Modulation of the heartbeat evoked cortical potential by hypnotizability and hypnosis.

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Abstract

Hypnotizability is a psychophysiological trait measured by scales and associated with several differences including interoceptive accuracy and the morpho-functional characteristics of interoception-related brain regions. The aim of the study was to assess whether the amplitude of the heartbeat evoked cortical potential (HEP), a correlate of interoceptive accuracy, differs in participants with low (lows) and high (highs) hypnotizability scores (assessed by the Stanford Hypnotic Susceptibility Scale, form A) before and after the induction of hypnosis. ECG and EEG were monitored in 16 highs and 15 lows during an experimental session including open eyes baseline (B), closed eyes relaxation (R), hypnotic induction (IND), neutral hypnosis (NH), post session baseline (Post). No significant difference was observed between groups and conditions in autonomic variables. The HEP amplitude was lower in highs than in lows at the right parietal site, likely due to hypnotizability-related differences in the functional connection between the right insula and parietal cortex. It increased in highs and decreased in lows across the session, possibly due to the highs' preeminently internally directed attention and to the lows' possible disengagement from the task. Since interoception is involved in several cognitive-emotional functions, its hypnotizability-related differences may contribute to the variability of experience and behavior in daily life.

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Abstract

Hypnotizability is a psychophysiological trait measured by scales and associated with several differences including interoceptive accuracy and the morpho-functional characteristics of interoception-related brain regions. The aim of the study was to assess whether the amplitude of the heartbeat evoked cortical potential (HEP), a correlate of interoceptive accuracy, differs in participants with low (lows) and high (highs) hypnotizability scores (assessed by the Stanford Hypnotic Susceptibility Scale, form A) before and after the induction of hypnosis.

ECG and EEG were monitored in 16 highs and 15 lows during an experimental session including open eyes baseline (B), closed eyes relaxation (R), hypnotic induction (IND), neutral hypnosis (NH), post session baseline (Post). No significant difference was observed between groups and conditions in autonomic variables. The HEP amplitude was lower in highs than in lows at the right parietal site, likely due to hypnotizability-related differences in the functional connection between the right insula and parietal cortex. It increased in highs and decreased in lows across the session, possibly due to the highs' preeminently internally directed attention and to the lows' possible disengagement from the task. Since interoception is involved in several cognitive-emotional functions, its hypnotizability-related differences may contribute to the variability of experience and behavior in daily life.

Keywords: interoception, heartbeat, HEP, hypnosis, hypnotizability.

Introduction

Hypnosis is a state of consciousness which can be self-induced or promoted through various procedures ("induction") enacted by other persons (Elkins et al., 2015). It is described as different from the ordinary state of consciousness (Pekala et al., 2006) and cannot be defined independently from self-reports, although many cortical correlates have been observed by imaging (Landry et al., 2017; Wolf et al., 2022) and EEG studies (Baghdadi & Nasrabadi, 2012; Hiltunen et al., 2021; Rho et al., 2021; Yargholi & Nasrabadi, 2015). Neutral hypnosis (NH) is a state following hypnotic induction without specific suggestions, i.e., requests to imagine perception, memory and behavior different from the actual ones (for instance, analgesia, hallucination, movement) and to experience them as real and involuntary. According to the bio-psycho-social model of hypnosis (Jensen et al., 2015), the proneness to enter the hypnotic state and accept suggestions is influenced by contextual and individual factors, one of them being the psychophysiological trait of hypnotizability. It is substantially stable through life (Piccione et al., 1989), is measured by scales (Elkins et al., 2015) classifying high (highs, 15% of the general population), medium (mediums, 70%) and low (lows, 15%) hypnotizable individuals, and displays physiological correlates observable in the ordinary state of consciousness even in the absence of suggestions (Bocci et al., 2017; Ibanez-Marcelo et al., 2019; Rashid et al., 2022; Santarcangelo & Scattina, 2016; Spina et al., 2020).

Hypnotizability and hypnosis could be relevant to the integration of bodily signals with ongoing conscious and unconscious mental processes at high levels of the central nervous system (Quadt et al., 2018). Their integration, in fact, differs according to cognitive-emotional states (Gentsch et al., 2019; Kritzman et al., 2022) and traits (Judah et al., 2018; Zhou et al., 2022), and interoceptive information is conveyed to a few brain structures displaying hypnotizability-related morpho-functional differences, i.e., insula, cingulate cortex and cerebellum (Landry et al., 2017; Picerni et al., 2019). Moreover, the highs' sensitivity to interoceptive signals - the self-reported mode of interpretation of bodily signals - is different and more "adaptive" than in lows and mediums, indicating a good relationship with the body and a tendency to positively interpret bodily signals (Diolaiuti et al., 2020). In contrast, the interoceptive accuracy - the ability to detect bodily

signals -, which can be tested using the heartbeats count, is lower in highs than in lows, although only during the first of three heartbeats count trials (Rosati et al, 2021).

The results of heartbeat count have been associated with the amplitude of the cortical potential evoked by heartbeat (HEP) which has been related to cardiac afferents, despite the presence of some non-interoceptive information (Desmedt et al., 2018). It is obtained by averaging electrophysiological signals (such as the EEG and MEG) synchronized to R-peaks or T-peaks of a simultaneously recorded ECG signal (Park & Blanke, 2019b). In contrast to exteroceptive cortical potentials, the HEP amplitude increases during deep sleep (N3) with respect to light sleep, and is like N2 during REM sleep (Lechinger et al., 2015), thus overcoming the effect of the thalamic gate during N3 and of the disrupted brain activity during REM. The amplitude of the HEP earlier component, which reflects cardiac interoceptive accuracy (200-350 ms), has been associated with heartbeat counting scores, although not unanimously (Park & Blanke, 2019b), and is more pronounced at the medial-right fronto-central sites. The amplitude of the later component (400-600 msec) is related to the proneness to not worry about body sensations, to stress-induced changes in cardiac output, emotional arousal, dysregulation of emotions and some clinical disorders (Baranauskas et al., 2021; Luft & Bhattacharya, 2015).

Since the heartbeat count indicated lower interoceptive accuracy in highs than in lows (Rosati et al., 2021), the aim of the present study was to assess whether this finding is supported by differences in the HEP amplitude, and whether the HEP amplitude changes during neutral hypnosis in highs and lows differentially.

Methods

Subjects

A priori power analysis performed by G*Power3.1 (Faul et al., 2009) for repeated measures ANOVA indicated that for the expected $\eta^2 = 0.3$ (Pollatos et al., 2005) and $\alpha = .05$ the sample size of 16 participants for each group would be enough to achieve power = 0.89. After the approval by the Bioethics Committee of the University of Pisa (n.17/2021), participants of both sexes were recruited among the right-handed (Edinburgh Handedness Inventory, score> 16) students at the University of Pisa who had undergone hypnotic assessment through the Italian version of the Stanford Hypnotic Susceptibility Scale, form A (SHSS, A (range: 0-12), Weitzenhoffer & Hilgard, 1959,) in the latest 6 months. Details regarding hypnotizability SHSS scales are available in Sheehan and McConkey (1981). After their written informed consent, 16 highs (SHSS score (mean + sd): 10.18 + 1.19; 9 females, age: 25.14+ 3.82 yrs) and 16 lows (SHSS score: 0.20 + .56; 7 females, age: 26.47 + 4.82 yrs) with medical, neurological and psychiatric negative anamnesis, no attention /sleep disturbance and drugs intake in the latest 6 months were enrolled. The final group was composed of 16 highs and 15 lows because one of the male lows was excluded from analyses owing to technical problems in the ECG recording. The two groups were homogeneous for education (master's students). Six highs and 3 lows reported basic experience of meditation. Medium hypnotizable individuals (mediums) were not enrolled to maximize the effects of hypnotizability on the studied variables during hypnosis (De Pascalis et al., 2000; Elkins et al., 2015).

Experimental procedure

The experimental sessions took place in the afternoon, between 3 and 5 p.m., at least 3 hours after the last meal and caffeine containing beverages intake, in a sound and light attenuated, temperature controlled (22°C) room. Alcohol consumption was prohibited during the preceding 24 hours. On the day of the experimental session, all participants completed the Tellegen Absorption Scale (TAS, Tellegen & Atkinson, 1974; Tellegen, 1981) whose score indicates the proneness to be deeply absorbed in mental activities (range: 1-34). They were also interviewed about the last night sleep satisfaction (range: 0-10) and were invited to sit in an armchair with their head, legs and arms supported, and prepared for EEG recording. Finally, they were informed that every instruction will be given to them by the same experimenter sitting nearby and that at a certain point they will have to listen to a pre-recorded voice (SHSS, A induction modified owing to the direct request to close eyes in R). The experimental session consisted of open eyes baseline (B, 3 min), closed eyes relaxation (R, 3 min), hypnotic induction modified from the SHSS, A (IND, divided into IND1 and IND2, 3 min each), neutral hypnosis (NH, 3 min), Post (post hypnosis, 3 min). At the end of the session participants were invited

to score the degree of change in the state of consciousness experienced during the session (range: 0-10). None of the participants showed EEG sleep episodes.

Signal acquisition and analysis

A telemetric Nautilus EEG system (g.tec, Schiedlberg) was used to acquire ECG and EEG signals according to a modified International 10-20 System. In details, leads were placed in F3, F7, C3, T7, P3, PO3, F4, F8, C4, T8, P4, PO4, Fz, Cz, Pz, Oz positions and referred to Cz. Two additional electrodes were placed on the skin near lateral cantus of left eye and in correspondence of left orbital ridge to detect eye movements. Another electrode, referred to Cz, was placed in proximity of left shoulder for ECG signal. All impedances were kept below 5 kΩ.

The ECG signal was analyzed with Kubios HRV (Tarvainen et al., 2014). First, the RR series were extracted from the ECG using the well-known Pan-Tompkins algorithm (Pan & Tompkins, 1985) and a cubic spline interpolation method was used to correct algorithm-related peak-detection artefacts. The obtained RR series were then resampled to 4Hz to derive the HRV signal (Malik, 1996). Starting from the HRV, we extracted several features in the frequency and time domain. Specifically, we computed the mean RR interval duration (RR, ms), the total RR variability (SD) the square root of the mean squared differences of successive normal-to-normal (NN) intervals (RMSSD), the power expressed as a percentage of total power in the low-frequency (LF, 0.04–0.15 Hz) and high frequency (HF, 0.15–0.40 Hz) ranges, the ratio of LF to HF power (LF/HF ratio). R peaks markers were saved for subsequent HEP analysis.

EEG signals were analyzed using EEGLAB (Delorme & Makeig, 2004) and MATLAB 2020b (The Mathworks, Inc., 2020) custom scripts. All EEG signals were downsampled to a sampling frequency of 125Hz after applying a proper low-pass anti-aliasing filter. Then, a high-pass filter of 0.1Hz was applied. Bad channels were removed through a semi-automatic procedure. First, the channels whose correlation coefficient with their neighbors was lower than a predefined threshold were discarded (here set to 0.8) (Mullen et al., 2013). Then, an expert visually inspected the data to eventually identify and remove those bad channels not captured by the correlation criterion. Afterwards, removed channels were recovered using a spline-spherical interpolation method. The obtained signals were re-referenced to the numeric average of all channels before undergoing to independent component analysis (ICA) (Makeig et al., 1995). ICA decomposes the signals into sets of maximally statistically independent components that represent both brain sources and different type of artefacts (e.g., muscular, ocular) (Onton et al., 2006). Artefact-related ICs were identified through visual inspection of their maps, spectra and time-course (Delorme et al., 2012). Each independent component was additionally described through its associated equivalent current dipole (Oostenveld, 2011). Finally, the EEG signals were reconstructed without the contribution of artefact-related ICs (i.e, ocular, muscular, cardiac, channel noise and other sources of artefacts). The HEP amplitude was obtained by averaging the EEG signals synchronized the R-peaks previously obtained with Kubios (Tarvainen et al., 2014). More specifically, we extracted EEG epochs from -200 ms to 600 ms around each R-peak followed by subtractive baseline correction estimated in 200ms preceding the R-peak. The epochs contaminated by abrupt signal changes in the ECG or EEG signal were also discarded from the analysis. At the end of this procedure, we obtained a collection of EEG epochs for each condition for each subject (% of retained epochs $> 95\%$).

Variables

Self-reports: TAS scores, last night sleep satisfaction, experienced change in the state of consciousness; *ECG* : RR, SD, RMSSD, LF/HF; *EEG* : point-by-point HEP amplitude across the 200-600 ms time interval following the R peak of ECG.

Statistical analysis

Kolmogorov-Smirnov test was used to study the variables distribution. Then, 1) self-reports were analyzed through separate univariate ANOVAs between highs and lows; 2) RR, SD, RMSSD and LF/HF were analyzed by repeated measures ANOVAs with a 2 groups (highs, lows) x 6 Conditions (B, R, IND1, IND2, NH, P) design. Bonferroni correction was applied for multiple comparisons; 3) the HEP amplitude was

analyzed through repeated measures ANOVA with hypnotizability (highs, lows) as between subject factor and Condition (B, R, IND1, IND2, NH, Post) as within-subject factor, using the Factorial Mass Univariate Toolbox (Fields & Kuperberg, 2020). Particularly, we used a permutation-bootstrap approach with 2000 permutations to test for significant condition, group and interaction effects. The analysis was performed for each time-point in (200, 600) ms time interval. The time interval from 0 to 200 ms was excluded from analysis because of the potential presence of residual cardiac artefacts on EEG signals. Multiple hypothesis testing was controlled with the cluster correction method (Oostevenld et al., 2011). Post hoc analyses were carried out by means of paired t-tests for condition main effect, unpaired t-test for group main effect, and by means of paired t-tests (for within factor) and unpaired t-tests (for between factor) for interaction main effect. All tests were carried out with significance level set at $\alpha = .05$.

Results

Self-reports

TAS scores were significantly higher (F (1, 25) = 5.547, p= .027, η^2 = .188, α = .618) in highs (mean +sd; 22.82 + 7.86) than in lows (14.20 + 7.16). The experience of change ([?]) in the state of consciousness was significantly more intense (F (1, 25) = 67.27, p = .0001, η^2= .714, α = 1.00) in highs ([?]: 6.90 + 1.17) than in lows ([?]:1.57 + 2.21).The last night sleep satisfaction was not different between highs (mean + sd; 7.34 + 1.35) and lows (7.03 + 2.15).

ECG

None of the variables exhibited significant Group and Condition effects and interactions. RR and LF/HF mean values are illustrated in Fig 1a, b. The SD mean value was 0.52 + 0.05 (mean + SD) sec, the RMSSD mean value was 0.04 + 0.03 sec^2.

Figure 1

RR duration and LF/HF (mean, SEM). B, baseline; R closed eyes relaxation; IND1 and IND2, earlier and later 3 minutes of hypnotic induction; NH, neutral hypnosis; Post, open eyes baseline. Blue, highs; brown, lows

Hosted file

`image1.emf` available at https://authorea.com/users/577186/articles/619682-modulation-of-the-heartbeat-evoked-cortical-potential-by-hypnotizability-and-hypnosis

EEG

HEP amplitude. Upward and downward directed HEP indicates positive and negative brain potentials, respectively (Fig. a Suppl El Mat).

Highs and lows exhibited similar HEP's amplitudes (Fig. 2, averaged conditions) all over the brain - with the highs' HEP sometimes slightly more positive than lows' - except for the right parietal site (P4). At this site (Table a Suppl El Mat), a significant Group effect (p< .045) was observed in a time-window ranging from 256 ms to 312 ms, with a significantly lower HEP amplitude in highs than in lows (Table b Suppl El Mat) in B, R, IND1, Post. Moreover, quasi significantly lower values were observed in highs with respect to lows in the time intervals from 424 to 488 ms (p = .053) and from 536 ms to 592 ms, as illustrated in Fig 3a.

Figure 2

HEP amplitude (averaged conditions). Frontal (upper panels), central (middle panels) and parietal (lower panels) HEP. For statistics, see text

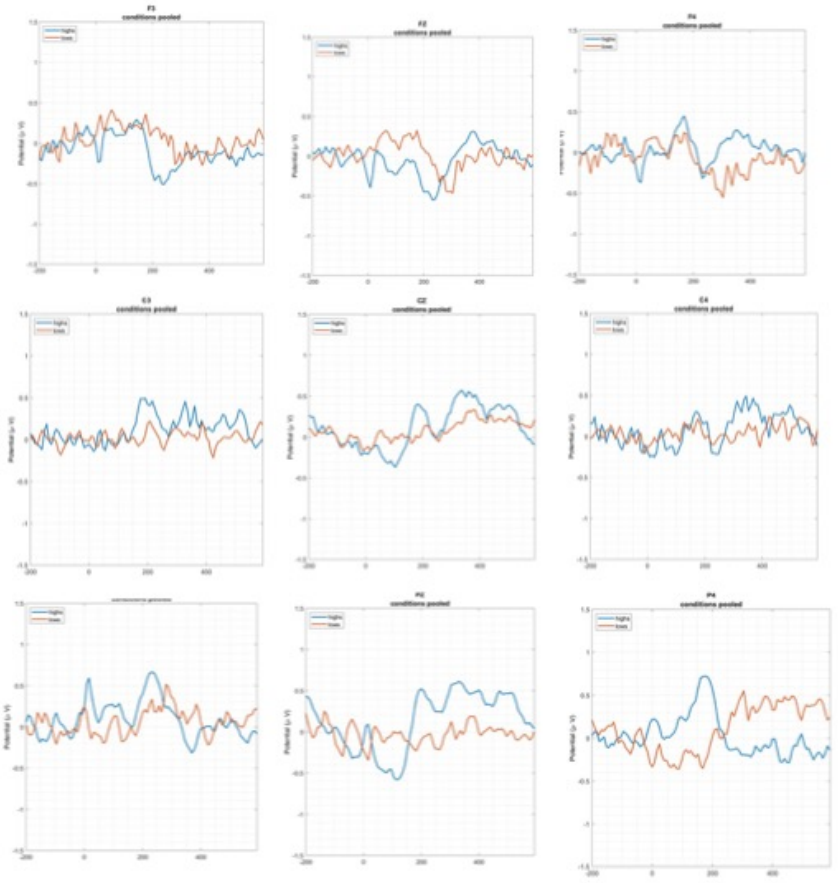
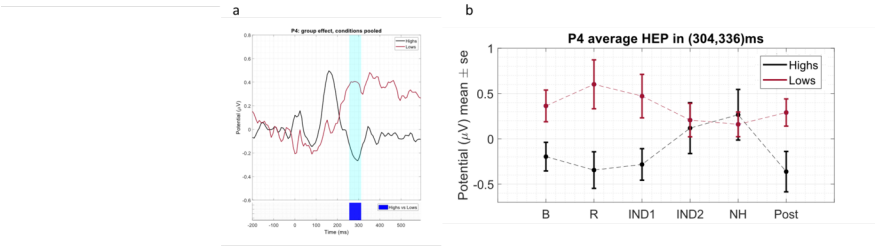


Figure 3

Group effect and Condition x Group interaction at P4. a) For each group, the conditions-pooled HEP amplitude is reported (left panel). The vertical area highlighted in cyan corresponds to the time points in which there was a significant main effect for the group ($p < 0.05$, cluster corrected). b) HEP amplitude (mean ± standard error). Group x Condition interaction at P4 for the time-points in the (304, 336) ms range.



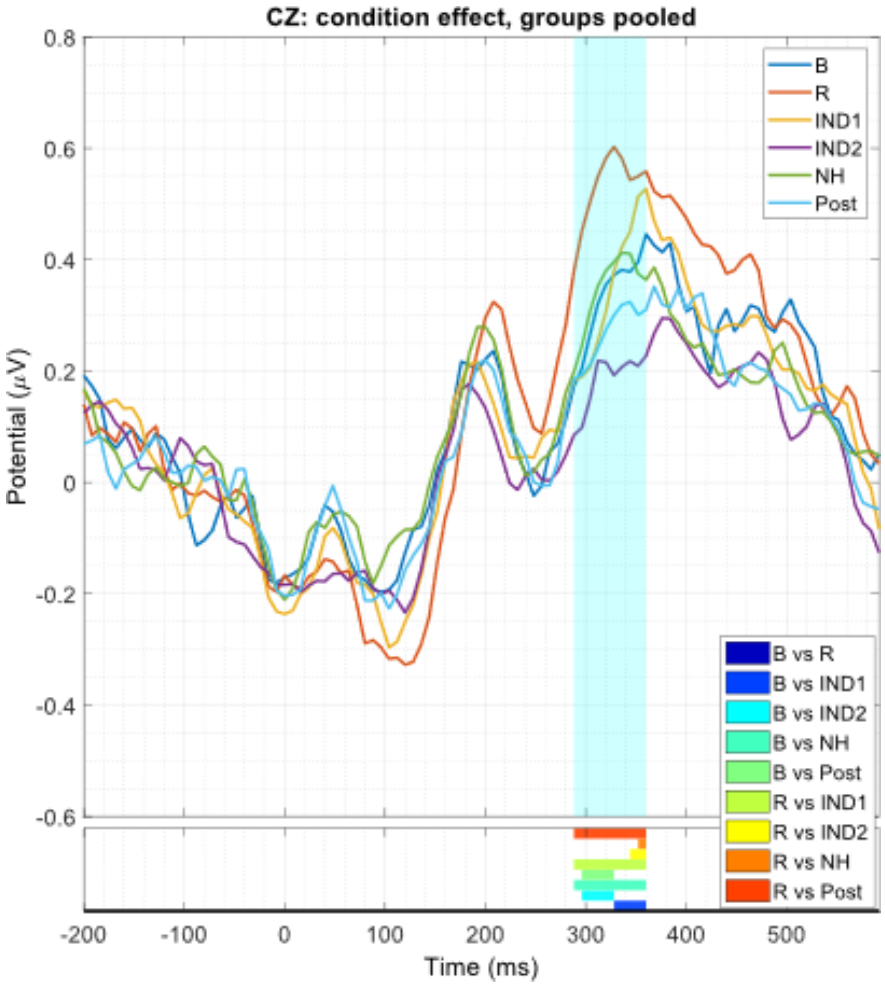
At P4 (Fig. 3b) we also observed a significant Group x Condition interaction ($p < .049$) in the time-range covering from 304 ms to 336 ms (Table a Suppl El Mat). Its decomposition revealed significant differences between conditions (Table c Suppl El Mat) in highs (NH vs R and Post) who increased their HEP amplitude, and in lows (Post vs R and IND1), who decreased it.

Moreover, we observed a significant Condition effect ($p< .004$) regarding both groups (Fig. 4, Table a Suppl

El Mat) at Cz (Fig. 4) in a time-window ranging from 288 ms to 360 ms after R-peak. The most extreme differences between the HEPs were between the R and the IND2 conditions, with R exhibiting the higher values of HEP and IND2 the lower ones. Among the other conditions, NH significantly differed from R (288-346) ms range and from B (352-360) ms range. Interestingly, the first and the second halves of the induction (IND1 and IND2) differed from B in different time windows: i.e., (296-320) ms for IND1 and (328-353) ms for IND2.

Figure 4

For each condition, the group-pooled HEP is reported (right panel). The vertical area highlighted in cyan corresponds to the time points in which there was a significant main effect for the condition ($p < 0.05$, cluster corrected). Post-hoc comparisons for which we observed a significant effect are reported below the results of the ANOVA and highlighted in different colors for each comparison)



Discussion

Interoception represents one of the most important information conveyed to the cerebral cortex, as it also influences somatosensory perception and its neural correlates (Al et al., 2020). The present study was aimed at investigating the relation between the HEP amplitude, considered an index of interoceptive accuracy, hypnotizability, which is associated with variations of interoceptive brain regions (Landry et al., 2017), and the state of consciousness, which changes during hypnosis in highs, but not in lows (Elkins, et al., 2015;

Pekala et al., 2017). Interoceptive signals (and thus, the HEP), in fact, are influenced by the state of consciousness differently from exteroceptive information (Baranauskas et al., 2021), and during wakefulness highs display lower interoceptive accuracy than lows, according to the heartbeat counting task.

In the present study, self-reports indicate that hypnotizability-related differences were not biased by sleepiness, and that only highs experienced a change in their state of consciousness, possibly facilitated by their greater attentional abilities enabling them to be deeply absorbed in the induction procedure.

ECG

No significant difference was observed in the autonomic state between groups and within conditions. Seemingly different findings with respect to other studies can be accounted for by differences in the experimental design. The absence of significant differences between groups in the closed eyes awake condition (R) lasting 3 minutes accords with the observation that significant differences between highs and lows appear during longer-lasting relaxation (15 minutes) (Santarcangelo et al., 2012). Moreover, a decrease in the absolute LF power and an increase in the absolute HF power have been observed during a 20 minutes neutral hypnosis, with consequent reduction of the LF/HF ratio (Santarcangelo et al., 1992). Finally, in other studies (De Benedittis et al., 1994), decreasing normalized LF and increased normalized HF have been observed during the second 10 minutes of a 20 minutes neutral hypnosis including imaginative suggestions promoting relaxation.

EEG

The absence of relevant group differences in the autonomic state allows to exclude that the HEP amplitude was influenced in highs and lows differentially, although the modulation of heart rate and heart rate variability is not necessarily associated with HEP modulation (Park & Blanke, 2019b).

No significant group difference in the HEP amplitude was observed all over the scalp except for the right parietal site (P4). Earlier findings in the general population (Baranauskas et al., 2021; Luft & Bhattacharya, 2015) indicate that the right hemisphere is more involved than the left one in the heartbeat detection task (Katkin & Reed, 1988). The highs' lower HEP amplitude at P4, with respect to lows, accords with their lower performance at the heartbeat detection test (Rosati et al., 2021). In this respect, a limitation of the study is the absence of medium hypnotizable participants, which prevents to associate the high or low hypnotizability with the performance of the general population (Jensen et al., 2017). The significant difference between highs' and lows' HEP observed in correspondence of sensori-motor areas (P4) is produced by negative and positive potentials in highs and lows, respectively. A possible interpretation of this finding, based on the bilateral connections of the posterior insula with the parietal cortex (Dionisio et al., 2019) is that the activation of the highs' right parietal cortex by insular volleys may be reduced by a diminished contribution of the left insula. The grey matter volume (GMV) of the left posterior (Huber et al., 2014) or entire insula (Picerni et al., 2019), in fact, is negatively correlated with hypnotizability.

The increase in the HEP amplitude occurring at P4 in highs during hypnosis supports the view of hypnosis as a state of consciousness associated with enhanced attention to internal signals (Demertzi et al., 2015). In the general population, indeed, the HEP is higher during interoceptive than exteroceptive attention (Petzschner et al., 2019). The same mechanism could be involved in the maintenance of HEP amplitudes during REM sleep in the general population (Baranauskas et al., 2021). On the other hand, disengagement from environmental information during hypnosis (Kramer et al., 2014) could be responsible for larger interoceptive representation (Luft & Bhattacharya, 2015). The lows, in contrast, might decrease their HEP amplitude during the session owing to distraction due to their low absorption abilities.

The absence of significant difference in the HEP amplitude between the second part of the hypnotic induction (IND2) and neutral hypnosis can be due to the highs' spontaneously entering the hypnotic state even independently from induction procedures. Unfortunately, an objective, discriminant index of hypnosis is not available yet.

The HEP amplitude at midline Cz (Condition effect) was lower during neutral hypnosis than in baseline

and relaxation independently from the group. Cz roughly corresponds to the dorsal anterior cingulus which is deactivated during hypnosis (Deeley et al., 2012; Demertzi et al., 2011; Jiang et al., 2017; McGeown et al., 2009). Thus, in highs the HEP reduction could be accounted for by reduced excitability of this region. In lows, who did not experience hypnosis, the HEP decrease could be accounted for by reduced arousal due relaxation. In this respect a limitation of the study is that the experience of relaxation was not scored.

Limitations and conclusions

Although moderate to large effects of attention and arousal on the HEP, and a moderate association between HEP amplitude and the heartbeats count have been observed (Coll et al., 2021), a limitation of the present study is that the HEP amplitude could not be correlated with the performance at the heartbeats counting task. This latter was not performed to prevent the effects of hypnotizability-related attentional abilities on the HEP amplitude (Raz, 2005). In summary, in highs, who display lower behaviorally assessed interoceptive accuracy than lows (Rosati et al., 2021), the HEP amplitude at parietal sites receiving insular information is lower than in lows. It increases in highs during hypnosis, which is associated with pre-eminent internally directed attention (Demertzi et al., 2015) and reduced activity of the anterior cingulate cortex (Deeley et al., 2012; Demertzi et al., 2011; Jiang et al., 2017; McGeown et al., 2009). In contrast, lows decrease their HEP amplitude possibly due to disengagement from the hypnosis task.

The reported findings provide further support to the view that hypnotizability is relevant to general aspects of life rather than merely to the proneness to accept suggestions (Diolaiuti et al., 2020; Ibanez.Marcelo et al., 2019; Santarcangelo & Carli 2021; Santarcangelo et al., 2016; Spina et al., 2020). Interoception, in fact, influences exteroceptive perception, contributes to self-consciousness, which includes bodily awareness, ownership and the experience of self as a global unity stable in time (Park & Blanke, 2019a), and could influence emotional experience and behavior (Parrinello et al., 2022).

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Figure legend

Fig.1. RR duration and LF/HF (mean, SEM). B, baseline; R closed eyes relaxation; IND1 and IND2, earlier and later 3 minutes of hypnotic induction; NH, neutral hypnosis; Post, open eyes baseline . Blue, highs; brown, lows

Fig 2 . HEP amplitude (averaged conditions). Frontal (upper panels), central (middle panels) and parietal (lower panels) HEP. For statistics, see text

Fig. 3 . Group effect and Condition x Group interaction at P4. a) For each group, the conditions-pooled HEP amplitude is reported (left panel). The vertical area highlighted in cyan corresponds to the time points in which there was a significant main effect for the group ($p < 0.05$, cluster corrected). b) HEP amplitude (mean $\pm$ standard error). Group x Condition interaction at P4 for the time-points in the (304, 336) ms range.

Fig. 4. For each condition, the group-pooled HEP is reported (right panel). The vertical area highlighted in cyan corresponds to the time points in which there was a significant main effect for the condition ($p < 0.05$, cluster corrected). Post-hoc comparisons for which we observed a significant effect are reported below the results of the ANOVA and highlighted in different colors for each comparison)

Fig a Suppl El Mat. HEPs during all conditions at frontal, Central and parietal sites.