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Cerebral mechanisms of hypnotic hypoesthesia. An ERP investigation on the expectancy stage of perception

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Abstract

The present study aims at identifying reliable markers of neural preparatory processes during hypnosis. To this goal, we recorded the electroencephalographic activity of 23 volunteers regardless of their hypnotizability score. Somatosensory evoked potentials (SEPs) were elicited while participants received non-painful electrical stimuli on the left median nerve in the conditions of relaxation and hypnosis with suggestions of reduced sensation. SEPs analysis was focused on the pre-stimulus activity and revealed two main components: the prefrontal negativity (pN) and the somatosensory negativity (sN) over the frontal and parietal areas of the scalp, respectively. Results showed reduced amplitudes for both components under hypnosis, mostly for the pN, suggesting a change of top-down control of parietal and prefrontal areas. Furthermore, the sLORETA source imaging showed a deactivation of the lateral and anterior portions of the prefrontal cortex (PFC) during the hypnotic state. The present study highlights the downregulation of the PFC as a core aspect of the adopted hypnotic task and confirms the ability of hypnosis to modulate the activity of frontal executive functions. Further, since the majority of participants fell into the medium range of hypnotizability, the present findings could reflect the hypnosis effects in most of the population.

KEYWORDS

ERP, expectancy, hypnosis, hypnotizability, prefrontal cortex, somatosensory perception

1 | INTRODUCTION

The definition of hypnosis has undergone a substantial evolution in the past decades and is still in progress. The Division 30 of the American Psychological Association has recently defined hypnosis as "A state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion" (Elkins, Barabasz, Council, & Spiegel, 2015). Unlike the previous definition (Daniel, 2005), it emphasizes hypnosis as a state of consciousness, highlighting the relevance of subjective experience for both its definition and assessment, rather than taking behavior only into account.

Despite the progress in the understanding of hypnotic phenomenology and the wealth of data available in the literature, the personality features related to hypnotic ability, as well as models and hypotheses attempting to explain it, do not allow for conclusive definitions. Among them, the neodissociation theory (Hilgard, 1973, 1974), the dissociated control model (Bowers, 1992) the cold control model (Dienes & Perner, 2007) and the transient hypofrontality hypothesis (Dietrich, 2003) have been introduced, which, despite some differences, all agree on the contribution of the frontal cortex in hypnotic phenomenology. In fact, the dissociation models suggest that hypnosis may depend on the dissociation of the supervisory attentional system and contention-scheduling mechanisms, while the cold control theory describes the hypnotic response as a metacognitive phenomenon leading to the subject being unaware of his/her intention in motor and cognitive actions. This reduced awareness, marked by intentional control related to inaccurate higher-order thoughts, has been associated with the deactivation of the left dorsolateral prefrontal cortex (DLPFC; Dienes & Hutton, 2013).

The neurophysiology and the neuropsychology of hypnosis are complex topics with variable and sometimes conflicting results since hypnosis is far from being a single monomorphic phenomenon, the neurocorrelates of which largely depend on hypnotic ability and tasks. This is especially true for the EEG, given its low spatial resolution, the high complexity and the great variability of its signals, as well as the variety of methods of signal processing, including the solution of the so called inverse problem. Neuroimaging techniques have shown that hypnosis engenders intentional, task related activation, and deactivation of several brain areas and circuits, including anterior cingulate cortex (ACC), somatosensory and motor cortex, temporal and occipital cortex, thalamus, brainstem, cerebellum, basal ganglia, and prefrontal cortex (Rainville, Carrier, Hofbauer, Bushnell, & Duncan, 1999; Rainville, Hofbauer, Bushnell, Duncan, & Price, ; Rainville & Price, 2003). Other authors have suggested that hypnotic susceptibility is linked to the efficiency of the frontal attentional system and that the hypnosis yields a functional dissociation of conflict monitoring and cognitive control processes (Egner, Jamieson, & Gruzelier, 2005; Schulz, Horstmann, Jokeit, Woermann, & Ebner, 2005). Furthermore, hypnosis has been reported to affect the activity of the default modality network (Deeley et al., 2012; Facco et al., 2019; Lipari et al., 2012; McGeown, Mazzoni, Venneri, & Kirsch, 2009). Increased functional connectivity between the left DLPFC—hub of the Control Executive Network (CEN)—and the salience network (SN) including the dorsal ACC, anterior insula, amygdala, and ventral striatum—has been recently shown in highly hypnotizable subjects, where a functional coupling between the dorsal ACC and the DLPFC has been found (Hoeft et al., 2012; McGeown, Mazzoni, Vannucci, & Venneri, 2015).

The abovementioned data look to converge on the capacity of hypnosis to intentionally modulate the activity of DMN, CEN, and SN (see Landry, Lifshitz, & Raz, 2017, as a review); this links the neuropsychology of hypnosis to the core of dissociative identity disorders and other psychiatric disorders, involving a loss of flexibility and an uncontrolled imbalance of these networks (Facco et al., 2019). Among these systems, the ACC, the anterior insula and the DLPFC seem to play a major role during hypnosis (see Casale et al., 2012; Kihlstrom, 2013, as reviews). Furthermore, the role of the frontal executive functions in hypnotizability was investigated with neuropsychological testing, both during and outside hypnosis (Aikins & Ray, 2001; Gruzelier & Warren, 1993; Kallio, Revonsuo, Hämäläinen, Markela, & Gruzelier, 2001). Woody and McConkey (2003) argued that hypnotized subjects share common characteristics with patients with frontal lesions. Accordingly, the performance of high hypnotizable individuals should be compromised in tests of executive functions like conflict monitoring, switching and active suppression, compared to the low hypnotizable counterpart. Kallio and colleagues (2001) observed that high hypnotizable individuals performed better than lows on frontal tests during baseline; however, under hypnosis, highs performed worse than lows, especially on the word fluency task. Similar results were obtained also by Gruzelier and Warren (1993), whereas Aikins and Ray (2001) observed that high-susceptible individuals performed better than lows on the Wisconsin card sorting test during baseline. Based on these findings, authors proposed that the hypnotic disposition is not associated to behavior akin to symptoms of frontal patients; rather, neuropsychological findings pointed to superior cognitive flexibility for highly susceptible people, a fact also suggested by the neuropsychophysiological model of Gruzelier (1998) and Crawford and Gruzelier (1992).

To summarize, previous research suggests that a high predisposition to hypnosis is associated with enhanced flexibility of the executive functions. However, some neuropsychological findings failed to reach a reliable statistical power (e.g., Kallio et al., 2001) and, more importantly, most studies on hypnosis suffered methodological limitations such as the categorical comparison between samples of high- and low-susceptible individuals (highs and lows), a fact which may lead to scarce generalizability of the results. On the contrary, the limited temporal resolution of brain imaging methods may not allow distinguishing the neural effects of hypnosis per se from those of the stimulus processing (e.g., the PFC activity changes along with the processing of painful sensation; Wik, Fischer, Bragée, Finer, & Fredrikson, 1999).

The aim of this study was to investigate the preparatory brain activity, especially over the PFC, during a passive stimulation task with hypnotic suggestions aimed at reducing sensations. As recommended by recent guidelines (Jensen et al., 2017), we adopted a within subjects design, where the susceptibility score was not considered as a categorical factor; indeed, most of the recruited participants fell into the medium range of hypnotizability. They received electrical pulses on the median nerve in the counterbalanced conditions of restful state and hypnosis with suggestions of hypoesthesia while the event-related potentials (ERPs) were recorded. Previous EEG investigations in this field focused on the brain activities of post stimulus processing: some of them reported modulations of the N140, P200, and P300 components, indicating the cognitive and the affective integration of the somatosensory stimulus as the locus of the hypnotic effect (Del Percio et al., 2013; De Pascalis, Cacace, & Massicolle, 2008; De Pascalis, Magurano, & Bellusci, 1999; De Pascalis, Magurano, Bellusci, & Chen, 2001; Ray, Keil, Mikuteit, Bongartz, & Elbert, 2002; Spiegel, Bierre, & Rootenberg,1989), while others observed modulations of the N20 component (Perri, Rossani, & Di Russo, 2019) and gamma oscillations (De Pascalis, Cacace, & Massicolle, 2004), suggesting also sensory (and not only attentional) alterations by hypnosis. On the contrary, in the present work, we investigated the preparatory brain activities, that are the ERPs preceding the somatosensory stimulation. To this aim, we focused on the so called prefrontal negativity (pN) component, a pre-stimulus and supramodal ERP activity reflecting the PFC contribution during the stimulus expectation stage (see Di Russo et al., 2017 as a review). This component has been analyzed checking both interindividual (Bianco, Berchicci, Perri, Quinzi, & Di Russo, 2017; Bianco, Di Russo, Perri, & Berchicci, 2017; Perri, Berchicci, Lucci, Spinelli, & Di Russo, 2015a; Perri, Berchicci, Spinelli, & Di Russo, 2014) and intraindividual differences (Lucci, Berchicci, Perri, Spinelli, & Di Russo, 2016; Perri, Berchicci, Lucci, et al., 2014; Perri, Berchicci, Lucci, Spinelli, & Di Russo, 2015b; Perri, Spinelli, & Di Russo, 2017), with its amplitude modulation reflecting the level of proactive and top-down attentional control during task performance (Bianco, Berchicci, Perri, Spinelli, & Di Russo, 2017; Perri, Berchicci, Lucci, Spinelli, & Di Russo, 2016; Perri & Di Russo, 2017). In addition, the analysis of pre-stimulus stage has been recently extended to include also sensory-specific ERPs (Di Russo et al., 2019; Perri, Berchicci, Lucci, et al., 2014), which showed an anticipatory negative slow cortical potential over the contralateral somatosensory area (Bianco et al., 2020): this sensory readiness activity was labeled as somatosensory negativity (sN) and was concomitant to the pN.

In the present study, we test the hypothesis that hypnotic suggestions of reduced sensations may attenuate the top-down control of prefrontal and somatosensory areas, as defined by the amplitude of the preparatory ERPs. Indeed, differently from hypnotic suggestions recruiting more PFC (e.g., during a cognitive-conflict resolution; Cojan, Archimi, Cheseaux, Waber, & Vuilleumier, 2013; Huber, Lui, & Porro, 2013; Zahedi, Abdel Rahman, Stürmer, & Sommer, 2019; Zahedi, Stuermer, Hatami, Rostami, & Sommer, 2017), we expect hypnotic hypoesthesia to recruit less PFC, thus, allowing external stimuli to be filtered out.

2 | METHOD

2.1 | Participants

Twenty-five healthy volunteers (12 males; mean age = 22.2 years, *SD* = 1.4) were selected from the same data set as Perri and colleagues (2019): they were recruited from the student population at the Universities of Rome "Foro Italico" and "Niccolò Cusano." Participants had a normal or corrected-to-normal vision, no previous experience with hypnosis and no history of neurological or psychiatric disorders; they gave their written informed consent. The procedures were approved by the local ethics committee and were in accordance with the ethical standards of the 1964 Declaration of Helsinki.

2.2 | Procedure and stimuli

For each volunteer, participation in the experiment consisted of two sessions at a distance of at least 1 week: in the first session, the individual level of hypnotic susceptibility was assessed; in the second session, electroencephalographic (EEG) activity under restful state (hereafter "control") and hypnosis state was recorded.

The hypnotic susceptibility was measured by the Italian version of the Harvard Group Scale of Hypnotic Susceptibility, Form A (HGSHS-A) within three group sub-sessions. During each sub-session, the 12 standard suggestions from HGSHS-A were administered orally by an experienced hypnotherapist (no audio recording was used). At the end of each session, participants were given a response booklet and were asked to report their experience filling in "objective" and "subjective" score forms. Only the objective score form was considered for the determination of the participants' individual score, following the standard procedure described by Shor and Orne (1962). For each of the first 11 items, a score of one was assigned if the subject reported having experienced the suggested response, otherwise the assigned score was zero. For the 12th item (posthypnotic amnesia), a score of one was assigned if less than four items had been reported in the response booklet before amnesia was lifted; otherwise a score of zero was assigned.

In the second session, the EEG was recorded during the left median nerve stimulation. The EEG session consisted of two conditions, provided in a counterbalanced order across participants: control and hypnosis. In the control condition, participants were asked to close their eyes and relax during SEP recording (about 18 min). During hypnosis, a suggestion of hypoesthesia was administered after the induction. Participants were given a 15 min break between conditions.

Hypnosis was induced as follows: the participant was invited to observe the tip of the operator's index finger, which was slowly moved to draw an eight shaped trajectory, while suggestions of heaviness of the eyelids were administered until participant's eyes were closed; then, suggestions of progressive body relaxation in craniocaudal direction and focused attention to one's breathing were delivered. The participant's hypnotic state was checked by observing the presence of signals, such as easing of facial tension, dropping of the lower jaw accompanied by a slight opening of the mouth, and slowing of the breathing rate (Casiglia et al., 2006). Following the induction, suggestions of hypoesthesia were administered before starting stimulation through suggestions of coldness of the left arm. After the end of stimulation, the participants were dehypnotized by slowly counting from 1 to 3, followed by eye opening.

At the end of each condition, participants were asked to rate the intensity and unpleasantness of the stimulation on two visual analog scales (VAS) from 0 to 10. For the measurement of the sensory VAS (s-VAS), participants were asked to indicate how clearly the stimuli were perceived, with 0 corresponding to “I did not feel the stimuli at all,” and 10 to “I felt the stimuli very clearly.” For the measurement of the affective VAS (a-VAS), participants were asked to indicate the level of unpleasantness associated with the stimuli, with 0 corresponding to “It was not unpleasant at all,” and 10 to “It was extremely unpleasant.”

2.3 | SEP recordings

Somatosensory stimuli consisted of 0.5 ms non noxious square waves generated by a constant current stimulator (STM 140; HTL, Udine, Italy) through surface skin electrodes placed over the median nerve of the nondominant (left) upper limb at the wrist joint, with the cathode about 2 cm more proximal to the anode. Stimulation intensity was determined for each participant by delivering series of stimuli of increasing intensity starting from 2 mA in steps of 1 mA until the motor threshold was reached, identified by a slight thumb twitching (mean intensity = 12 ± 2 mA). The interstimulus-interval (ISI) randomly varied between 600 and 1,200 ms (mean 900 ms). Each condition consisted of three 6 min runs during which 400 stimuli were delivered, for a total of 1,200 stimuli per condition. Participants were tested in a sound attenuated, dimly lit room: they were comfortably seated with the left arm comfortably resting on a pillow. The EEG signal was recorded using two BrainAmp amplifiers connected with 64 ActiCap active electrodes (BrainProducts GmbH, Munich, Germany) mounted according to the 10–20 International system. The ground electrode was positioned on the left forearm, and all electrodes were referenced to the left earlobe. Electrode impedances were kept below 5 KΩ, and signals were digitized (rate of 1 kHz) and stored for offline averaging. Artifact rejection was performed to discard epochs contaminated by signals exceeding the amplitude threshold of ±60 μV. After this procedure, two subjects had to be removed from the data set, due to the high number of artifacts, mostly due to the head drops during hypnosis. Accordingly, 23 subjects (11 males; mean age = 22.1 years, *SD* = 1.5) were considered for EEG analysis. On average, about 15% of the trials in each condition were rejected due to the presence of artifacts, and, on average, 1,020 artifact-free trials were collected for each condition.

The EEG recording was segmented in epochs of 1,100 ms (from −700 to 400 ms after stimulus onset) with the first 100 ms serving as the baseline. Subsequently, the artifact-free, segmented EEG was low-pass filtered (Butterworth cutoff frequency 70 Hz, slope 24 dB/octave). For each condition, the segmented trials were averaged so that grand average traces for the control and hypnosis conditions were obtained. To exclude that late post stimulus ERPs may interfere with the pre-stimulus activity in the subsequent trial, we also segmented the signal from −500 to 400 ms with a −500/-400 ms baseline. The comparison between the two segmentations yielded not significant differences.

2.4 | Data analysis

To reduce the high number of possible comparisons across multiple sites, the choice of the electrodes has been established a priori based on the literature (e.g., Perri et al., 2016). Accordingly, the prefrontal negativity (pN) component was calculated on the frontopolar derivations (Fp1, Fpz, Fp2), while the somatosensory negativity (sN) was calculated on the central-parietal derivations (CP1, CPz, CP2), analyzing the mean amplitude recorded in the 400 ms preceding the stimulus onset.

The subjective ratings were compared between control and hypnotic condition with *t* tests for paired samples, whereas analysis on the SEP amplitude was performed with repeated measures analysis of variance (ANOVAs) with order of conditions (hypnosis-control, control-hypnosis), condition (hypnosis, control), area (prefrontal, central-parietal), and laterality (left, midline, right) as factors. The results were corrected for multiple comparisons using the Bonferroni test, and the effect sizes were calculated as partial eta squared (η_p^2). According to Cohen (2013), η_p^2 greater than .01, .06, .14 were interpreted as small, medium, and high effects, respectively. Finally, the susceptibility scores, the SEP amplitude, the a-VAS and s-VAS were correlated to each other (Pearson's *r*). The overall alpha level was fixed at .05.

2.5 | Neuroelectric source imaging

The neural source of pre-stimulus SEPs was estimated using sLORETA software, which is a functional imaging method based on electrophysiological and neuroanatomical constraints (Pascual-Marqui, 2002), able to localize both superficial and deep brain structures (Pizzagalli et al., 2004; Zumsteg, Friedman, Wieser, & Wennberg, 2006) using EEG data. Afterward, reference free current source density (CSD) waveforms of the representative regions of interest (ROIs) were obtained (single voxel at ROI centroid), yielding high resolution temporal curves.

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3 | RESULTS

3.1 | Hypnotizability and subjective reports

The mean level of hypnotizability (as defined by the HGSHS-A) was 7.3 ± 1.8 corresponding to a moderate susceptibility. In particular, the sample was composed of $N = 7$ highs (HGSHS from 9 to 12, mean = 9.7), $N = 10$ mediums (HGSHS from 6 to 8, mean = 7.2), and $N = 6$ lows (HGSHS from 0 to 5, mean = 4.8). Figure 1 shows the histograms for the two VAS: perceived intensity (s-VAS) was reduced in the hypnosis condition (mean = 6.3, $SD = 2.6$) compared to control (mean = 8.8, $SD = 1.2$; $t = 5.5$, $p < .0001$); similarly, affective rating (a-VAS) scores decreased in the hypnosis condition (mean = 2.8, $SD = 2.3$) compared to control (mean = 3.9, $SD = 2.5$; $t = 2.4$, $p < .05$). Therefore, hypnotic suggestions decreased the self-rates by the 28.4% and 28.2% for the sensory and affective perception, respectively.

3.2 | Electrophysiological data

Figure 2 shows the grand averages of the pre-stimulus SEPs in the two conditions. At frontopolar derivation (Fpz) the onset of pN was at about 500 ms prior to the stimulus in the control condition, and at about 200 msec in hypnosis. On the central and central-parietal derivations (Cz and CP2), a slowly rising negativity was detectable as well: this component, mainly reflecting a readiness potential involving the areas close to stimulation, was slightly reduced in hypnosis, especially in the 200 ms range before stimulus occurrence. Figure 3 shows the scalp topography of the SEPs in two temporal windows of 200 ms each (i.e., from −400 ms to the stimulus onset).

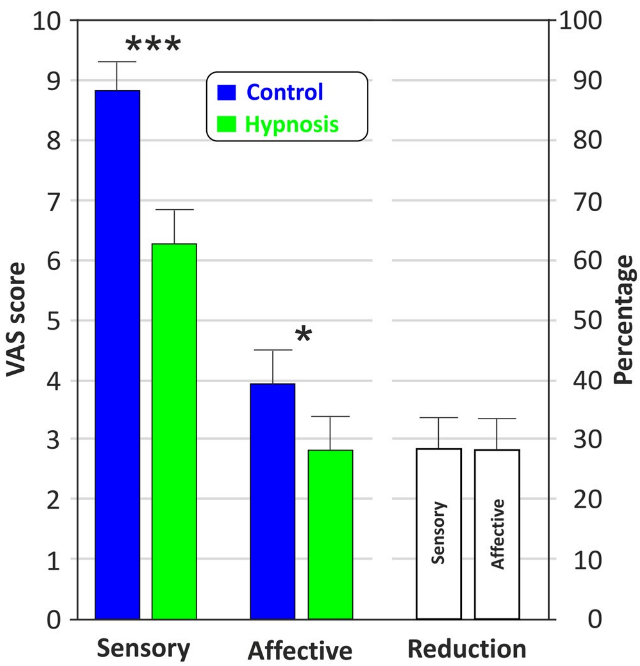

FIGURE 1 Histograms of the sensory and affective visual analog scales (VAS) of the somatosensory perception in the two conditions. Reduction refers to the control minus hypnotic state values. The error bars show standard error of the mean (*SEM*). $*p < .05$, $***p < .001$. The reduction rate between control and the hypnotic condition is expressed in percentage

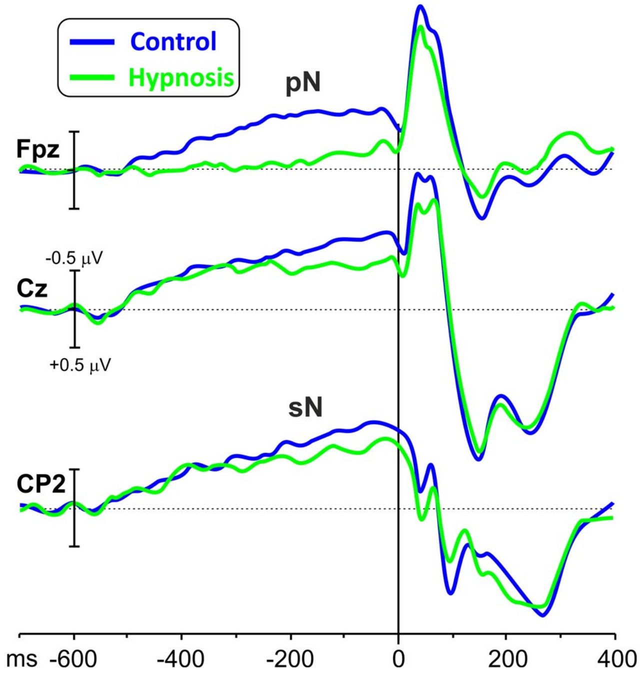

FIGURE 2 Grand-average waveforms of the pre-stimulus ERPs in the control and hypnotic condition

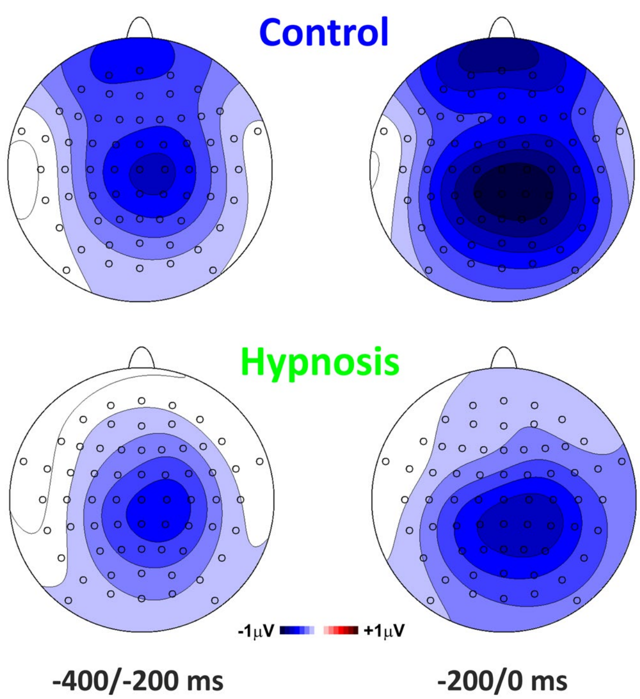

FIGURE 3 Topographic maps of the −400/0 ms activity in the control and hypnotic condition

The control condition was marked by two areas of activity in prefrontal and central-parietal derivations, with slight lateralization toward the right hemisphere; instead, only the central-parietal activity was detectable in hypnosis.

ANOVA did not show significant results for the order of condition (i.e., hypnosis or control first) neither when considered as the main effect nor as an interaction effect (all *ps* > .05), thus, excluding any habituation effect on the observed findings. At the opposite, significant results emerged for the main effects of laterality ($F_{1,21} = 5.1$, $p = .03$, $\eta_p^2 = .19$) and condition ($F_{1,21} = 11.7$, $p = .002$, $\eta_p^2 = .35$), indicating greater amplitudes for the right than the left hemisphere, and for the control than the hypnotic condition. Further, a significant effect emerged for Condition x Area interaction ($F_{1,21} = 5.3$, $p = .03$, $\eta_p^2 = .20$), indicating that the hypnotic reduction of pre-stimulus activity was greater in the prefrontal than central-parietal areas.

The pre-stimulus ERP activity was not correlated to hypnotizability scores and subjective ratings of the somatosensory stimulation. However, for descriptive purposes only, we also provide data relating to the power of the ERP components for the three subgroups of hypnotizability (see Table 1).

As for the pN component, Table 1 suggests that amplitude reduction in hypnosis was generally greater for the mediums, while the highs showed a laterality-like effect consisting of a more pronounced reduction over the left than the right hemisphere. At the opposite, pN activity of mediums and lows was equally reduced on the two hemispheres as the effect of hypnotic suggestion. As for the sN component, the reduction of activity during hypnosis was nearly absent for lows, moderate for mediums and larger for highs: results were comparable between hemispheres. However, no implications can be drawn from these observations, and they must be taken with caution for two main reasons: (i) the size of the three subgroups was rather small and they are not suitable for a reliable ERP analysis, and (ii) the mean HGSHS of lows was 4.8, meaning that no participants scored below 4. Overall, ERP analysis indicated reduced amplitude over prefrontal and the parietal areas during hypnosis. Further, in order to exclude that this finding reflected a more general effect on EEG amplitude, we also performed a control analysis over a posterior site. Mean amplitude of the medial occipital site (Oz) in the −400/0 ms time window was compared between conditions, but no differences emerged between hypnosis (mean = −0.27 μV, *SD* = 0.28) and control (mean = −0.31 μV, *SD* = 0.29; *p* > .05).

3.3 | sLORETA source analysis

The LORETA global field power reached the maximum amplitude at about −100 ms. The source analysis identified three ROIs in the middle frontal gyrus: the BA 10 (frontopolar cortex), the BA 11 (orbitofrontal cortex), and the BA 47 (lateral frontal cortex). As shown in the 3D and 2D rendering of Figure 4a, the activity of the prefrontal areas was enhanced and more left-lateralized in the control than the hypnotic condition: note that laterality was not necessarily related to the stimulated hand's side, as no motor areas were included in the prefrontal ROIs. The CSD waveforms of Figure 4b reflect the time course of voxel activation in these ROIs, confirming a pre-stimulus activity close to the baseline in the hypnotic condition, and a larger left activity in the control condition. As shown in the 3D cortex (top view) of Figure 4c, source analysis identified the best match of parietal activity deeply in the BA7 (corresponding to the somatosensory associative cortex), though less active than the prefrontal cortex. BA7 activity was strongly reduced in the hypnotic condition.

4 | DISCUSSION

The aim of this study was to test the hypothesis of reduced top-down processing before the stimulus administration in hypnosis with the suggestion of hypoesthesia. ERP analysis showed that the pre-stimulus activity included two different slow waves: the pN and the sN, reflecting the PFC top-down processing and the secondary somatosensory area preparatory process, respectively (Bianco et al., 2020; Perri et al., 2015a). Compared to the control condition, hypnosis reduced both pre-stimulus activities, with the pN to a greater extent. Accordingly, the source imaging confirmed that the pre-stimulus activity mainly involved the PFC, especially the BA 10, BA 11, and BA 47. The activity of these areas was

TABLE 1 Mean amplitude of the prefrontal negativity (pN) and somatosensory negativity (sN) components for the three subgroups of hypnotic susceptibility (HGSHS)

	pN left			pN right			sN left			sN right		
HGSHS	**C**	**H**	**Diff**	**C**	**H**	**Diff**	**C**	**H**	**Diff**	**C**	**H**	**Diff**
Highs	−0.42	0.03	−0.45	−0.43	−0.3	−0.13	−0.67	−0.32	−0.35	−0.78	−0.44	−0.34
Mediums	−0.89	−0.16	−0.73	−0.85	−0.2	−0.65	−0.82	−0.65	−0.17	−0.94	−0.82	−0.12
Lows	−0.29	0.07	−0.36	−0.34	0.08	−0.42	−0.29	−0.31	0.02	−0.43	−0.36	−0.07

Abbreviations: C, control; Diff, differential value (C–H); H, hypnosis.

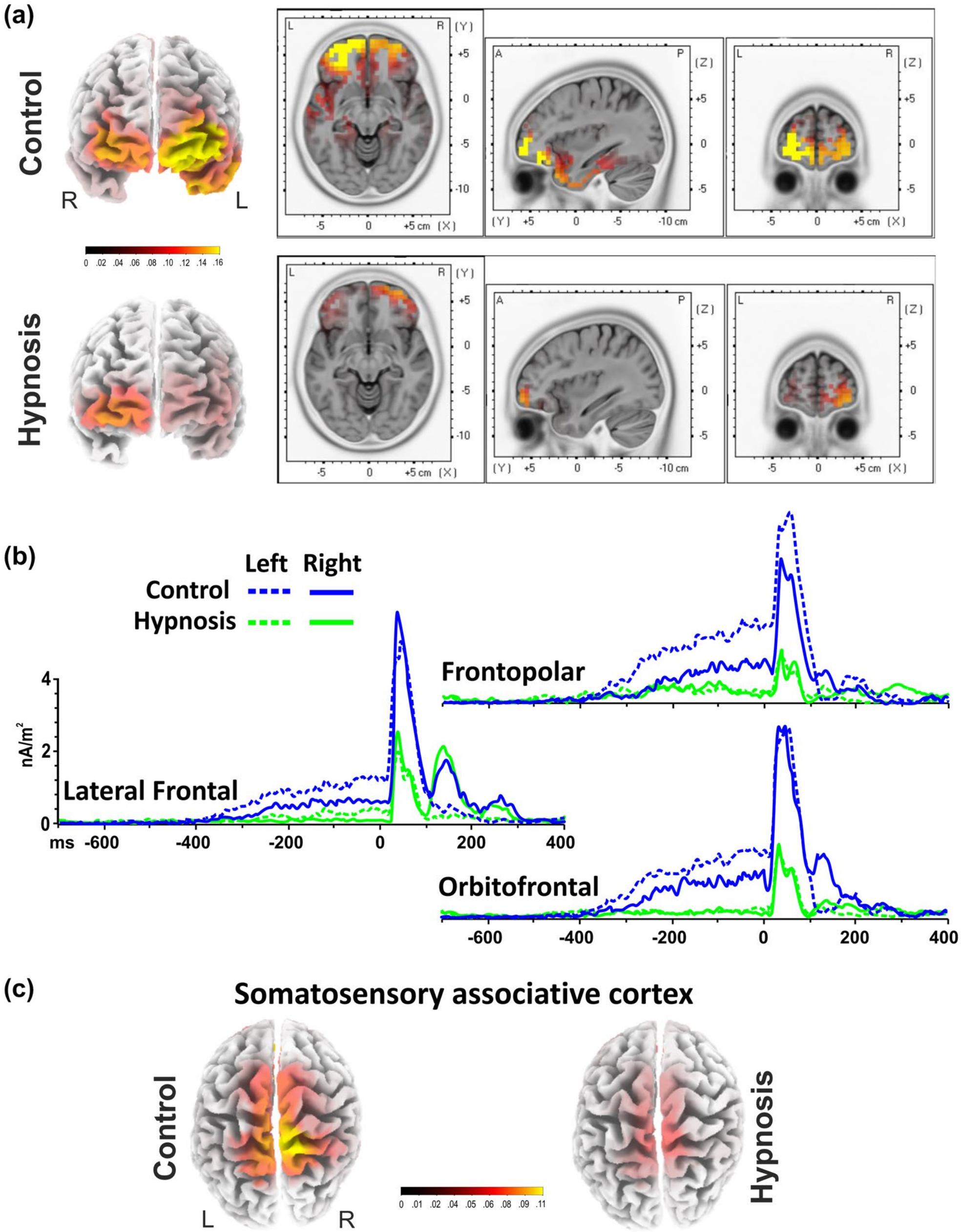

FIGURE 4 sLORETA source analysis showing (a) brain activities at 100 ms before the stimulus in the control and hypnotic condition (slices are settled on the best match), (b) current source density (CSD) waveforms of the most active prefrontal ROIs, and (c) 3D cortex (top view) at −100 ms (best match of activity at parietal BA7)

mainly left-lateralized in the control condition, and it was strongly reduced in hypnosis. Our results are in line with those by Crawford and Gruzelier (1992), who suggested the centrality of frontal lobe deregulation in hypnosis, such as with McGeown and colleagues (2009) who reported deactivation of the anterior part of the default mode network (DMN) during hypnosis. Since the DMN has been linked to spontaneous mind wandering in the resting state (Mason et al., 2007), the authors interpreted the PFC deactivation in terms of inhibition of irrelevant thought processes during hypnosis (see also Lynn, Laurence, & Kirsch, 2015). Likewise, inhibitory repetitive transcranial magnetic stimulation (rTMS) of the DLPFC has been shown to increase the responsivity to hypnosis (Dienes & Hutton, 2013), and the DLPFC is the hub of the CEN (Sridharan, Levitin, & Menon, 2008). The complex interplay between CEN, SN, and DMN allows for a proper balance between processing systems managing external/internal channels of information, and their dysfunctional interaction is at the base of severe psychiatric disorders, including psychosis, posttraumatic stress disorder, and dissociative identity disorders (Cole, Repovš, & Anticevic, 2014; Khadka et al., 2013; Lanius, Bluhm, & Frewen, 2011) (Menon & Uddin, 2010). Changes of connectivity within the DMN and between DMN, SN, and CEN are also related to hypnosis and hypnotic ability (Deeley et al., 2012; Hoeft et al., 2012; Landry et al., 2017; Lipari et al., 2012; McGeown et al., 2009). Therefore, it is not surprising that hypnosis may yield relevant changes in PFC activity. Overall, our data confirm the involvement of the anterior part of the brain in the hypnotic experience as well as a decreased activity in parietal somatosensory associative cortex: this is in line with the results of previous studies, showing the attention-related changes of somatosensory activity (Bianco et al., 2020; Johansen-Berg, Christensen, Woolrich, & Matthews, 2000; Mima, Nagamine, Nakamura, & Shibasaki, 1998) and suggest the capacity of hypnosis to decrease top-down attention to the attended somatosensory stimuli. The pre-stimulus stage of processing allowed us to tell expectancy-related activity from the one yielded by the stimulus administration. Since it was previously shown that with such a signal segmentation the late stimulus-evoked ERPs do not contaminate the analysis of the preparatory activity in the next trial (Quinzi, Berchicci, Bianco, Perri, & Di Russo, 2019), we may assume that our findings are not driven by post stimulus processing for which hypnosis effects emerged until the P250 component (Perri et al., 2019). In other terms, unlike brain imaging techniques, ERPs allowed a sharp separation of the neural correlates of the disposition in receiving the stimulus from the activities of stimulus processing. With such a distinction, we are more confident in suggesting that our hypnotic protocol is associated with the inhibition of the PFC top-down control, as reflected by the source analysis and the reduced amplitude of the pN component (see Di Russo et al., 2017; Perri, 2020 as reviews). The deactivation of the lateral and anterior portions of the PFC, and the reduced experience of the electrical stimuli (as measured by the subjective ratings) confirm the key-role of the frontal cortex in hypnotic phenomenology (e.g., Gruzelier, 1998) such as the definition of hypnosis in terms of "reduced peripheral awareness characterized by an enhanced capacity for response to suggestion" (Division 30 of the APA, Elkins et al., 2015).

Further studies are needed to check the relationship between the amplitude of the pN component and the executive functioning during hypnosis, and whether it might reflect a general index of hypnotic state and depth; perhaps, ERPs might help to overcome the limits of EEG, given its great variability and the lack of reliable EEG markers of hypnosis (Vanhaudenhuyse, Laureys, & Faymonville, 2014).

As far as the sN component is concerned, it has been suggested that the pre-stimulus modality-specific ERPs reflect the anticipatory attention to the stimuli to be processed (Brunia & Van Boxtel, 2004; Perri, Berchicci, Lucci, et al., 2014; Van Boxtel & Böcker, 2004). Accordingly, its reduction in hypnosis may reflect a reduced of attention to the somatosensory stimulation, a claim that would be consistent with the concept of absorption in hypnosis (e.g., Price & Barrell, 1990), as well as to the great capacity of hypnosis to modulate thermal and pain thresholds, up to full analgesia (Casiglia et al., 2007; Conversa et al., 2019; Facco et al., 2011; Facco, Pasquali, Zanette, & Casiglia, 2013). The lack of correlation between pN and sN components and the subjective estimation of stimulus intensity suggests that sensory and affective perception are not mediated by isolated activities in the brain, but rather by the integration of neural activities in a wider network of brain areas. Likewise, the neurophysiological parameters were not associated to the HGSHS-A score, a fact which may depend on two different factors: (a) Hypnotic ability is a complex phenomenon, the personality features of which are ill-defined yet, while the Harvard and Stanford scales are essentially based on a construct of suggestibility (Facco et al., 2017); (b) being hypnosis a matter of a complex subjective, introspective activity it is reasonable to speculate that phenomenological measures (e.g., Pekala et al., 2010) may be more appropriate to define it, than a behavioral parameter.

Finally, the interpretation of the hypnotic state as a matter of hypofrontality (Dietrich, 2003) may be an ambiguous and, thus, misleading concept requiring a short analysis to be properly understood. The whole of abovementioned theories of hypnosis as dissociation and hypofrontality, well analyzed in the systematic review by Landry et al. (2017), emphasize the following possible components of hypnotizability: (a) top-down changes in the cognitive and executive control and other higher-order activities; (b) deactivation of medial PFC and/or involvement of the DMN, affecting mind wandering; (c) disconnection between executive and supervisory process, cognitive monitoring systems and/or impaired retroactive connections, allowing for proneness to suggestions. Taken as a whole, from a strictly reductionist perspective these theories seem to hint to hypnosis as a condition of loss of control, a less-than-normal state of consciousness. However, when hypnosis is associated to specific tasks such as hypnotic focused analgesia it involves the activation rather than deactivation of DLPFC (Casiglia et al., 2018, 2020): this indicates subject empowerment allowing for an intentional control of pain threshold and pain neuromatrix up to the level of surgical analgesia. Also, this implies that the hypnotized subject has critically accepted the procedure and related instructions, while remaining able to recover the control, whenever should he/she deem it necessary. In other words, hypnosis is far from being a plain loss of control, but, rather, the paradoxical result of enhanced metacognitive control and cognitive flexibility, able to intentionally stop the executive control when useful to participant's purpose. As far as our study is concerned, the "paradox" emerges through the less recruitment of PFC activity that might reflect the metacognitive ability to achieve the hypnotic task by letting the electrical stimuli go and, as a result, affecting the perception. In other terms, our opinion is that modulation of PFC activity should not be interpreted simply in terms of increased or decreased cognitive control in hypnosis. Indeed, it is noteworthy to point out that an increase (and not a decrease) of anticipatory activity has also been observed in the DLPFC of subjects who accomplished a specific hypnotic suggestion (Huber et al., 2013); further, EEG findings on the posthypnotic suggestion reported additional proactive control with enhanced frontal activity during cognitive-conflict resolution (Zahedi et al., 2017, 2019). Crucially, the increased recruitment of the right PFC would even represent a distinctive feature of highs outside of hypnosis, again suggesting a more efficient attentional focusing for the more hypnotizable individuals (Cojan, Piguet, & Vuilleumier, 2015). Taken together, these findings challenge the notion of hypofrontality and loss of control as a marker of hypnosis, suggesting that hypnosis leads to greater executive flexibility instead, which allows a more effective regulation of PFC activity in the top-down control of perception and attention.

5 | CONCLUSIONS

Most neurophysiological studies on hypnosis used to consider distinct samples of high- and low-susceptible participants. However, this approach might fail to provide reliable generalizability of the results, given that almost 80% of people fall into the medium range of hypnotizability (Bongartz, 1985). The marked opposite clustering between highs and lows individuals may partly explain the difficulty to identify reliable neural markers of hypnosis; indeed, this approach carries the unavoidable exclusion of the mediums, with the risk to ignore the more common aspects of hypnosis and hypnotizability. Instead, the present study selected participants irrespective of susceptibility scores, allowing a more representative generalization of the hypnosis effects on the majority of the population (see also Jensen et al., 2017 on the importance of studying mediums).

Further, the present work emphasizes the relevance of EEG measures, especially the ERP method, which allows investigating the fast sequence of neural events emerging under hypnosis. Indeed, as we were able to isolate and describe distinctive preparatory activities before stimulus administration, these findings may shed new light on brain processing during hypnosis. In particular, we showed that hypnotic hypoesthesia was associated with less recruitment of the somatosensory and prefrontal cortex during the expectancy stage; as for the hypnotic effects in the post stimulus stage, in a previous investigation (Perri et al., 2019) we reported reduced engagement of a neural network composed mainly by thalamocortical radiations, anterior insula, and cingulate gyrus. Taken together, these findings allow a more complete description of the entire neural processing than what emerges from the investigation of single processes. We suggest that hypnotic hypoesthesia acts through a combination of top-down and bottom-up mechanisms whose link could be the thalamocortical connections. The hypnotic-guided metacognitive control might be responsible for the changes in the activities from the brain areas concerned with the particular type of processing (reduced pN and sN in the present study): in particular, the frontal control is responsible for the top-down modulation of the nucleus reticularis which serves as a gating mechanism for regulating the preparatory activities of the cerebral cortex (Birbaumer, Elbert, Canavan, & Rockstroh, 1990; Skinner & Yingling, 1976). As a consequence, the thalamic nuclei altered the gating mechanism in the transmission of sensory information to the cortex (Brunia, 1993) and affected the bottom-up processing of the stimuli (i.e., reduced N20 during hypnosis; Perri et al., 2019).

Future studies might consider similar methods of signal processing to shed new light on the cerebral mechanisms of hypnosis and hypnotic suggestion; it would also be interesting to look at the EEG in the frequency domain in order to understand which frequency bands are modulated mostly by hypnotic suggestions in the expectancy stage. For example, analysis on the alpha power of the present data could have provided some information about participants vigilance level to make sure that the observed results were not due to no specific consequences of the hypnotic condition. For the same reason, it would be useful for future studies to overcome the limitations of the present work by combining the EEG data with specific measures of vigilance.

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