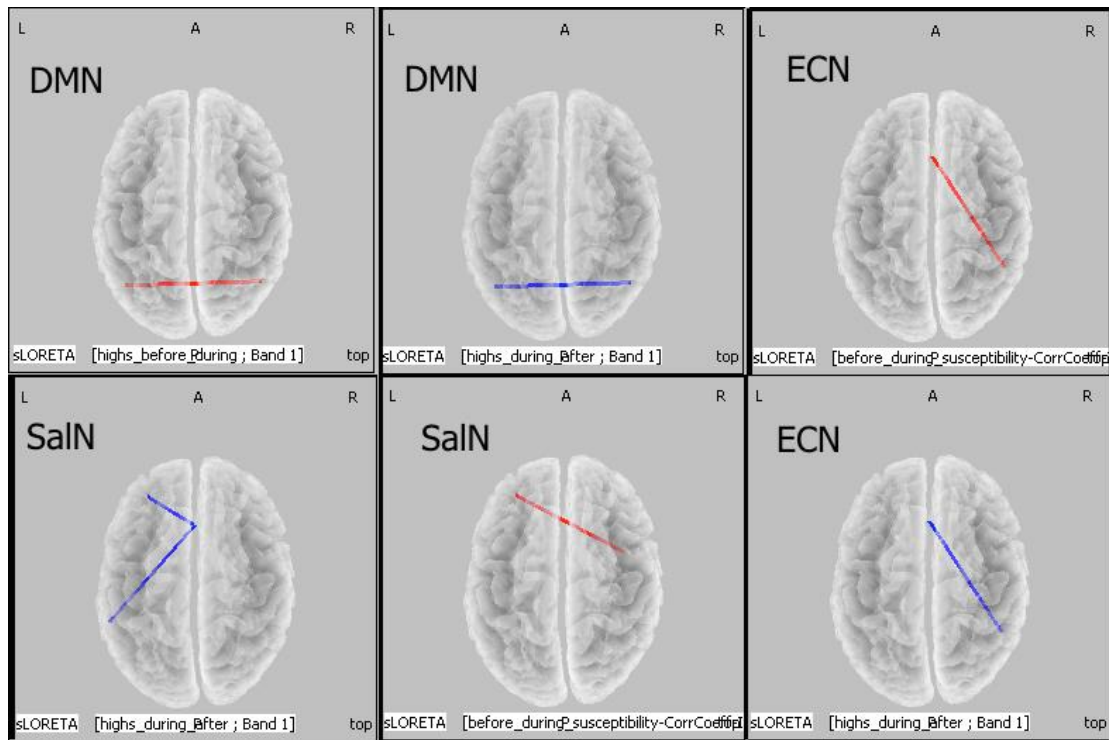


Figure 4. Significant hypnosis related functional connectivity changes in the theta frequency band in different networks (DMN = default mode network, ECN = executive control network, SalN = salience network). Left is anatomical left. All the axial views are views from the top. The red wires indicate relative increases, whereas the blue wires show relative decreases. The ends of the lines (points) represent centroids of the defined ROIs. An overview shows increases in all networks in the before-during condition and decreases in the during-after condition (the condition can be read at the bottom of each picture). The first picture indicates an increase in theta connectivity between the left and right lateral parietal cortex for highs before-during, whereas the second picture shows a decrease in the same area for highs during-after. The top right picture shows an increase in connectivity between dorsal medial PFC and right superior parietal lobe for highs and lows before-during with susceptibility, whereas the bottom right picture shows a decrease in the same area for highs during-after. The bottom center picture indicates an increase in functional connectivity between the left anterior PFC and the right insula (highs and lows before-during with susceptibility), whereas the bottom left picture shows decreases between left anterior PFC and dACC and between dACC and left lateral parietal cortex.

In the ECN, an increase in LLFC was found between the dorsal medial PFC and the right superior parietal lobe when comparing differences before – during between highs and lows, modulated by hypnotic susceptibility ($r = 0.56, p < 0.05$). Consistent with this, the exact inverse trend was observed for the susceptibility-related changes during – after hypnosis, although this was not significant. Moreover, when comparing only highs during – after hypnosis, there was a significant decrease in theta connectivity between the dorsal medial PFC and the right superior parietal lobe ($t = 3.4, p < 0.05$).

Beta1. Figure 5 shows the significant beta1 band LLFC results. For beta1, we found the postulated decrease in LLFC to occur between nodes of the dorsal attention network (DAN) and the ECN. However, an unexpected hypnosis related increase in beta1 connectivity was also observed between specific nodes within the SalN and the DAN. In the DAN there was a decrease in beta1 connectivity between the left frontal eye-field and the left middle temporal complex (MT), when testing for changes before – during hypnosis related to hypnotic susceptibility ($r = 0.59, p < 0.05$). Moreover, when comparing only highs before – during hypnosis, there was a decrease in beta1 LLFC between the left and right frontal eye-field and a synchronous increase between the left and right MT ($t = 3.4, p < 0.05$). In the ECN, a decrease in beta1 connectivity between the dorsal medial PFC and the left superior parietal lobe was found when testing the changes from before to during hypnosis related to hypnotic susceptibility ($r = 0.47, p < 0.1$). A finding inconsistent with predictions was found in the SalN: an

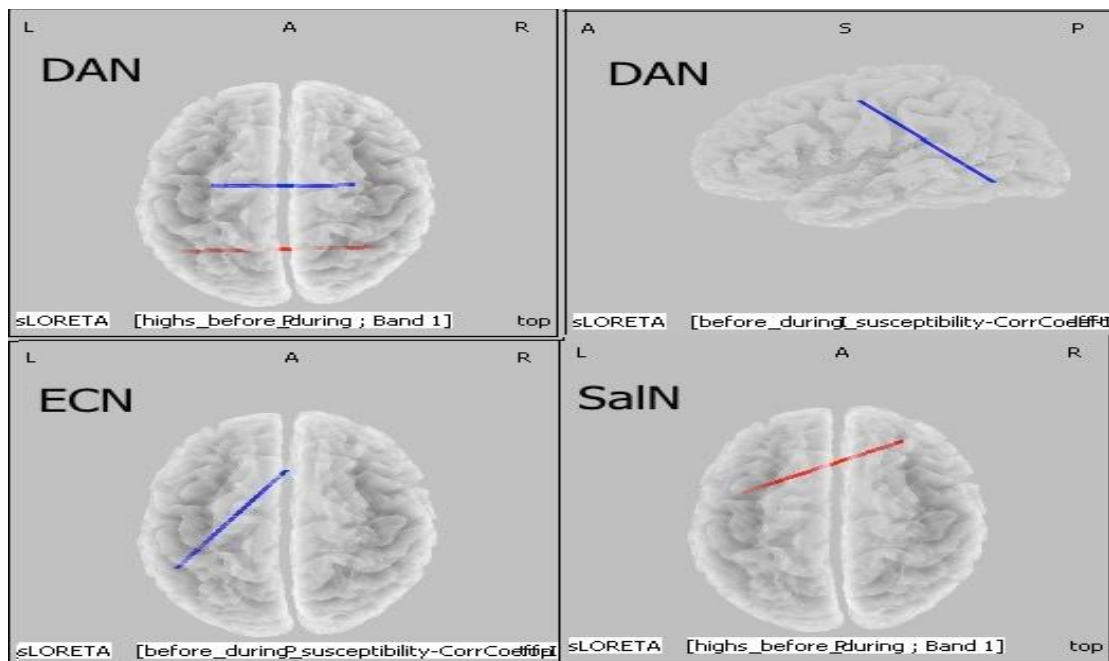


Figure 5. Significant hypnosis related functional connectivity changes in the beta1 frequency band in different networks (DAN = dorsal attention network, ECN = executive control network, SalN = salience network). Left is anatomical left. All the axial views are views from the top, except the top right picture, which represents a sagittal view from the left. The blue wires indicate decreases between regions, whereas the red wires indicate increases in connectivity. The dots connected by the wire represent the centroids of the defined ROIs. All the pictures are representations of changes between the conditions before during. Top left: decreased connectivity between left and right frontal eye-field and increased connectivity between left and right MT. Top right: decreased connectivity between left frontal eye-field and left MT. Bottom left: decrease in connectivity between dorsal medial PFC and left superior parietal lobe. Bottom right: increase in connectivity between left insula and right anterior PFC.

increase in beta1 connectivity for highs before – during hypnosis between the left insula and the right anterior PFC ($t = 4.00$, $p < 0.01$).

Discussion

This study aimed firstly at quasi-replicating the core results reported by Jamieson & Burgess (2014) of hypnosis-related increases in functional connectivity in the theta band and increases in the beta1 band. Secondly, it aimed to extend those results from sensor space into source space and to examine those changes within the major networks involved in regulating the content of experience. For this purpose, the eLORETA source localization method was used.

The results confirm that spectral analysis is not recommended for identifying “state” changes in hypnosis. This finding supports similar recent results by Jamieson and Burgess (2014). As expected, no significant differences were found between groups or conditions, except an interaction between gender and trait (low versus high susceptible) in mean scalp delta and theta power. As the pattern of the interaction was identical, and delta and theta are adjacent frequency bands, this interaction may represent a more general low frequency effect. This unexpected result suggests that there are important gender differences in neurophysiological expression of hypnotic susceptibility.

The extension of the spectral band power analysis from sensor to source space by eLORETA analysis of CSD differences failed to identify any significant regional differences. Specifically, we tested each frequency band for differences in CSD between high and low susceptible participants, which are modulated by hypnotic susceptibility. This expected null result further confirms both the scalp-based spectral band power results reported above, and those of Jamieson and Burgess (2014). It highlights either the inadequacy of spectral band power measures alone to define hypnotic states of consciousness or the essential unreality of such ‘states’.

Results of the connectivity analysis broadly support the connectivity findings of Jamieson and Burgess (2014). Using measures of coherence (iCOH versus LLFC), both this analysis and the one presented by Jamieson and Burgess (2014) indicate an increase in functional connectivity in the theta band and a decrease in the beta1 band. It is increasingly plausible that susceptibility related changes in functional

connectivity in the theta and beta1 bands, contingent upon hypnotic induction, represent neurophysiological correlates of the hypnotic state. Moreover, these findings were shown to include changes in functional relationships between core nodes of the principal cortical networks discovered to govern the contents and dynamics of awareness. These results provide a real advance towards establishing hypnosis as an altered state of the mind-brain system and also towards identifying some of the key components of that state.

Functional roles of the theta and beta1 rhythms

Theta. Baghdadi & Nasrabadi (2012b) found that the ratio of phase synchrony in the delta, theta and beta band successfully characterize high susceptibles and dissociate them from low susceptible individuals. When trying to find a faster, more reliable test for assessing hypnotic susceptibility than current available lengthy procedures (such as SHSS:C), the authors found that the ratio of phase synchrony in these three frequency bands in hypnosis as compared to a pre-hypnosis baseline was lower than in low susceptibles (Baghdadi & Nasrabadi, 2012b). Based on these results, the researchers propose a system of EEG monitoring during a hypnotic induction and imagine the application of an algorithm, which would instantaneously calculate the phase synchrony in these bands. This would lead to a more concise and practical assessment of an individual's susceptibility level. Moreover, Baghdadi & Nasrabadi (2012a) found that the theta frequency band seems to be related to hypnotizability more than other bands. They conclude that the raise in theta band may be due to the repression of frontal functions, as theta was shown to spike when an individual was trying to suppress a response or an action (Kirmiziansan et al, 2006). However, theta has also been shown to appear during mental activity, such as focusing on a task (Wang, 2010), and has been postulated as a mechanism of selective attention (Vinogradova, 1995). In addition, as emphasized by Jamieson and Burgess (2014), theta is also known to act in the facilitation of transmission between distant brain structures. Moreover, theta also spikes in orienting exploring activities (Vinogradova, 1995). Nevertheless, it still supports the "active ignoring" mechanism of the hippocampus (Vinogradova, 1995, p 571).

Beta. It is known that beta signals primarily originate in the deep layers of the cortex (Wang, 2010). This frequency band is thought to also be involved in long distance signaling along feedback pathways, where top-down signals encode

expectations that guide learning (Wang, 2010). Moreover, there is evidence of implication of the beta rhythm in attention, movement behavior, response inhibition and broader cognitive processes, such as selective attention, working memory, guided search, object recognition, perception (involving top-down signaling from the frontal eye-field) and sensorimotor integration. In addition, given that beta1 is increased when a specific response is withheld, this rhythm has been associated with preparation and inhibitory control as well (Wang, 2010).

Given the implication of these two frequency bands in such various activities, it is difficult and precarious to make direct assumptions regarding the functions of the two rhythms. While caution must be taken in interpreting such results, one can nevertheless make reasonable suggestions of their roles in the case of hypnosis.

First of all, the results indicate an increase in theta band connectivity in the DMN. The DMN is a network of regions active during resting states. During a default mode state, specific midline brain structures, such as the posterior cingulate cortex/precuneus, mesiofrontal areas (including the dACC) and temporoparietal junction areas (Heine et al, 2012; Raichle, 2011; Greicius, 2003) are collectively activated. DMN activity has been linked to self-related and internal processes (e.g. stimulus-independent thought), mind-wandering, social cognition, introspection, monitoring of the “mental self” and integration of cognitive processes (Heine et al, 2012). Furthermore, deviations from a normal functioning of the default mode network during hypnosis might support the hypnotic state account (McGeown et al, 2009).

This study found an increase in theta band connectivity in the DMN, between the left and right lateral parietal cortex, after a hypnotic as compared to before a hypnotic induction. Moreover, a decrease a decrease in connectivity was observed between the exact same nodes after de-induction was observed, which strengthens the importance of this result. No significant changes were found in this network for the beta1 band. Previous studies focusing on the DMN have shown decreased activity in this region following a hypnotic induction (McGeown et al, 2009; Heine et al, 2012). However, Heine et al (2012) observe that in the hypnotic state there may be only little or no connectivity decreases within the DMN. Our results show increased connectivity between the dorsal nodes (left and right lateral parietal cortices) of the DMN. Although functional connectivity and activation are often related, McGeown et al (2009) report results, which seem contradictory to ours. Specifically, they identified a

decrease in activity in the anterior midline node of the DMN, without a concurrent decrease in the posterior midline node or other increases in activity in task-related structures. Nevertheless, Greicius, Krassnow, Greiss & Menon (2003) and Uddin, Kelly, Biswal, Castellanos & Milham (2009) report differences between the anterior and the posterior midline nodes of the DMN, concluding that there must be a functional specialization within nodes of this network. When studying the anti-correlation of activity in other networks with anterior (ventro-medial pre-frontal cortex, vmPFC) and posterior nodes (posterior cingulate cortex, PCC) of the DMN, Uddin et al (2009) found that their internetwork connectivity was dissociable. The networks which were anti-correlated with the anterior node (PCC) were prefrontal motor planning and control circuits and the insula. The authors argued that given that the insula is closely connected with the human mirror neuron system (HMNS), the DMN and the HMNS may interact during self-related cognition. Moreover, the authors indicate that the DMN as a whole may coordinate activity between these two regions (Uddin et al, 2009). Consequently, Uddin et al (2009) also remark that failure to suppress activity in dorsal nodes (PCC) of the DMN is associated with attentional lapses.

Thus, the suggestion that hypnosis may involve an altered functioning of the DMN (as compared to normal eyes-closed resting conditions) finds support within our results. Moreover, as Heine et al (2012) suggest, these changes in functional connectivity might be linked with modified self-related mentation. This is important, as it further contributes to the state-non-state debate by adding evidence of differences in neural organization between hypnosis – when devoid of any specific suggestion other than the induction – and a normal resting state.

Whether these differences are further linked with a disrupted pattern of attentional control can only be indicated by the specific results found in the networks, which direct and modulate attention. Nevertheless, only the beta1 rhythm showed significant susceptibility differences in LLFC before hypnosis – during hypnosis between specific nodes of the DAN. No other differences during hypnosis – after hypnosis were found. However, both decreases and increases between various nodes of the DAN were found.

The DAN is a fronto-parietal network (Corbetta, Kincade & Shulman, 2002; Ptak & Schneider, 2010) activated by presentation of cues, which indicate perceptual and response features of stimuli to which participants should direct their attention

(Corbetta & Shulman, 2002). This network includes structures such as the bilateral frontal eye-fields, the bilateral anterior and posterior intraparietal sulcus and the bilateral middle temporal complex (see also Ossandón et al). These regions have been shown to activate during voluntary top-down attentional selection (Jha, Krompinger & Baime, 2007), working memory, directed visuomotor behaviour (Corbetta et al, 2002), spatial attention as well as covert attentional shifts (Corbetta et al, 1998). Moreover, the frontal eye-fields and the intraparietal sulci play critical roles in spatial coding (Corbetta et al, 2002).

The decreases in beta1 LLFC in the DAN were observed between the left and the right frontal eye-field and between the left frontal eye-field and the left middle temporal complex, whereas increases in LLFC were seen between the left and right middle temporal complex (MT). It has been shown that there is a joint network for attention and eye-movements (Corbetta et al, 1998). Rossi, Pessoa, Desimone and Ungerleider' (2009) also observed that the frontal eye-fields are important PFC sites, being activated during cognitive control. Jha et al (2007) also demonstrate the role of the frontal eye-field in attentional orienting. In addition, Corbetta et al (1998) emphasize that regions activated by attention shifts include the MT and that the mechanisms for covert and overt attention shifts overlap in the brain. Moreover, Kastner and Ungerleider (2000) suggest that the MT is an area where top-down attentional mechanisms operate by enhancing responses to stimuli at the attended location, while biasing general processing in favour of stimuli which appear at the that location. The increases in beta1 functional connectivity were observed between corresponding left and right temporal regions, which are involved in auditory processing and speech perception. This result may indicate attention towards the hypnotists' voice. Even though the hypnotist was not talking during the recordings, the participants may have kept their attention focused in order to respond when the hypnotist would address them again. The decreases in beta1 activity between the left and right frontal eye-field and the left frontal-eye field and left MT might indicate inhibition or decoupling of conflict monitoring processes and cognitive control processes of the frontal attention network (see e.g. Egner et al, 2005; Jamieson & Sheehan, 2004). In sum, the changes in the organization of the DAN in hypnosis might indeed include dissociation of attentional control processes, although hypnosis requires that attention be allocated to the hypnotists' voice, yielding, in sum, a discrete pattern of attentional organization.

The results for the SalN were more consistent. As described by Heine et al (2012), the SalN encompasses fronto-insular and ACCs and their connections to subcortical and limbic structures. This network has been shown to activate during orientation towards salient emotional stimuli (Seeley et al, 2007), conflict monitoring, information integration, and response selection; and has been linked to pain-related processes (Heine et al, 2012).

The increases in theta band connectivity between the right insula and the left anterior PFC and the increases in beta1 connectivity between the exact opposite part (left insula and right anterior PFC) both indicate increased communication between these brain locations. These increases in functional connectivity are supported by decreases in the SalN after hypnosis as compared to during hypnosis, between the dACC and the left anterior PFC and between the dACC and the left lateral parietal cortex). Moreover, the salience network is known to integrate highly processed sensory data with visceral, hedonic and autonomic information so that the organism can decide what to do next (Seeley et al, 2007). Sridhara, Leviton and Menon (2008), and Menon and Uddin (2010) argue that the SalN, in particular the anterior insula, plays a crucial role in switching between DMN and ECN. Moreover, research indicates that the dACC is implicated in conflict monitoring and evaluation (Botvinick, Cohen & Carter, 2004; MacDonald, Cohen, Stenger & Carter, 2000), without being involved in conflict resolution. Although, at first glance, this rather frontal pattern of distribution might resemble frontal-midline (FM) theta (Wang, 2010; Kubota et al, 2001), current results suggest that, in the case of hypnosis, it is not the DAN or the ECN that are affected by such increases, as usually associated with FM theta. Particularly, these results indicate a functional role of the theta rhythm in the SalN, with a core node in the anterior insula, the dACC and the PFC. This discrete organization in functional connectivity indicates an increased association between information integration and conflict monitoring processes.

Finally, the ECN is a network whose activity has been related not only to the control of goal-directed behavior, target detection, error detection, conflict resolution, and inhibition of automatic responses, but also to tasks which require mental effort such as dealing with conflict, handling novelty and developing anticipations (Berger & Posner, 2000). This network includes regions such as bilateral middle, inferior and superior frontal cortices (Heine et al, 2012) and bilateral inferior and superior parietal cortices.

In what regards the results for the ECN, increases in theta band functional connectivity have been found during hypnosis as compared to before hypnosis between the dorsal medial PFC and the right superior parietal lobe, which were complemented by successive decreases in the same hubs after hypnosis as compared to during. The right-sided distribution of this increase is clearly visible. Regarding this, Heine et al (2012) remark that the right executive control network is engaged in perceptual, nociceptive and somesthetic processing. Furthermore, as Bhagdhadi et al (2012a, b), and Jamieson and Burgess (2014) remark, it is possible that this decrease in functional connectivity reflects a dissociation of frontal functioning and higher executive functions. Moreover, this interpretation would be supported by the decreases in beta1 functional connectivity between the dorsal medial PFC and left superior parietal lobe, which might indicate a dissociation of executive functions. This finding is rather supportive of dissociation theories of hypnosis (Egner et al, 2005; Jamieson & Sheehan, 2004).

An important next step is further replication of these results in source space. Without replication, these observed changes remain merely suggestions and speculations. It is important that the changes in connectivity observed in the different functional networks are confirmed, as this would lead to further clarity about the exact mechanisms involved in the hypnotic state. Moreover, an interesting issue that arises from this pursuit is the functional connectivity between the networks themselves. Although these preliminary analyses have been made, the presentation of these results is beyond the scope of this study. However, the study of interactions between different functional networks during hypnosis would further shed light on the mechanisms involved, contributing immensely for example to the resolution of dissociation versus focused attention debate on the mechanism of various hypnotic responses. In regards to state – non-state debate, it seems that an increasing amount of research in functional connectivity is indicating that the theta band is important in implementing hypnotic responses. If changes in the organization of theta band functional connectivity represent a neurophysiological marker of the hypnotic state, the next question for researchers is whether and if so, how, this state causally contributes to the generations of responses to hypnotic suggestions. By combining behavioral, phenomenological as well as neuroimaging or electrophysiological measures, such questions can be answered.

Finally, the importance of finding answers to questions as the ones suggested above is shown by the wide application of hypnotic procedures in the clinical field. Hypnosis has been shown to have successful application in various pathological settings, such as cancer care (Lioffi, 2006), rehabilitation after stroke (Diamond, Davies, Schaechter & Howe, 2006), and treatment of phantom limb pain (Bamford, 2006). Moreover, a meta-analysis by Schnur, Kafer, Marcus and Montgomery (2008) showed that there is a large effect size in favour of hypnosis being able to reduce stress associated with medical procedures. Another meta-analysis by Adachi, Fujino, Nakae, Mashimo and Sasaki (2014), studying the effects of hypnosis in chronic pain treatment, found results suggesting the efficaciousness of such procedures in this field. Given the wide application of hypnotic procedures to the relief and ailment of individuals, more clarity about the functional mechanism of hypnosis contribute to extending its applications.

Limitations of this study. First of all, it is important to address the study design. Although containing additions to the design used in Jamieson and Burgess (2014), there is always room for improvement. For example, the current study did not include any ratings of the self-perceived levels of hypnosis (i.e. hypnotic depth, Cardena et al, 2013) ratings. Although we controlled for differences between hypnosis and no hypnosis by including low susceptible people and by using susceptibility scores as regressors when analyzing the data, it could be possible that inclusion of participant's hypnotic depth self-ratings would give us higher precision when interpreting the results. In addition, it would have been useful to study neurophenomenological correlates of these neurophysiological changes. Although the PCI was administered, it was not included in these analyses. Another important step, therefore, will be the inclusion of phenomenological analyses, in order to map the relationship between subjective experience and neural activity (see Cardeña et al, 2013). It is important to emphasize that our aim here was the exploration of the neural organization of the hypnotic state, in order to identify correlates that may mark the on-set of such a state. Although behavioural data has previously been regarded as the gold standard in determining such questions, EEG data is more precise and is not cued or motivated by demand characteristics, which is a main problem when only self-report and behavioural responses are being studied. However, the combination of all three types of measure may lead to the most valid results.

The present study restricted connectivity analysis to the theta and beta1 frequency bands. It may be useful to conduct exploratory analyses in other frequency bands. Another objection could be brought to our method of ROI construction, which allowed for quite large areas to be included (all voxels within a radius of 20mm). It is possible that a method of ROI construction, using more restricted ROI volumes, would yield results that are more informative. In addition, although each 2-minute recording was independently visually inspected for artifacts, eLORETA is extremely sensitive to such biases. Furthermore, it is also important to remind that the present analysis was based on 2-minute resting segments. Although studying linear lagged functional connectivity, which has provided a better picture of hypnosis state changes than spectral band power or conventional coherence, these results are still limited by the fact that state changes are continuous and cannot be reduced to activity recorded in two minute segments at different points in the hypnosis session. In order to fully represent such changes, a continuous time series functional connectivity analysis of the whole induction and later hypnosis procedure should be undertaken. Pioneering work in this direction is available, but only in the form of single case studies (see e.g. Fingelkurts et al, 2007b). Such an investigation would involve an immense computational cost, given current data preparation and analysis procedures available for EEG data. Therefore, comprehensive applications of such methods must await further technological developments.

Conclusion

This study examined the neural organization in specific functional networks following a hypnotic induction, in order to continue the search for a hypnotic state ‘marker’. Results suggest that changes in functional connectivity in the theta and beta1 bands following a hypnotic induction are linked with a reorganization of operations within networks involved in the production and regulation of conscious experience, thus supporting the altered state account of hypnotic phenomena.

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Appendix

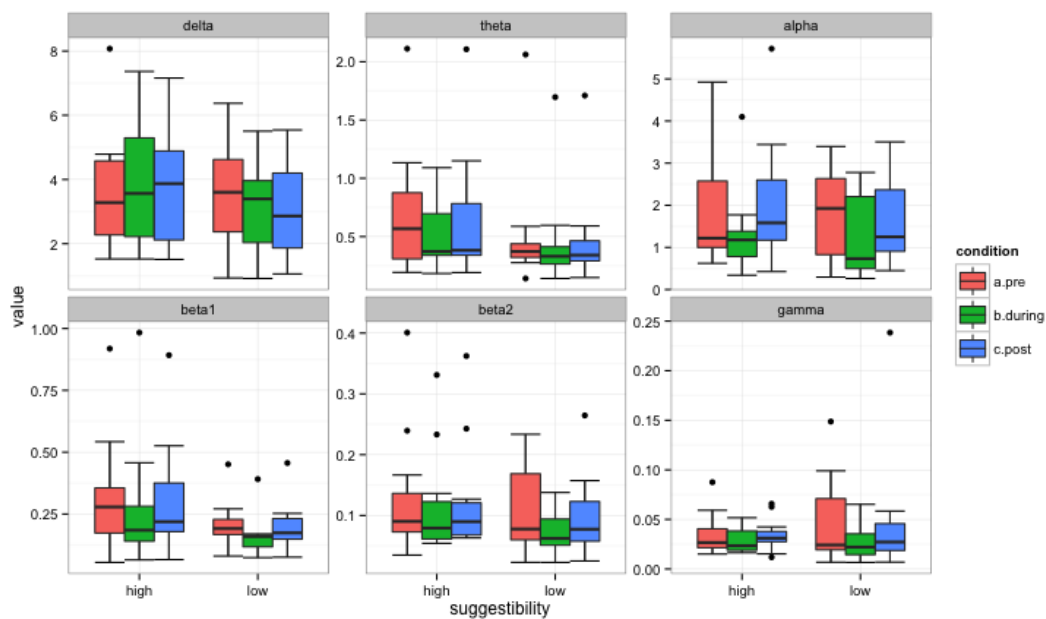


Figure 2. Differences in the natural logarithm of mean power in each frequency and condition, modulated by susceptibility, are here depicted for illustrative purposes. The red boxplots represent the “before” hypnosis condition, the green ones the “during” hypnosis condition and the blue ones the “after” hypnosis condition. The three left boxplots in the pictures stand for the highs, whereas the other three boxplots on the left hand side represent the lows. As is visible, slight differences exist in each frequency band. The more prominent differences can be seen in delta, theta (highs), alpha (lows), and beta1 (highs). However, none of these differences were significant.

R code.

```
library('compute.es')
library('reshape')
library('car')
library('xlsx')
library('ggplot2')
library('multcomp')
```

```

library('pastecs')
setwd("/Users/ruxi/Documents/MSc/Dissertation/Pooled_FFTdata/stats")
data <- read.table("anovaordered.txt", header = TRUE)
View(data)
summary(data)
attach(data)
options("scipen"=100, "digits"=4)
shapiro.test(delta)
shapiro.test(theta)
shapiro.test(alpha)
shapiro.test(beta1)
shapiro.test(beta2)
shapiro.test(gamma)
a <- log(alpha)
b1 <- log(beta1)
b2 <- log(beta2)
d <- log(delta)
g <- log(gamma)
t <- log(theta)
leveneTest(a, interaction(sex, condition), center = median)
#contrasts(suggestibility) <- cbind(c(-2, 1, 1), c(0, -1, -1)) when planned comparisons
alpha.model <- aov(a~suggestibility*condition*sex)
summary(alpha.model)
summary.lm(alpha.model)
beta1.model <- aov(b1~suggestibility*condition*sex)
summary(beta1.model)
summary.lm(beta1.model)
beta2.model <- aov(b2~suggestibility*condition*sex)
summary(beta2.model)
summary.lm(beta2.model)
delta.model <- aov(d~suggestibility*condition*sex)
summary(delta.model)
summary.lm(delta.model)
gamma.model <- aov(g~suggestibility*condition*sex)
summary(gamma.model)
summary.lm(gamma.model)
theta.model <- aov(t~suggestibility*condition*sex)
summary(theta.model)
summary.lm(theta.model)
da <- aov( d~ suggestibility*sex)

```

```
TukeyHSD(da)
ta <- aov(t~suggestibility*sex)
TukeyHSD(ta)
```

Hypnotic Induction Script.

Just settle back comfortably in your chair and relax. We are going to do a hypnotic induction procedure that will allow you to enter a hypnotic state, and then we will ask you to perform the tasks that you have practiced on the computer. Before we do this we will first show you a relaxation procedure, which will allow you to relax.

After relaxing your body, we will show you how to calm your mind. We will count backwards from "10" to "1", while you let your mind become more and more calm and at ease. As I count back from "10" to "1", I will ask you to count along silently with me, so that by the time we get to "1", your mind will be deeply and calmly at ease. As this happens you may feel yourself moving into a hypnotic state, a state, which many people report feels somewhat like falling asleep, but with the difference that you will still hear me clearly, you will be able to respond and move if you need to, and to perform the tasks that you have practiced. Do you have any questions before we start? (IF NO QUESTIONS, THEN PROCEED.)

OK. Whenever you are ready, just allow your eyes to close. Just rest for a few minutes with your eyes closed now and we will soon start with the relaxation procedure.

[Resting EEG recording 1 – Pre-Hypnosis (1min)]

[Administer PCI]

Now just forget about any other sounds and noises you may hear and bring your attention inwards. Let's begin by becoming aware of your breathing. Just become aware of your breathing, and with each breath that you take, notice how relaxed you can become every time you breathe out. Let your breathing be rhythmic and natural and as you inhale and as you exhale, notice how much more relaxed you can become. That's right. With each breath that you take, let yourself become more and more calm and more and more relaxed, as you forget about any other sounds or noises you may hear except for my voice. While being aware of your breathing, let yourself relax, more and more deeply, more and more fully relaxed with each breath that you take.

I now want you to focus your attention on the muscles of your forehead and scalp and let them relax. That's right, focus on the muscles of your forehead and scalp and let any tension and tightness just fade and vanish away, fade and vanish away. Feel how relaxed and at ease you can let the muscles of your forehead and scalp become.

Now, feel the relaxation moving down into the muscles around your eyes and your temples. Focus on the muscles around your eyes and temples, and let any tension and tightness there just fade and vanish away. Feel how relaxed and at ease you can let the muscles around your eyes and temples become. Let your eyes relax. Let your eyelids become heavy, very, very heavy; very, very relaxed. See how relaxed and at ease you can let the muscles around your eyes become. Now imagine the relaxation moving down into your cheeks and nose, and now, down across your chin and jaw. Focus

on the muscles of your chin and jaw, your cheeks and nose, and let all tension and tightness just fade and fade and vanish away, as you become more and more relaxed, more and more relaxed.

Feel the relaxation now move down into the muscles of your neck. Focus in on the muscles of your neck and shoulders and let any tension and tightness there just fade and vanish away. Visualize the muscles of your neck and shoulders becoming more and more relaxed, more and more at ease, as all tension and tightness in your neck and shoulders just fades, and vanishes away. With each breath that you take, with every word that I say, feel the muscles of your neck and shoulders relax, more and more relaxed, more and more at ease.

Now, let the relaxation move down into your upper arms. Let the muscles and tissues of your upper arms become more and more relaxed, more and more at ease, as all tension and tightness fades away and vanishes. Feel wave upon wave of deep, soothing relaxation now move down through your elbows into your lower arms, and into your wrists, hands and fingers. Let all the muscles and tissues of your upper and lower arms, your hands and fingers become more and more relaxed, more and more at ease, letting go of all tension, as you forget about any noises and sounds other than my voice. Feel how heavy and relaxed the muscles of your arms and hands can become.

Now let the relaxation in your arms and hands, move back up into your shoulders and down into your chest and upper back. Let the muscles and internal organs of your chest and upper back become more and more relaxed, more and more at ease. Feel and imagine the muscle fibers relax and become more and more soft and loose, so that your heart and lungs can work more efficiently, more at ease. Just relax, relax deeply, relax fully.

Now let the relaxation continue down into your stomach and abdomen, your hips and lower back. Let the muscles and internal organs of your hips and lower back, your stomach and abdomen become more and more relaxed, more and more at ease. Feel how deeply relaxed and fully at ease you can let yourself become. More and more relaxed and at ease with every word that I say, with every breath that you take. See how relaxed you can let yourself become.

Feel the relaxation now gently move down into the muscles of your upper legs. Feel the relaxation permeate each and every muscle fiber as the muscles there become more and more relaxed, more and more heavy and deeply relaxed. Let the relaxation continue now down through your knees into your lower legs, and finally, your ankles, your feet, and your toes. Let all the muscles and tissues of your legs, and feet, and toes, become more and more relaxed, more and more at ease. Let all the muscles of your body relax.

Now scan your body for any tension and tightness that may remain, and let it all just fade away. See how even more relaxed you can let yourself become. Your body is now very relaxed, completely at ease. You can let your mind now become as calm and at ease as your body is relaxed. In a few moments, I am going to count back from "10" to "1" and with each number that I say, I would like you to count along silently with me.

With each number that I say, with each number that you say silently, your mind will become more and more calm, more and more serene, more and more empty, so that when we get to "1", your mind will be completely calm, completely still. And as we count back from "10" to "1" you will feel

yourself drifting off into a pleasant and relaxed hypnotic state, a state that many people report feels very much like falling asleep, but with the difference that you can clearly hear me.

You will always hear me no matter how relaxed, how calm, how deeply hypnotized you feel yourself to be, and you will be able to speak if you need to, to open your eyes and move and perform the task on the computer, while always remaining deeply hypnotized. You feel very safe, very secure, and very at ease. Very safe, very secure, and very at ease.

Here we go. Ten. . nine. . . let your mind become more and more calm, more and more clear, more and more still, as all worries and problems just fade and fade and vanish away. See how clear and calm and serene you can let your mind become. Eight . . . seven . . . , let go of all worries and thoughts as your mind becomes still more at ease, more and more quiet, more and more serene, as you begin to drift off into a pleasant relaxed and calm hypnotic state. Calm, relaxed, and at ease; calm . . . , relaxed . . . , and at ease. More and more calm, more still and serene.

See how relaxed and at ease you can let yourself become. Forget about anything except for my voice, just focus on my voice as you go more and more deeper still.

Six . . . five . . . , feel your mind becoming more and more calm as you begin to go more and more deep, more and more deeply at ease, as you drift off into a very pleasantly relaxed and quiet hypnotic state. A state a bit like falling asleep, but with the difference that you will still hear me clearly, and be able to perform the tasks you have practiced with ease, remaining deeply hypnotised. Four, feel yourself going deeper and deeper into a pleasantly relaxed and quiet hypnotic state, deeper and deeper, more and more calm, relaxed and at ease.

Three, going deeper and deeper, as your mind and body become more and more calm, more clear, more relaxed and at ease. Two, letting go deeper and deeper still, more and more relaxed, more and more calm. One . . . You are so deeply at ease, almost asleep, nothing will disturb you as you feel so calm, clear, quiet and deeply relaxed, deeply at ease. Although deeply hypnotised, you can clearly hear me; you will always hear me no matter how relaxed or asleep you may feel.

Now just rest for a few minutes with your eyes closed and we will soon continue with the rest of the procedure.

[Resting EEG recording 2 – Hypnosis (1min)]

Ok, in a little while, I will ask you to open your eyes while remaining just as deeply hypnotized as you are now. You will be able to adjust your posture, ask questions if you need to, to respond and perform the task you have practiced, while remaining comfortably relaxed and deeply hypnotized, calm, aware and at ease.

After you complete the happy-face sad-face task, you can rest for a while, and then I will give you some instructions before continuing to the next part.

Now, slowly open your eyes, look at the screen, and take a moment to let your eyes adjust to the light. Please read the instructions on the screen, and if you have any questions about the task, just let me know. Adjust your body if you need to so you can reach the mouse and the keyboard on the desk. Then whenever you are ready, you can start. When you complete the task, you can just close your eyes again and relax.

[Memory Acquisition Task]

(Ok, just let your eyes close now and relax.) You have concentrated well upon the task, so allow yourself some time to rest now and relax, and settle even deeper into a calm, clear, quiet state of mind, always deeply at ease. 10s

Now as you keep listening to my voice, you are becoming more and more deeply relaxed, with each breath, deeper and deeper, more and more relaxed, breathing regularly and with ease.

In a little while, I will ask you to open your eyes and remain just as deeply hypnotized as you are now. You will be able to adjust your posture, ask questions if you need to, respond and perform the new-old face task that you have practiced earlier, while remaining comfortably relaxed and deeply hypnotized, calm, aware and at ease.

All right, remain deeply relaxed now but listen carefully to what I tell you next. In a little while I will ask you to open your eyes and perform this task on the computer.

You will find however that you are unable to remember the faces you saw previously. You will be unable to remember any of those faces until I tell you that you can remember them. Even now your memory of them is fading. You are becoming less and less able to recall them, less and less. Soon you will be unable to recall any of the faces which you saw previously. You will forget all the faces you have just seen until I say to you: *Now you can remember everything!* You will not be able to remember any of those faces until then. When I tell you that you can remember you will be able to remember all the faces that you saw previously.

Now open your eyes slowly, look at the screen, and take a moment to let your eyes adjust to the light. Please read the instructions on the screen, and if you have any questions about the task, just let me know. Adjust your body if you need to so you can reach the mouse and the keyboard on the desk. Then whenever you are ready, you can start. When you complete the task, you can just close your eyes again and relax.

[Recognition Task 1]

(Ok, just let your eyes close now and relax.) You have concentrated well upon the task, so allow yourself some time now to rest and relax, and settle even deeper into a calm, clear, quiet state of mind, always deeply at ease. 10s

Now as you keep listening to my voice, you are becoming more and more deeply relaxed, with each breath, deeper and deeper, more and more relaxed, breathing regularly and with ease.

All right, remain deeply relaxed now but listen carefully to what I tell you next: *Now you can remember everything. Now, you can remember everything.* You are now able to remember all the faces that you saw previously. Your memory for those faces is completely normal again and you can recall them just as you were able to do so before I made any suggestion for you to forget. In a little while I will ask you to open your eyes again and perform the final task on the computer. You will be shown more faces on the screen and you will be asked whether you have seen each face before. You may have seen some of these faces before during the happy face – sad face task after the beginning of hypnosis. You will have no trouble now remembering the faces that you saw then.

Now open your eyes slowly, look at the screen, and take a moment to let your eyes adjust to the light. Please read the instructions on the screen, and if you have any questions about the task, just let me know. Adjust your body if you need to so you can reach the mouse and the keyboard on the desk.

Then whenever you are ready, you can start. When you complete the task, you can just close your eyes again and relax.

[Recognition Task 2]

HYPNOTIC DREAM SHSS:C

(Ok, just let your eyes close now and relax.) You have concentrated very well and have completed all the tasks now. You are still deeply relaxed and at ease. In a few moments I am going to count from "one" to "ten" and as I do so, you will begin to wake up. I am going to count from "one" to "ten" and as I do you will become more and more aware and alert, so that at "five", your eyes will begin to open and you will become increasingly alert, relaxed, and awake. At "ten" you will be fully alert, in your normal state of wakefulness, feeling relaxed and refreshed.

Here we go. *One*, . . . (VOICE BECOMING Slightly LOUDER/Excited AS YOU COUNT FROM "ONE" TO "TEN.") *Two*, . . . *Three*. Becoming more and more awake, more and more aware, more and more alert. *Four*. Waking up more and more, more and more alert. *Five*. Eyes beginning to open now, becoming more and more alert and aware of your surroundings, more and more clear. *Six*,... *Seven*... *Eight*..., more alert and refreshed, relaxed and at ease. *Nine*..., *Ten*. Eyes open, fully alert now, feeling refreshed, relaxed, and at ease, in your ordinary state of wakefulness. Alert . . . , refreshed . . . , relaxed . . . , and at ease.

[Brief Debrief: Check alertness/orientation

Now please just rest with your eyes closed for awhile and we will soon stop the EEG recording and reach the end of the experiment.

[Resting EEG recording 3 – Post-Hypnosis (1min)]

[Administer PCI]

[Full Debrief: Check alertness/orientation]