

Altered Brain Connectivity and Network Topological Organization in a Non-ordinary State of Consciousness Induced by Hypnosis

Rajanikant Panda^{1*}, Audrey Vanhaudenhuyse^{1*}, Andrea Piarulli^{1,3}, Jitka Annen^{1,2}, Athena Demertzi¹, Naji Alnagger^{1,2}, Srivas Chennu⁴, Steven Laureys^{1,2,5}, Marie-Elisabeth Faymonville^{1†}, and Olivia Gosseries^{1,2†}

Abstract

■ Hypnosis has been shown to be of clinical utility; however, its underlying neural mechanisms remain unclear. This study aims to investigate altered brain dynamics during the non-ordinary state of consciousness induced by hypnosis. We studied high-density EEG in 9 healthy participants during eyes-closed wakefulness and during hypnosis, induced by a muscle relaxation and eyes fixation procedure. Using hypotheses based on internal and external awareness brain networks, we assessed region-wise brain connectivity between 6 ROI (right and left frontal, right and left parietal, upper and lower midline regions) at the scalp level and compared across conditions. Data-driven, graph-theory analyses were also carried out to characterize brain network topology in terms of brain network segregation and integration. During hypnosis, we observed (1) increased delta connectivity between left and right

frontal, as well as between right frontal and parietal regions, (2) decreased connectivity for alpha (between right frontal and parietal and between upper and lower midline regions) and beta-2 bands (between upper midline and right frontal, frontal and parietal, also between upper and lower midline regions), and (3) increased network segregation (short-range connections) in delta and alpha bands, and increased integration (long-range connections) in beta-2 band. These higher network integration and segregation were measured bilaterally in frontal and right parietal electrodes, which were identified as central hub regions during hypnosis. This modified connectivity and increased network integration-segregation properties suggest a modification of the internal and external awareness brain networks that may reflect efficient cognitive-processing and lower incidences of mind-wandering during hypnosis. ■

INTRODUCTION

Over the past decade, research on hypnosis has made unique contributions to cognitive neuroscience and various clinical applications, such as pain management, depression, treatment of phobia, drug addiction, and psychotic disorders (Vanhaudenhuyse, Nyssen, & Faymonville, 2020; Oakley & Halligan, 2009). Hypnosis is a non-ordinary state of consciousness that can result in experiencing a range of phenomena, including feelings of increased inner absorption and dissociation from the environment, in addition to decreased self-agency and spontaneous thoughts (Vanhaudenhuyse et al., 2020; Oakley & Halligan, 2009). Although there is no consensus regarding definitions and description of hypnotic phenomena, hypnosis can be viewed as having four main components: absorption (tendency to be involved in a perceptual, imaginative experience), dissociation (involves a mental

severance of the behavioral components of the experience that normally are processed together, with a particular disconnection from the “here and now”), suggestibility (individual tendency to comply with given suggestions), and automaticity (non-voluntary responses relevant to the content of a communication intended to be a suggestion; Weitzenhoffer, 2002; Spiegel, 1991). Despite established knowledge regarding the subjective experiences during hypnosis, the identification of the neurobiological underpinnings of hypnosis is still unclear.

In the field of consciousness research, two anti-correlated brain networks have been intensively studied: the internal and external awareness networks (Kyeong, Kim, Kim, Kim, & Kim, 2017; Demertzi, Soddu, & Laureys, 2013; Smallwood, Brown, Baird, & Schooler, 2012; Vanhaudenhuyse et al., 2011). The internal awareness network is related to self-related stimuli, whereas the external awareness network is associated with environmental awareness (Demertzi et al., 2013; Smallwood et al., 2012; Vanhaudenhuyse et al., 2011). The internal awareness network involves midline regions (i.e., medial prefrontal cortex, anterior cingulate, posterior cingulate cortex), whereas the external awareness network involves mainly

¹University of Liège, Belgium, ²University Hospital of Liège, Belgium, ³University of Pisa, Italy, ⁴University of Kent, Medway, United Kingdom, ⁵Laval University, Québec, Canada

*Equally contributed authors.

†These authors jointly supervised this work.

bilateral frontal and parietal regions. Regarding phenomenology, the hypnotic state is characterized by a modification of the internal (self-related) and external (environment-related) awareness as subjectively evaluated by volunteers (i.e., higher for internal awareness and lower for external awareness; Demertzi, Vanhaudenhuyse, Noirhomme, Faymonville, & Laureys, 2015). fMRI studies on hypnosis have reported the involvement of both frontoparietal (associated with external awareness network) and midline (associated with internal awareness network) regions (Jiang, White, Greicius, Waelde, & Spiegel, 2017; Demertzi et al., 2011; McGeown et al., 2009). However, these studies provide contrasting findings of increased and decreased connectivity in those regions during hypnosis (Landry, Lifshitz, & Raz, 2017). In line with fMRI studies, EEG studies also showed the involvement of frontoparietal network during hypnosis (Li et al., 2017; Jamieson & Burgess, 2014). Decreased alpha and increased delta power spectral density were noted in the frontoparietal regions during hypnosis compared with normal wakefulness (Li et al., 2017; Jamieson & Burgess, 2014). A study on one “virtuoso” (i.e., highly hypnotizable participant) also reported frontoparietal changes during hypnosis using concurrent fMRI and EEG (Lipari et al., 2012). Increased fMRI activation was observed in the precuneus, posterior cingulate cortex, and occipital and right frontal areas, whereas from source reconstruction EEG, increases in delta (1.5–4 Hz) and beta-1 (12.5–18 Hz) bands were found in the parietal cortex, and decreases in theta (4.5–8 Hz), alpha (8.5–12), beta-2 (18.5–21 Hz), and beta-3 (21.5–30 Hz) bands were noted in the left visual cortex, supramarginal gyrus, ACC, and anterior prefrontal cortex (Lipari et al., 2012). These previous studies consistently reported that the frontoparietal and midline regions are key regions during conscious perception (Demertzi et al., 2013; Kjaer, Nowak, & Lou, 2002). Looking specifically at the connectivity of these regions may help explain the alteration of the internal and external awareness networks during hypnosis.

Beyond brain region synchronization or connectivity, there is a growing interest in understanding the brain network topological organization as it seeks to provide some mechanistic insights into the specificities that substantiate specific patterns of altered connectivity. Generally, brain dynamics and neural synchronicity display distinct topological patterns organized in segregated modules (richer short-range connections) with specific and independent functions, in addition to possessing connections (long-range) that ensure the integration within and between those modules (Mohr et al., 2016; Deco, Tononi, Boly, & Kringelbach, 2015; Sporns, 2013). Brain topology follows specific small-world network properties during brain states through the integration of the segregated functional modules aided by network hubs, which ensure efficient communication (Deco et al., 2015). Furthermore, segregation and integration have been reported to reach a balance during higher cognitive processes

(Keerativittayayut, Aoki, Sarabi, Jimura, & Nakahara, 2018), whereas this balance is disrupted in pharmacological and pathological states of reduced consciousness (López-González et al., 2021; Rizkallah et al., 2019; Monti et al., 2013). Thus, in addition to brain connectivity, network topological organization, commonly measured using methods based on graph theory, may provide further details pertaining to the network topological alteration, which could complement to the frontoparietal–midline connectivity changes that underpin the neural correlates of hypnosis.

We thus aim to study the internal–external awareness networks and network topological properties during hypnosis. The internal–external awareness network dynamics can be studied through a simple model, such as hypothesis-based connectivity by considering ROIs with frontal, parietal, and midline brain regions. Hence, here, we study EEG connectivity at the scalp level focusing on frontal, parietal, and midline region electrodes, which may provide information on the altered network dynamics during hypnosis. Furthermore, we will study brain network topology (i.e., network segregation and integration) using graph theory. The changes in network topology at the regional (i.e., electrodes) level could overlap with the areas of altered connectivity. Identifying these overlapping changes could help to explain the underlying brain properties of altered connectivity. Finally, to evaluate the link between brain network dynamics and subjective experiences reported during hypnosis, we will analyze correlations between the modified brain connectivity and network topological properties with hypnotizability scores, as well as self-assessed scores of absorption and dissociation.

METHODS

Participants and Hypnosis Protocol

Twelve healthy participants were recruited for this study. This number was chosen based on previous related studies on healthy individuals (e.g., Martial et al., 2019; Timmermann et al., 2019; Nieminen et al., 2016; Jamieson & Burgess, 2014; Deeley et al., 2012). All participants had a high level of hypnotizability according to the Stanford Hypnotic Susceptibility Scale, Form C (SHSS:C; Weitzenhoffer, Hilgard, & Kihlstrom, 1996) and the Hypnosis Liège Scale (Vanhaudenhuyse et al., 2019). Participants underwent high-density EEG recordings during ordinary consciousness (i.e., normal wakefulness) and during hypnosis. In both conditions, participants were asked to keep their eyes closed. Inclusion criteria were to be older than 18 years old and no history of neurological or psychiatric disease. Written informed consent was obtained for each participant, and the study was approved by the Ethics Committee of the Medical School of the University of Liège.

All participants underwent a hypnosis session to assess their level of hypnotizability using the SHSS:C (A.V. and O.G.; Weitzenhoffer et al., 1996). The SHSS:C scale defines

participants as highly hypnotizable if the score is superior or equal to 8, as moderately hypnotizable if the score is between 7 and 5, and as lowly hypnotizable when the score is below or equal to 4. Participants underwent a second session of hypnosis (M-E.F.) with the induction technique used in clinical practice (i.e., 3-min induction using eye fixation and progressive muscle relaxation). Participants were then invited to increase their sensation of relaxation by closing their eyes and experiencing a neutral hypnosis (i.e., to deepen their experience by listening to white noise) without any specific suggestion (Vanhaudenhuyse et al., 2019). Only during the induction procedure, permissive and indirect suggestions were used to develop and deepen the hypnotic state. The exact words and specific suggestions during the induction varied depending upon the experimenter's observation of participant behavior and on her judgment of participant's needs. The hypnosis induction procedures were chosen based on participants' preference from a number of methods: visual fixation of a point, focusing on the sensations of well-being in the body, focusing on the breathing, or a combination of these procedures. Hypnosis was maintained for 15 min, accompanied by a white noise. Immediately after, participants self-assessed their absorption: ("Estimate on a 0–not at all–to 10–fully–scale, how deeply you felt absorbed and your attention was focused on the experience you have just lived?"), dissociation: ("Estimate on a 0 to 10 scale, how much you felt dissociated from your bodily reality in the actual environment? 0 means you were in the reality of this room; 10 means you completely escaped within your subjective experience, entirely disconnected from the reality"), and time perception (estimation of the time elapsed, in minutes, since you started the hypnotic exercise; Vanhaudenhuyse et al., 2019). M.-E. F. then provided a subjective index of hypnotizability (Hypnosis Liege Scale [Vanhaudenhuyse et al., 2019]), which considers mean score superior or equal to 8 as high, between 7 and 5 medium, and below or equal to 4 low. The two hypnotizability assessments (SHSS:C and Hypnosis Liege Scale) took place in two different days and were delivered in a randomized and balanced order. We included only those participants who obtained both a high level of hypnotizability according to the SHSS:C and a high score on the Hypnosis Liège Scale. Participants underwent a third session in conjunction with the EEG recording. During this last session, the hypnotic procedure was the same as in the second session (neutral hypnosis), with the addition of the EEG recording only during the hypnotic state (and not during the induction procedure). In three participants, EEG data were discarded because of technical issues during the data recording, leading to a sample of 9 highly hypnotizable participants (six females, mean age 23.8 ± 3.4 years).

EEG Acquisition

EEG data were acquired using a 60-channel EEG system (Nexstim eXimia, Nexstim Plc). EEG signals were acquired

as per 10–20 electrode placement system, and taking as a reference an additional electrode placed on the forehead, at a sampling rate of 1450 Hz and were band-pass filtered between 0.1 and 500 Hz; EEG channels impedances were kept below 5 k Ω throughout the recording. Two additional electrodes were used to record the electrooculogram (Nexstim eXimia, Nexstim Plc). EEG was recorded for 5 min in an eyes-closed "ordinary consciousness (normal wakefulness)" condition, and for 5 min during an eyes-closed "hypnosis" condition after the induction procedure. Note that the EEG data were acquired just before recording TMS coupled with EEG (not reported here).

Data Analysis

Preprocessing and Power Spectral Analysis

EEG signals were bandpass filtered between 1 Hz and 48 Hz band using Butterworth filter. Filtered EEG recordings were visually inspected to detect both noisy channels and epochs. Noisy epochs showing nonstationary artifacts (i.e., sudden movements) were removed. EEG recordings were then submitted to an independent component analysis to remove nearly stationary artifacts (eye-blinks, saccades, ECG), in line with Chennu et al. (2017). The EEG signals were then rereferenced to the scalp average and down sampled to 250 Hz. Finally, noisy channel signals were substituted with signals obtained via spline interpolation as in Junghofer et al. (2000). After preprocessing, we consider 4-min EEG data to be consistent with each participant postprocessing analysis. For each recording and EEG channel, the power spectral densities in five bands of interest (delta, 1–3.75 Hz; theta, 4–7.75 Hz; alpha, 8–11.75 Hz; beta-1, 12–19.75 Hz; and beta-2, 20–29.75 Hz) were estimated using a Hanning-windowed fast Fourier transform on 4-sec epochs (overlap between contiguous epochs 50%). For each band, the mean channel absolute power density was estimated averaging among epochs and the resulting value was log-transformed.

Connectivity Analysis

Connectivity between each pair of electrodes was estimated for each condition and each band using the weighted Phase Lag Index (wPLI; Hardmeier et al., 2014; Vinck, Oostenveld, Van Wingerden, Battaglia, & Pennartz, 2011). wPLI is considered as a robust estimate of the effective phase coupling between two signals because it does not consider coupling at zero phase-lag as, at the scalp level, the instantaneous coupling reflects the effects of volume conduction rather than any real coupling (Hardmeier et al., 2014; Vinck et al., 2011). wPLI values vary between 0 and 1, indicating the extent to which two signals have a phase coupling; Higher wPLI values indicate stronger coupling between two signals (i.e., brain regions).

Regional Connectivity

Frontoparietal and midline connectivity patterns were divided in six ROIs: right and left frontal, right and left parietal, upper and lower midline. Between-regions connectivity was estimated for each condition and band of interest as the average over the related wPLI indices: Let us consider two regions i and j . The connectivity between these regions was estimated by averaging among the wPLIs of all pairs of electrodes x, y such that $x \in i$, and $y \in j$ (Teipel et al., 2018; Tóth et al., 2014). The electrodes included in each ROI were composed of the following electrodes: left frontal (FP1, AF3, F1, F3, F7), left parietal (CP1, CP3, CP5, P1, P7, P9), right frontal (FP2, AF4, F2, F4, F8), right parietal (Cp2, CP4, CP6, P2, P4, P8, P10), upper midline (FPZ, AFZ, Fz, FCZ), lower midline (CPZ, Pz, POZ, OZ).

Graph Theory Analysis

In addition to region-specific connectivity analysis, we assessed the brain topological organization using a data-driven graph-theory approach. Our aim is to evaluate brain network integration and segregation, as modulation of network integration and segregation in consciousness is a key factor as per our previous studies (López-González et al., 2021; Rizkallah et al., 2019; Chennu et al., 2017). Starting from the wPLI matrices, we used a binary graph approach for network analysis. A graph consists of elements called “vertices” or nodes (N) connected by links or edges (E). Here, electrodes were taken as network nodes and between-electrodes connectivity (i.e., wPLI) as a measure of link strength. The connectivity matrix was consecutively thresholded to maintain from 75% down to 5% of the strongest connection in steps of 2.5%. The lower limit was chosen to avoid excessive network fragmentation because of sparser adjacency matrices at lower thresholds (Holla et al., 2017). Topological properties of the functional brain networks segregations and integration were characterized using two popular graph theory measures: (1) the normalized clustering coefficient (NCC) as a measure of network segregation, and (2) the normalized participation coefficient (PC) as a measure of network integration (Holla et al., 2017; Sporns, 2013; Fornito, Zalesky, & Bullmore, 2010). Previous studies have shown that these two graph theory measures characterize altered conscious states (Rizkallah et al., 2019; Chennu et al., 2017; Chennu, O’Connor, Adapa, Menon, & Bekinschtein, 2016). To ensure the comparability of results across different network sparsity and across different conditions, we used normalized graph measures.

The CC of a node (C_i) is the ratio between the number of existing connections (links, E) and the number of all possible connections within its neighborhood. C_{avg} is the average of the CCs over all nodes in the network:

$$C_{avg} = \frac{1}{n} \sum_{i \in N} C_i = \frac{1}{n} \sum_{i \in N} \frac{E_i}{K_i(K_i - 1)/3} \quad (1)$$

The NCC was obtained as the ratio between the network CC (C_{avg}) and the random CC (C_{rand}) obtained by averaging 100 random generated networks keeping the same number of nodes, edges, and degree distribution of the real network (Guimerà & Amaral, 2005). High NCC values denote the presence of densely connected short-range connections that form local clusters of nodes (i.e., modules/communities) within the network and, hence, a high level of functional segregation.

The PC gives an estimate of the intermodule connectivity strength thus characterizing the levels of functional integration and long-range connections within the network. To compute the PC, first we made the partition of modular structure of the same network. The exact determination of the modular structure in terms of modularity maximization requires the evaluation of modularity value for all possible partitions, which is computationally challenging (Miyachi & Sukegawa, 2015). In this study, we used the Louvain algorithm (Blondel, Guillaume, Lambiotte, & Lefebvre, 2008), as implemented in the Brain Connectivity Toolbox (Rubinov & Sporns, 2010) to generate a set of partitions of the same network. This algorithm allows computationally efficient module detection through modularity maximization and provides hierarchical information (the detection of modules within modules). With the aim to assess the consistency of modules affiliation, we generated a set of partitions of the same network 100 times and took the average modularity. The PC of a node (P_i) is the ratio between the number of links of the node i (included in a given module m) to nodes in other modules of the network, and the total degree of the node (i.e., its total number of links). P_{avg} is the average of the PC over all nodes in the network:

$$P_{avg} = \frac{1}{n} \sum_{i \in N} P_i = \frac{1}{n} \sum_{i \in N} \left(1 - \sum_{m \in M} \left(\frac{k_i(m)}{k_i} \right)^2 \right) \quad (2)$$

where m is a specific module in a set of modules M (composing the whole network), and $k_i(m)$ is the connection (number of links/edges) between node i and all nodes in a given module m (Baum et al., 2017; Chennu et al., 2017). A P_i value close to 1 indicates that the node has a high connectivity with other modules of the network (other than its own), thus contributing to the between-modules information integration, whereas a P_i close to 0 indicates that a brain region (node) is highly connected with nodes of its own module and its contribution to the network integration is low. The normalized participation coefficient (NPC) is the ratio of the average participation coefficient (P_{avg}) of the network and the random participation coefficient (P_{rand}) obtained by averaging 100 random generated networks (obtained as above, maintaining the same number of nodes, links, and degree distribution of the real network).

The hub regions (electrodes) were computed from both the network-segregated hubs using nodal CC (i.e., nodal NCC) and integrated hubs using nodal participation

coefficient (i.e., nodal NPC). The segregated hubs are the nodes (i.e., regions/electrodes) that have higher connections to the neighbor nodes within the modules, whereas integrated hub regions represent the nodes with higher connections with intermodular connections. The network segregated hub regions consist of higher short-range connections, whereas integrated hub regions consist of higher long-range connections (Bertolero, Yeo, & D'Esposito, 2015; van den Heuvel & Sporns, 2013; Guimerà & Amaral, 2005). The nodal NCC and NPC were estimated by averaging the series of NCC and NPC values obtained at each threshold for each node.

Statistical Analysis

Regarding power spectral analysis, between-conditions differences in band-wise spectral density distribution over the scalp were assessed by performing for each electrode a between-conditions paired *t* test. For each band, 60 tests were conducted, and the *t*-value significance of each comparison was corrected for multiple comparisons using a single-threshold permutation test for the maximum *t* statistics (1000 permutations; Nichols & Holmes, 2001). For connectivity analysis, two-tailed paired *t* tests were used to assess between-conditions (ordinary consciousness vs. hypnosis) statistical differences. Corrections for multiple comparisons were performed using false discovery rate (FDR) at 0.05 level, for hemispheric regional connectivity

pairs ($n = 15$ pairs) and for each frequency band. For the graph-theory analysis, between-conditions difference for global NCC and NPC were calculated using two-tailed paired *t* tests with $p < .05$ significance level. For the nodal NCC and nodal NPC, between-conditions difference were assessed for each brain region/node ($n = 60$ nodes) using two-tailed paired *t* tests with FDR correction at $p < .05$ for each frequency band. To assess the associations between phenomenology and its putative cortical correlates, hypnotizability variables (i.e., SHSS:C, Hypnosis Liege Scale, absorption, and dissociation scores) were correlated with brain connectivity measures and graph-theory measures using Pearson correlations.

RESULTS

The nine highly hypnotizable participants (median score SHSS:C = 8.9 ± 1.1 , mean Hypnosis Liege Scale = 9.3 ± 0.8) obtained a mean absorption score of 7.7 ± 1.0 , a mean dissociation score of 8.5 ± 0.5 , and a mean time perception difference of 14.4 ± 6.8 min (difference between actual and perceived hypnosis duration). Individual demographical data and hypnotizability scores are presented in Table 1.

Alteration to the configuration of neural activity and interactions were assessed using connectivity and network topological reorganization. First, we looked at the absolute power spectrum of the EEG signal and found an

Table 1. Participant Demographics and Hypnotizability (as Measured with the SHSS:C and the Hypnosis Liège Scale), Absorption and Dissociation Scores, As Well As Time Perception Difference Score as Self-Evaluated by Participants

Name	Gender	Age (Years)	SHSS: C Total Score (0–12)	Absorption (0–10)	Dissociation (0–10)	Hypnosis Liège Scale Total Score (0–10)	Δ Time Perception (Minutes)
Participant 1	F	27	8	8	8	10	0
Participant 2	M	19	10	7	8.5	9.5	20
Participant 3	M	20	11	7.5	8.3	8	-10
Participant 4	F	29	9	9	8	9	15
Participant 5	M	23	8	6	8	8	20
Participant 6	F	25	9	7	8.5	9	15
Participant 7	F	22	8	8	9	10	-10
Participant 8	F	22	8	8	9.5	10	20
Participant 9	F	27	9	9	9	10	20
Mean \pm SD	6F/3M	23.8 \pm 3.4	8.9 \pm 1.1	7.7 \pm 1.0	8.5 \pm 0.5	9.3 \pm 0.8	14.4 \pm 6.8

Note that the time perception difference is calculated as the difference between the actual and the perceived hypnosis duration (in minutes), with positive values corresponding to the perception of a shorter duration of the hypnosis session (compared with the actual duration). F = female; M = male; SHSS:C = Stanford Hypnotic Susceptibility Scale, Form C.

increase of power in delta (especially in frontal regions electrodes) and concurrent decreases in alpha and beta-2 bands during hypnosis compared with ordinary consciousness. Notable decreases in alpha and beta-2 bands

were prevalent in posterior and midline electrodes, respectively (Figure 1).

We next observed a significant increase of connectivity in delta band between the right and left frontal regions

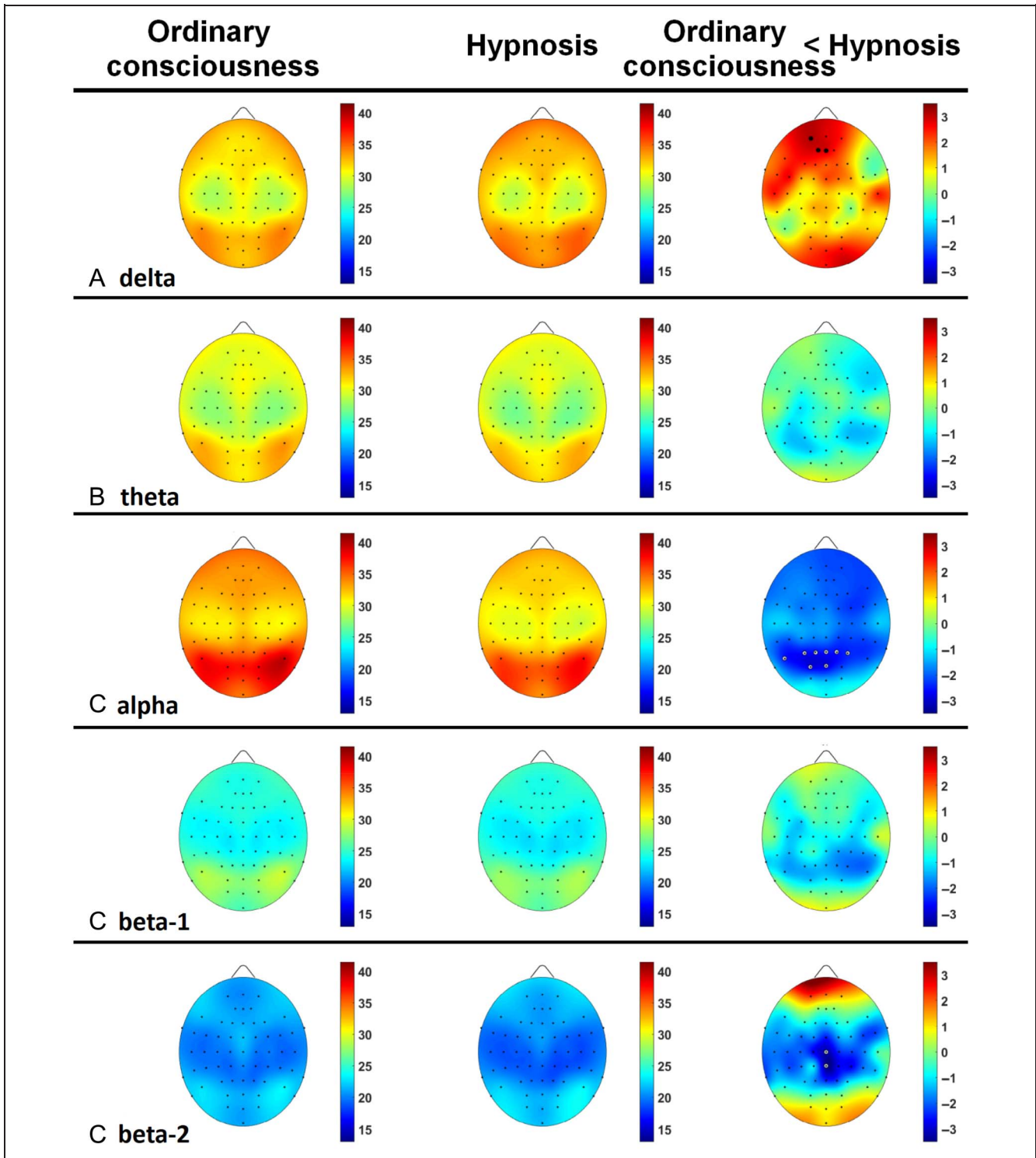


Figure 1. Power spectral changes during hypnosis. Absolute power spectral distribution of delta, theta, alpha, beta-1, and beta-2 for ordinary consciousness, hypnosis and the difference between ordinary consciousness and hypnosis. During hypnosis, the power spectrum was increased in delta frequency in frontal electrodes and decreased in alpha and beta-2 frequencies at posterior and midline electrodes, respectively. The black circles on the electrodes indicate significantly increased power, and white circles on the electrodes indicate significantly decreased power during hypnosis compared with ordinary consciousness.

Table 2. Frontoparietal and Midline Regions Connectivity of Ordinary Consciousness and Hypnotic State, along with Statistical Values

	<i>Brain Connectivity</i>	<i>Ordinary Consciousness</i>	<i>Hypnosis</i>	<i>t Values</i>	<i>p Value</i>
Delta	right frontal to left frontal	2.63 ± 0.17	2.91 ± 0.14	4.17	.001
	right frontal to right parietal	3.17 ± 0.24	3.40 ± 0.25	3.51	.004
Alpha	upper midline to lower midline	2.53 ± 0.75	1.88 ± 0.69	-3.41	.004
	right frontal to right parietal	4.70 ± 1.76	3.65 ± 1.19	-3.00	.008
Beta-2	upper midline to lower midline	0.59 ± 0.07	0.49 ± 0.06	-3.68	.003
	right frontal to right parietal	1.17 ± 0.19	0.98 ± 0.10	-2.75	.012
	right frontal to upper midline	0.87 ± 0.12	0.70 ± 0.06	-3.70	.003

The p values were corrected for multiple comparisons with FDR $p < .05$ for all the between-pairs connectivity comparisons ($n = 15$).

electrodes, $t(8) = 4.17$; $p = .001$, and between the right frontal and right parietal regions electrodes, $t(8) = 3.51$; $p = .004$, at the scalp level during hypnosis compared with ordinary consciousness. During hypnosis,

we also observed a decreased connectivity in the alpha band between upper and lower midline regions electrodes, $t(8) = -3.41$; $p = .004$, and between right frontal and right parietal regions electrodes, $t(8) =$

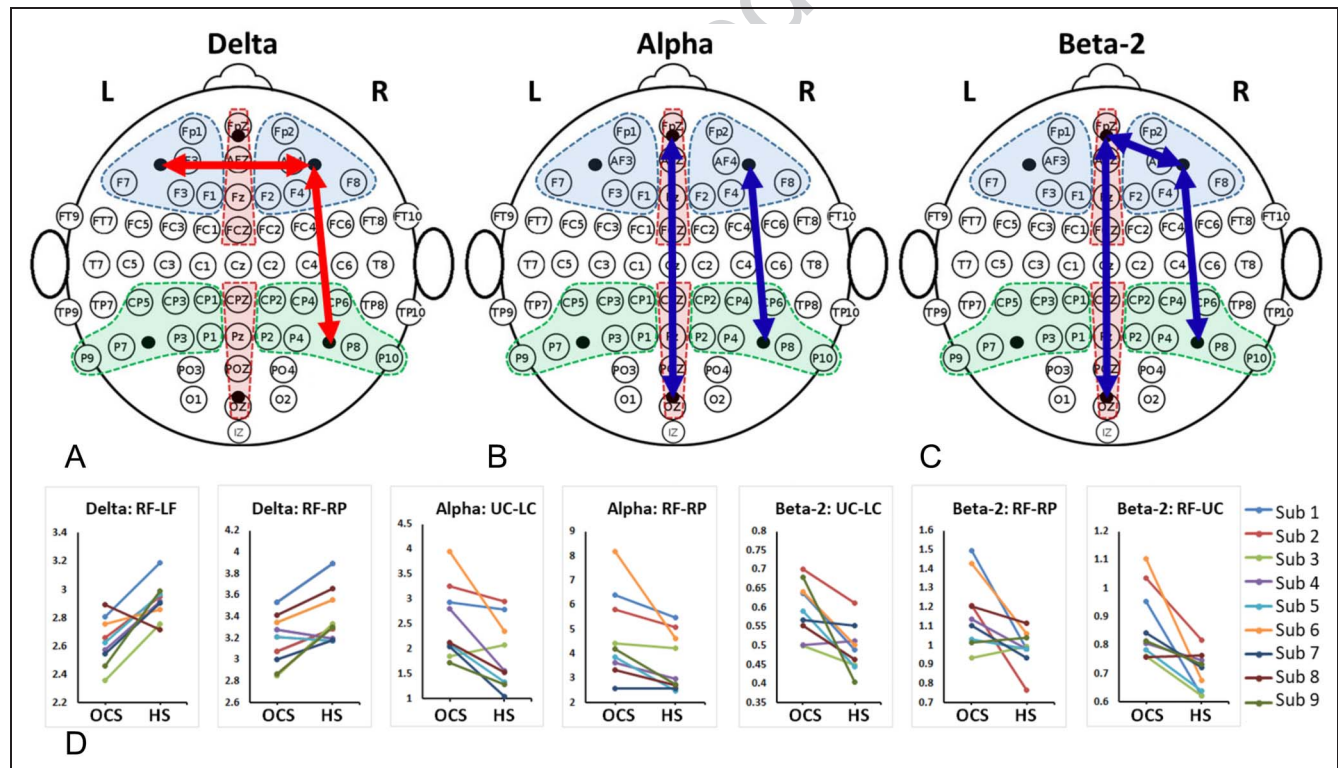


Figure 2. Regional brain connectivity alteration during hypnosis. Frontoparietal and midline regions connectivity of hypnotic state compared with ordinary consciousness for delta, alpha, and beta-2 frequency bands. Increased frontal and right frontoparietal regions connectivity (red arrow) in (A) delta band and decreased connectivity (blue arrow) at midline, right frontoparietal, and upper midline to right frontal regions during hypnosis compared with ordinary consciousness in (B) alpha and (C) beta-2 frequency bands. Blue, red, and green colors represent bilateral frontal, midline, and bilateral parietal brain regions at the scalp level. (d) Represents individual participant mean connectivity (arbitrary unit) during ordinary consciousness state (OCS) and hypnotic state (HS). Colors represent each individual participant. L = left hemisphere; R = right hemisphere; RF = right frontal; LF = left frontal; RP = right parietal; UM = upper midline; LM = lower midline. The statistical significant level was set at $p < .05$ (FDR corrected for regional connectivity pairs [$n = 15$ pairs]).

-3.00; $p = .008$. When considering the beta-2 band, hypnosis also decreased connectivity between: (1) upper and lower midline electrodes, $t(8) = -3.68$; $p = .003$; (2) right frontal and right parietal regions electrodes, $t(8) = -2.75$; $p = .012$; (3) upper midline and right frontal regions electrodes, $t(8) = -3.70$; $p = .003$ (Table 2 and Figure 2). For intrasubject connectivity variation, the individual participant connectivity value of ordinary conscious state and hypnosis are reported in the graph plot (Figure 2D).

The topological properties of network segregation (i.e., NCC) and integration (i.e., NPC) increased during hypnosis compared with ordinary consciousness at both the global (whole brain) and local (brain region/electrode) level. We found an overall increase of whole brain segregation (NCC) in hypnosis when considering delta, $t(8) = 2.40$; $p = .021$, and alpha, $t(8) = 3.18$; $p = .006$, band

networks. In addition, an increase of whole brain network integration (NPC) was apparent for beta-2, $t(8) = 2.75$; $p = .012$ (Table 3 and Figure 3). In further assessing the altered local topological organization, we found that the increased network segregated hubs (i.e., short-range connections) are in the frontal area (F1, Fz, and F2) in the delta frequency band and frontoparietal (F8, AF1, AF2, AFz, F1, Fz, P4) in the alpha frequency band. On the other hand, increased integrated hubs (i.e., long-range connections) were found in the frontoparietal area (FC5, FC7, and P4) in beta-2 frequency bands (Table 3 and Figure 4).

Parameters characterizing the hypnotizability level such as SHSS:C, Hypnosis Liege Scale, absorption score, and dissociation score did not show any significant correlation with brain connectivity measures (i.e., regional connectivity and graph theory measures).

Table 3. Graph Theory-based Network Measures of Clustering Coefficient (CC) and Participation Coefficient (PC) for Hypnotic State and Ordinary Consciousness Values and Statistical Values

	<i>Brain Regions</i>	<i>Ordinary Consciousness</i>	<i>Hypnosis</i>	<i>t Values</i>	<i>p Value</i>
Delta: CC	global (whole brain)	1.52 ± 0.25	1.79 ± 0.32	2.40	.021
Delta: CC	F1	1.18 ± 0.09	1.36 ± 0.07	6.92	< .001
	Fz	1.21 ± 0.07	1.38 ± 0.11	5.36	< .001
	F2	1.26 ± 0.12	1.40 ± 0.13	3.63	.003
Alpha: CC	global (whole brain)	1.12 ± 0.16	1.4 ± 0.31	3.18	.006
Alpha: CC	F8	1.14 ± 0.13	1.22 ± 0.15	5.15	< .001
	AF1	1.17 ± 0.07	1.33 ± 0.15	4.60	< .001
	AF2	1.16 ± 0.08	1.33 ± 0.13	4.50	.001
	Afz	1.19 ± 0.08	1.34 ± 0.16	4.01	.002
	F1	1.19 ± 0.09	1.28 ± 0.12	4.12	.002
	Fz	1.12 ± 0.08	1.27 ± 0.14	3.66	.003
	P4	1.07 ± 0.15	1.16 ± 0.16	3.44	.005
Beta-2: PC	global (whole brain)	0.65 ± 0.05	0.71 ± 0.03	2.75	.013
Beta-2: PC	FC5	0.77 ± 0.08	0.88 ± 0.05	4.80	< .001
	F7	0.77 ± 0.06	0.87 ± 0.03	4.44	.001
	P4	0.82 ± 0.07	0.91 ± 0.03	4.11	.002

The statistical significance level was noted at $p < .05$ (uncorrected) for the global CC and PC; however, the nodal CC and PC (individual electrodes) p values were corrected for multiple comparisons (FDR $p < .05$).

Figure 3. Brain topological organization in terms of network segregation and integration during hypnosis. During hypnosis state (HS; red) compared with ordinary consciousness state (OCS; blue), (A) the network segregation (CC) increases in the delta and alpha bands, and (B) the network integration (PC) increases in the beta-2 band at the whole brain level (i.e., average of all electrodes/nodes). The error bars represent the standard deviation. Statistical significant level was set at $p < .025$ (for both global CC and PC).

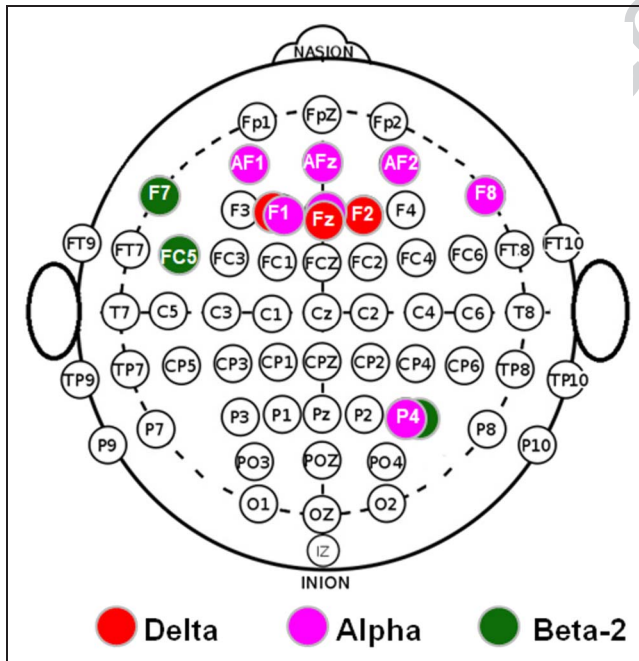
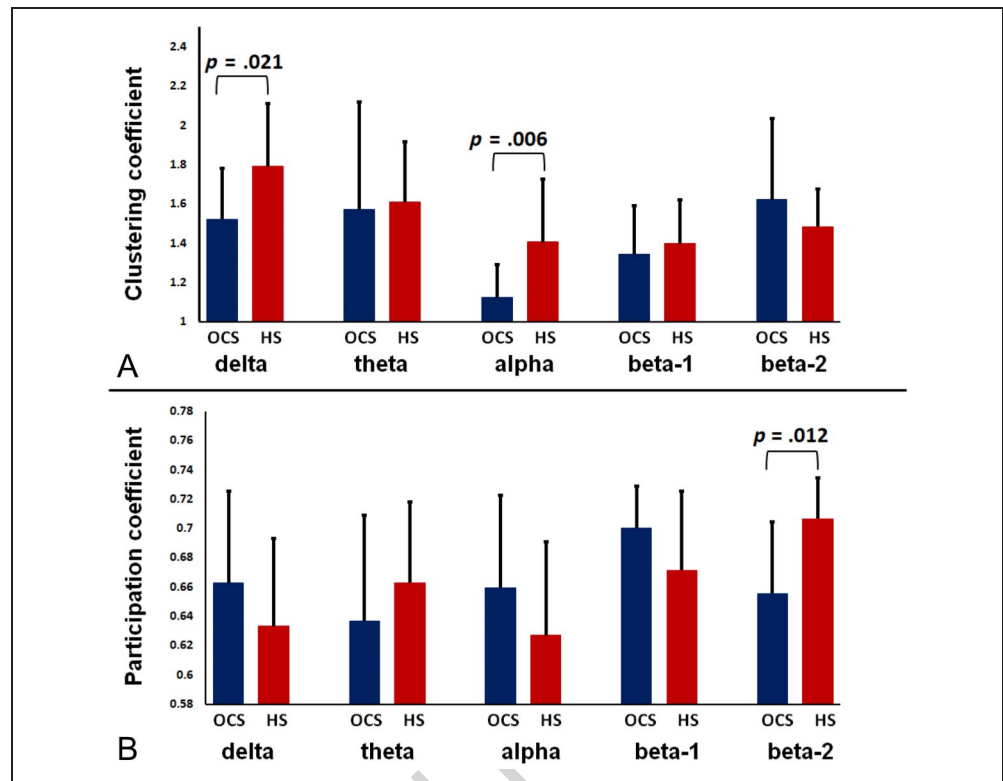


Figure 4. Local region wise (i.e., electrodes) topological differences in terms of network segregation (nodal CC) and integration (nodal PC) for hypnosis state. Surface visualization of the hub brain regions (electrodes), which showed increased nodal clustering (short-range connections) and PC (long-range connections) at bilateral frontal and right parietal during hypnosis compared with ordinary consciousness. The statistically significant level was set at $p < .05$ (FDR corrected across all electrodes).

DISCUSSION

We assessed neurophysiological correlates of hypnosis in nine highly hypnotizable participants focusing on brain connectivity in frontoparietal and midline region electrodes and brain topological organization using high-density EEG. We observed brain connectivity changes in high and low frequencies during hypnosis, with increases in delta band and decreases in alpha and beta-2 bands in frontoparietal and midline region electrodes. These modifications during hypnosis were more lateralized to the right hemisphere. Furthermore, the data-driven graph-theory analysis revealed a richer network topological organization in terms of network integration and segregation globally and locally during hypnosis. The local regional network topology showed an increased number of segregated hubs in the delta and alpha bands, and an increased number of integrated hubs in the beta-2 bands in frontoparietal regions during hypnosis compared with ordinary consciousness (i.e., normal wakefulness).

First, we analyzed the EEG spectral power changes, finding increased power in delta and concurrent decreases in alpha and beta-2 in hypnosis in comparison with ordinary consciousness, consistent with previous studies (Rho et al., 2021; Li et al., 2017; Lipari et al., 2012; Montgomery, Dwyer, & Kelly, 2000). Beta rhythms are known to be involved in sensorimotor processes. Decreases in beta activity were previously reported in participants in the hypnotic state and were suggested to be linked to

multisensory disruption (Li et al., 2017; Lipari et al., 2012). Participants included in our study have reported high levels of dissociation (from the outer environment). This indicates that decreased beta rhythms observed in our results could be interpreted as related to an alteration in somatosensory perceptions during hypnosis. Interestingly, decreases in alpha and beta activity have also been reported in other non-ordinary states of consciousness including meditation and the psychedelic state (Timmermann et al., 2019; Carhart-Harris et al., 2016; Amihai & Kozhevnikov, 2014). Decreases in alpha power are recognized as the most robust brain effect of psychedelics. This has been suggested to represent disruptions in top-down predictive processing and high-level psychological functioning, a commonality of most, if not all non-ordinary states of consciousness. However, some previous studies on hypnosis also reported increased alpha and beta activity, specifically in the right occipital cortex (Ulett, Akpınar, & Itil, 1972) and parietal region (Crawford, Clarke, & Kitner-Triolo, 1996). Parallel to decreases alpha and beta-2, we also found increased low-frequency delta activity in frontal electrodes, consistent with previous studies (Li et al., 2017; Lipari et al., 2012), suggested to reflect an attentional shift toward internal processing during cognitive tasks (Dimitriadis et al., 2010; Harmony et al., 1996) and sustained attention to internal mental processes (Harper, Malone, & Bernat, 2014). Despite several studies reporting brain activity modulation through power spectral changes during hypnosis, contradicting findings are rife. This could be because of different methods used, in either frequency analysis or the method of hypnotic procedure.

Moving beyond power spectrum analysis, we evaluated brain connectivity and network topological reorganization via graph theoretical measures, hypothesizing a hypnosis-induced alteration in frontoparietal and midline connectivity. Indeed, neuroimaging studies have consistently reported that frontoparietal and midline regions facilitate conscious processes and cognitive flexibility (Winter et al., 2020; Demertzi et al., 2011, 2013; Northoff & Bermpohl, 2004; Aftanas & Golocheikine, 2002). During hypnosis, we observed increased connectivity in the delta band between left and right frontal regions as well as between right frontal and right parietal electrodes. In contrast, alpha and beta-2 bands showed decreased connectivity in midline, between right frontal and right parietal, and between right frontal and upper midline region electrodes. Our results of decreased frontoparietal region connectivity in alpha and beta bands are consistent with previous results in the hypnotic state (Li et al., 2017; Jamieson & Burgess, 2014). Studies have shown that alpha activity and connectivity are ubiquitous during everyday conscious experience and that it is strictly linked to both attention and awareness (Harris, Dux, & Mattingley, 2020; Horschig, Jensen, van Schouwenburg, Cools, & Bonnefond, 2014). Indeed, studies on disorders of consciousness have shown that unresponsive wakefulness

syndrome patients (who do not have any awareness of the external environment) have reduced alpha activity and connectivity, whereas minimally conscious states patients who do retain awareness and a link with the external environment (to a certain degree) show a partial preservation of alpha oscillations (both in terms of activity and connectivity [Naro et al., 2018; Chennu et al., 2017]). Furthermore, lower levels of alpha connectivity have been also reported in sleep (Imperator et al., 2019; 2021), ketamine-induced anesthetized states (Blain-Moraes, Lee, Ku, Noh, & Mashour, 2014), and meditative state (Jiang, Stieger, Kreitzer, Engel, & He, 2021; Winter et al., 2020). These studies brought further evidence about the link between alpha oscillations and both the level of awareness and the degree of engagement with the external environment. During hypnosis, participants reported high levels of dissociation; therefore, we hypothesized that the decrease of alpha and beta band activity and connectivity could be associated with reduced awareness and with a disconnection from the external environment. A recent study on different sleep stages with a different connectivity and classification approach showed that alpha functional connectivity was highly relevant for distinguishing between wakefulness and REM sleep (Imperator et al., 2021). This represents further evidence corroborating the speculation that decreased alpha functional connectivity could be associated with a disconnection from the external environment (Vanhaudenhuyse et al., 2019). This disconnection has also been referred to “disconnected consciousness” in previous studies on other non-ordinary states of consciousness (Martial, Cassol, Laureys, & Gosseries, 2020). Furthermore, we also showed decreased connectivity in midline regions that could be because of a partial disruption of internal awareness and self-referential processing during hypnosis. These results echo fMRI studies on hypnosis (McGeown, Mazzoni, Vannucci, & Venneri, 2015; Deeley et al., 2012), in addition to mindfulness practice and raj-yoga meditation that showed reduced connectivity in midline regions associated with reduced mind-wandering and internal awareness (Panda et al., 2016; Brewer et al., 2011; Farb et al., 2007), supporting again the disconnected consciousness hypothesis induced by hypnosis.

In contrast to decreased connectivity in higher frequency bands, we also noted increased connectivity in the delta band between left and right frontal regions electrodes as well as between right frontoparietal region electrodes. Increased delta band connectivity is also associated with the neural integration in complex domains, such as top-down processing (Park, Thut, & Gross, 2020; Helfrich, Huang, Wilson, & Knight, 2017), mental imaginary tasks and mental imagery of visual art (Bhattacharya & Petsche, 2002; Von Stein & Sarnthein, 2000), and cognitive processes (Harmony, 2013; Tóth et al., 2012), and has also been linked to high levels of focus and absorption (Soffer-Dudek, Todder, Shelef, Deutsch, & Gordon, 2018). fMRI studies on meditation, and gratitude thinking have

reported increased functional connectivity in frontal, insula, and parietal areas (Kyeong et al., 2017; Panda et al., 2016; Hasenkamp, Wilson-Mendenhall, Duncan, & Barsalou, 2012; Brewer et al., 2011). This goes in line with our hypothesis that increased delta connectivity in frontal and frontoparietal electrodes during hypnosis could be associated with an engagement with mental imagination, the enhancement of somatic and emotional control and to high levels of absorption.

The network topological reorganization underlying the emergence of the observed contrasting brain connectivity during hypnosis was further investigated using a data-driven, graph-theory approach. Overall, these analyses indicated a richer brain network configuration during hypnosis. Specifically, we found higher brain network segregation (i.e., brain regions with short-range connections) in low-frequency bands (delta and alpha) and richer network integration (i.e., brain regions with long-range inter modular connections) in higher frequency bands (beta-2). This suggests that during hypnosis, the brain network forms a critical balance between low and high frequency bands for information processing locally at low frequencies (high segregation), and globally at high frequencies (high integrations). Indeed, the balance between brain network segregation and integration is the basis for optimal brain functioning and stable information processing in higher-order cognitive processes (Keerativittayayut et al., 2018; Cohen & D'Esposito, 2016; Bertolero et al., 2015; Cole, Ito, & Braver, 2015) and the ability to effectively adapt to novel circumstances (i.e., fluid intelligence; Gard et al., 2014). The increase in network integration is consistent with a flattened energy landscape in the dynamical working point of the brain during non-ordinary states of consciousness. This flattened energy landscape, proposed by the entropic brain hypothesis (Girn et al., 2023; Carhart-Harris et al., 2014), refers to a flattening in a dynamical systems sense, as the energy required to transition between brain states and to induce interactions between brain networks is minimized. This behavior has been consistently observed in previous studies about non-ordinary states of consciousness such as dreaming and psychedelic drug-induced experiences (Girn et al., 2023). Furthermore, locally segregated and global integrated hub regions were mainly observed in bilateral frontal, upper-midline, and right parietal regions electrodes measured at the scalp level. These data-driven findings support our hypothesis that frontoparietal and midline region connectivity is associated with non-ordinary states of consciousness by hypnosis induction.

Our connectivity results were dominated by right hemispheric alterations during hypnosis. Right hemisphere brain activity/connectivity is associated with several functions including creativity, imagination, intuition, free-thinking, and holistic thought (Lanfranco, Rivera-Rei, Huepe, Ibáñez, & Canales-Johnson, 2021; Prete, Tommasi, & Tommasi, 2020; Chen et al., 2019; Villafaina, Collado-Mateo, Cano-Plasencia, Gusi, & Fuentes, 2019;

Calvo & Beltrán, 2014). A number of studies have previously suggested the lateralization of the neural correlates of hypnosis to the right (Lanfranco et al., 2021; Kihlstrom, Glisky, McGovern, Rapcsak, & Mennemeier, 2013; Naish, 2010). In addition, Bakan (1969) reported that hypnotizable participants showed more reflective eye movements to the left than participants insusceptible to hypnosis, presumably indicating greater right hemisphere activation (Bakan, 1969). In fact, those who are highly susceptible to hypnosis are able to generate unusual experiences; this can be achieved while in a state where their brains show a hemispheric asymmetry that is reversed from their normal waking state (Naish, 2010). Because a speculated neuro-physiological mechanism for the induction of hypnosis highly implicates imaginative capacity, unusual thought processes, and holistic approaches, our lateralized results here possibly reflect this underlying lateralization of function. Despite the early popularity of right lateralization of hypnosis function, driven by a romantic idea of brain lateralization more generally, the point should be cautiously considered (Gruzelier, 2006) because of previous evidence showing left-hemispheric involvement in hypnosis (Maquet et al., 1999; Jasiukaitis, Nouriani, & Spiegel, 1996). However, most of these studies proposed verbal suggestions during hypnosis whereas the specificity of our method was a neutral hypnosis with only a white noise used to deepen the hypnotic state.

Lastly, we did not find any significant correlations between brain metrics and behavioral measures. This could be because of small sample size, which is a clear limitation of our study. Note however that previous studies on consciousness have comparable numbers of participants (Martial et al., 2019; Bharath, Panda, Saini, Sriganesh, & Rao, 2017; Nieminen et al., 2016). Despite the small sample size, as well as the lack of a control group of lowly hypnotizable participants, our findings of a group difference in connectivity were also prominent at the individual participant level (i.e., out of nine, eight participants have similar patterns; Figure 2D). This further supports the group-level indications of brain connectivity alterations during hypnosis. Previous results of EEG studies on hypnosis are heterogeneous. Discrepancies observed within the literature may be because of the differing analysis methods and methods of hypnosis induction (neutral hypnosis vs. other suggestions). Therefore, we would encourage future studies with larger sample sizes, possibly performing analysis on EEG-based cortical source reconstruction and/or EEG combined with fMRI. These techniques may provide further insights on brain dynamics in hypnosis, specifically to explore brain regional modification that we reported in the scalp electrode level in our study.

Finally, one can argue that the absence of randomization order of the two conditions (i.e., ordinary consciousness and hypnosis) does not allow to fully distinguish the effects of hypnosis. However, the risk of inducing hypnosis before the control condition could result in a post-

hypnosis effect affecting the recordings during ordinary consciousness. A “wash-out” delay between conditions could be a solution to avoid this post-hypnosis effect. Studies have been conducted both without (Lee & Koo, 2012) and with randomized order (Rimbert, Zaepffel, Riff, Adam, & Bougrain, 2019; Schmidt, Hecht, Naumann, & Miltner, 2017) for the two conditions of data recording, but the wash-out period in the randomized studies is unclear. Future studies could propose both conditions in a randomized order, including a wash-out delay between the conditions. To our knowledge, there are nevertheless no clear guidelines regarding the minimum time needed as wash-out period to avoid any delayed effect of hypnosis. Furthermore, in this study, we have adapted the induction procedure to allow the participants to experience the hypnotic process. Future studies could potentially compare the effect of different types of procedures on the brain activity recorded during hypnotic process.

In conclusion, the present study demonstrates that during hypnosis, brain connectivity decreases in alpha and beta-2 bands at midline and frontal-midline, which could be associated with reduction of external awareness and dissociation from the outer environment. On the other hand, increased delta band connectivity in frontal and frontoparietal regions may be associated to high levels of dissociation. This modified connectivity pattern was prominent in the right hemisphere. Furthermore, during hypnosis, the brain network reconfiguration became richer by reconfiguring the network segregation and integration in low- and high-frequency bands respectively, within bilateral frontal and right parietal hub regions.

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Reprint requests should be sent to Olivia Gosseries, Department of Coma Science Group, GIGA-Consciousness, University of Liège, Belgium Centre du Cerveau², University Hospital of Liège, Belgium, or via e-mail: ogosseries@uliege.be or Audrey Vanhaudenhuyse, Department of Algology Interdisciplinary Center; University Hospital of Liege; Belgium Sensation and Perception Research Group, GIGA-Consciousness, University of Liège, Belgium, or via e-mail: avanhaudenhuyse@chuliege.be.

Data Availability Statement

The EEG data used in this experiment are available upon reasonable request to the corresponding author with appropriate procedures.

Author Contributions

Rajanikant Panda: Formal analysis; Investigation; Methodology; Software; Validation; Visualization; Writing—Original draft; Writing—Review & editing. Audrey Vanhaudenhuyse: Conceptualization; Data curation; Funding acquisition; Investigation; Project administration;

Resources; Supervision; Validation; Writing—Original draft; Writing—Review & editing. Andrea Piarulli: Formal analysis; Investigation; Methodology; Visualization; Writing—Review & editing. Jitka Annen: Formal analysis; Methodology; Supervision; Writing—Review & editing. Athena Demertzi: Data curation; Writing—Review & editing. Naji Alnagger: Visualization; Writing—Review & editing. Srivas Chennu: Methodology; Software; Writing—Review & editing. Steven Laureys: Conceptualization; Funding acquisition; Resources; Supervision; Validation; Writing—Review & editing. Marie-Elisabeth Faymonville: Conceptualization; Data curation; Project administration; Writing—Review & editing. Olivia Gosseries: Conceptualization; Data curation; Funding acquisition; Investigation; Project administration; Resources; Supervision; Validation; Visualization; Writing—Original draft; Writing—Review & editing.

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Diversity in Citation Practices

Retrospective analysis of the citations in every article published in this journal from 2010 to 2021 reveals a persistent pattern of gender imbalance: Although the proportions of authorship teams (categorized by estimated gender identification of first author/last author) publishing in the *Journal of Cognitive Neuroscience (JoCN)* during this period were $M(an)/M = .407$, $W(oman)/M = .32$, $M/W = .115$, and $W/W = .159$, the comparable proportions for the articles that these authorship teams cited were $M/M = .549$, $W/M = .257$, $M/W = .109$, and $W/W = .085$ (Postle and Fulvio, *JoCN*, 34:1, pp. 1–3). Consequently, *JoCN* encourages all authors to consider gender balance explicitly when selecting which articles to cite and gives them the opportunity to report their article’s gender citation balance.

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