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Subjects' hypnotizability level affects somatosensory evoked potentials to non-painful and painful stimuli

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HIGHLIGHTS

- We test the relationship between hypnotizability and SEPs to non-painful and painful stimuli.
- N1–P2 complex was lower in high than low hypnotizability group.
- Subjects' hypnotizability level affects SEPs to non-painful and painful stimuli.

ABSTRACT

Objective: We evaluated the working hypothesis that the EEG activity associated to non-painful and painful stimuli in condition of waking state (no hypnotic procedure) was related to the hypnotizability level.
Methods: Hypnotizability level was measured in 16 healthy subjects through the Italian version of the Stanford Hypnotic Susceptibility Scale (SHSS, score: 0–12). EEG data (56 electrodes) were recorded during non-painful and painful electrical stimuli applied to the left index finger. Cortical activity (vertex N1–P2 complex) was compared in subjects with low hypnotizability level (N = 8, SHSS:0–6) vs. subjects with high hypnotizability level (N = 8, SHSS:7–12).
Results: The amplitude of the N1–P2 complex was lower in the High-hypnotizability compared to the Low-hypnotizability group over primary sensorimotor cortex (C3 and C4 electrodes) and centro-parietal midline areas (Cz and Pz electrodes) for non-painful and painful stimuli. The SHSS showed a statistically significant negative correlation with the vertex N1–P2 complex at C3 and Cz ($r = -0.5$, $p < 0.05$) electrodes for non-painful stimuli.
Conclusion: Compared to the Low-hypnotizability subjects, High-hypnotizability subjects showed a reduced cortical activity related to non-painful and painful stimuli.
Significance: The results suggest a relationship between hypnotizability and cortical activity related to non-painful and painful stimuli in the condition of waking state (no hypnotic effect).

1. Introduction

The level of hypnotizability is a stable personality trait that has high test–retest reliability (Piccione et al., 1989; Kumar et al., 1996). It has been shown that the level of hypnotizability varied greatly in healthy individuals (Gibson, 1988; Dixon et al., 1990) and correlated with attentional abilities, vividness of imagery, fantasy proneness, creativity, and emotionality (Crawford, 1989; Crowson et al., 1991; Crawford et al., 1993, 1995; Gruzelier, 2002). Furthermore, level of hypnotizability has important implications to predict the positive response to a range of psychological therapies (Gruzelier, 2002; Spiegel, 2007; Kirenskaya et al., 2011).

Several studied have shown that electroencephalography (EEG) is a viable approach to understand the relationship between cortical activity and hypnotizability. EEG techniques analyzed the data in frequency and time domains. For the frequency domain, it has been reported that the theta power (4–8 Hz) was higher in subjects with high hypnotizability compared to subjects with low hypnotizability in both waking and hypnotic conditions (Sabourin et al., 1990; Crawford and Gruzelier, 1992; Crawford, 1994; Graffin et al., 1995; De Pascalis et al., 1998; De Pascalis, 1999; Williams

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and Gruzelier, 2001). Furthermore, conflicting results were found at gamma band (around 40 Hz; De Pascalis, 1999; De Pascalis et al., 1989, 1998; Ray and Bjick, 1997). Some studies reported an increase of gamma power in subjects with high hypnotizability compared to subjects with low hypnotizability (De Pascalis et al., 1998; Ray and Bjick, 1997). The opposite was found in another study (De Pascalis et al., 1989).

For the time domain analysis, event-related potentials (ERPs) studies have shown that compared to subjects with low hypnotizability, subjects with high hypnotizability are characterized, in both waking and hypnotic state, by a reduction of N100 (N = negativity, 100 = voltage peak at about 100 ms post-stimulus) and/or P300 (P = positivity, 300 = voltage peak at about 300 ms post-stimulus) components related to auditory (Crawford et al., 1996; Barabasz et al., 1999; Gruzelier et al., 2002), visual (Spiegel et al., 1985; Nordby et al., 1999; Barabasz et al., 1999; Jensen et al., 2001), and olfactory (Barabasz and Lonsdale, 1983; Spiegel and Barabasz, 1988) stimuli.

In the last years, several studies have investigated the relationship between hypnotizability and pain, a critical process for the survival of the organism, which allows for immediate awareness concerning potential injury. Hypnotic procedures were able to reduce pain perception under a variety of both chronic (i.e. cancer) and acute (i.e. painful medical procedures) conditions (Hilgard and Hilgard, 1994; Holroyd, 1996). Furthermore, compared to subjects with low hypnotizability, subjects with high hypnotizability have shown a stronger reduction of pain perception following hypnotic procedures (Hilgard and Hilgard, 1994; De Pascalis and Perrone, 1996; Holroyd, 1996; Chapman and Nakamura, 1998; Crawford et al., 1998; Milling et al., 2010). It has also been reported a decrease of late somatosensory ERP components in response to electrical or laser painful stimuli during hypnotic procedures compared to baseline condition (no hypnosis; Arendt-Nielsen et al., 1990; De Pascalis and Carboni, 1997; Crawford et al., 1998; De Pascalis, 1999; De Pascalis et al., 1998, 1999, 2008; Ray et al., 2002). In this regard, compared to baseline condition, hypnotic analgesia provoked a reduction of P300 peak related to a laser painful stimuli in healthy subjects (Arendt-Nielsen et al., 1990). Similarly, healthy subjects showed a decrease of P300 peak related to electrical painful stimuli during hypnotic suggestions of deep relaxation, dissociated imagery, focused analgesia compared to baseline condition (De Pascalis et al., 1999). Compared to subjects with mid and low hypnotizability, subjects with high hypnotizability showed a stronger reduction of P300 peak related to electrical painful stimuli during hypnotic analgesia compared to baseline condition (Ray et al., 2002; De Pascalis et al., 1999, 2008). Furthermore, compared to baseline condition, a hypnotic obstructive hallucination produced a reduction on electrical painful perception in parallel with reduction on P300 peak in healthy subjects with high hypnotizability (De Pascalis and Carboni, 1997). Finally, hypnotic analgesia induced a reduction of P200 and P300 peaks related to a electrical painful stimuli in subjects with chronic back pain (Crawford et al., 1998).

To contribute to the vivid debate on relationship among hypnotizability, pain, and cortical activity, the present study tested the hypothesis that somatosensory ERPs associated to electrical stimuli were related to the level of hypnotizability also in a simple waking state without hypnosis procedures. Compared to the previous studies, we evaluated two different levels of predictable electrical stimulation, i.e. non-painful (No-Pain) and moderately painful (Pain).

2. Methods

2.1. Subjects

Sixteen young (8 female) right-handed healthy volunteers participated to the present study. The mean subjects' age was 24.8 (±0.9 standard error, SE) years. For each subject, the hypnotizability level was measured through the Italian version of the Stanford Hypnotic Susceptibility Scale, form C (SHSS, score: 0–12; De Pascalis et al., 2000). The enrolled subjects were then subdivided in two sub-groups of 8 persons: subjects with low hypnotizability level (Low-hypnotizability, SHSS: 0–6, 3 female, mean subjects' age: 23.8 ± 1.2 SE) and subjects with high hypnotizability level (High-hypnotizability, SHSS:7–12, 5 female, mean subjects' age: 25.6 ± 1.3 SE). T-testing for independent population was computed to evaluate the presence or absence of statistically significant differences between the two sub-groups for age ($p < 0.05$). Furthermore, Fisher exact test was computed to evaluate the presence or absence of statistically significant differences between the two groups for gender ($p < 0.05$). No statistically significant difference was found (age: $p > 0.35$; gender: $p > 0.3$).

All subjects gave their written informed consent according to the Declaration of Helsinki and could freely request an interruption of the investigation at any time. The general procedures were approved by the local institutional ethics committee.

2.2. Experimental design

A sketch of the experimental design is shown in Fig. 1. Visual warning stimuli (red screen, duration 500 ms) were followed (2500 ms) by visual target stimuli (green screen, duration 200 ms) associated with an electrical stimulation at left index finger (forefinger). The interval between electrical stimulations of two subsequent trials was 10000 ms, a time period sufficient to make negligible the effects of habituation to stimulation and to reset the brain processes specifically related to such kind of stimulation (Bromm and Lorenz, 1998). The experimental design included two conditions: No-Pain and Pain. In the No-Pain, a non-painful electrical stimulation was applied, whereas in the Pain condition, a moderately painful electrical stimulation was applied. For both conditions, 100 trials were collected. Of note, the order of the two conditions was randomly changed across the subjects.

2.3. Electrical stimulation

In all conditions, the somatosensory stimulus consisted of a constant current monophasic pulse of 5 ms, which was intracutaneously applied to the tip of the left index finger (forefinger). This electrical stimulation was delivered at the beginning of visual

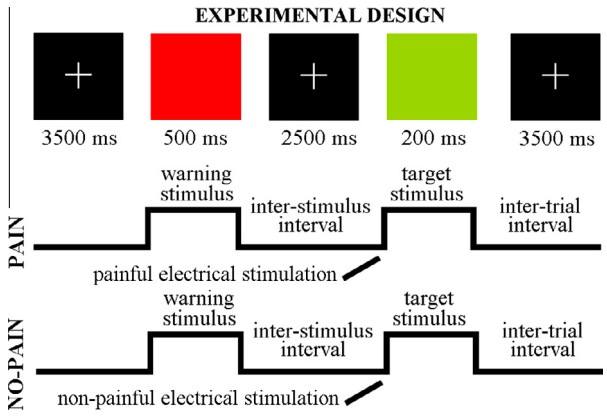

Fig. 1. Sketch of the experimental design. This design included two conditions, namely Pain, No-Pain. In all conditions, a visual warning stimulus (red screen, duration 500 ms) preceded the electrical (painful or non-painful) stimulation of 2500 ms. Immediately after the electrical stimulation, a visual target stimulus (green screen, duration 200 ms) appeared. The interval between electrical stimulations of two subsequent trials was 10 s. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

stimulus. After drilling a hole in the stratum corneum of the first phalanx of the left forefinger, a specially constructed electrode was inserted and fixed on the skin (Bromm and Meier, 1984; Bromm et al., 1989). This electrode was made of a gold pin (cathode) with a ring electrode (anode), and it did not interfere with the finger movement. A conductive bracelet located at wrist served as a ground.

Experimental design included two levels of predictable electrical stimulation, i.e. non-painful (No-Pain) and moderately painful (Pain). Non-painful and moderately painful stimuli were given in separate recordings blocks and subjects were told the level of the simulation at the beginning of each recording block. Therefore, they could reliably predict the kind of stimulation (i.e. painful, non-painful) across that recording block. The magnitude of the stimulation was determined by a series of increasing and decreasing stimulus intensities at the beginning of each recording block. In particular, the procedure was as follows. During the setting of the stimulus intensity, subjects had to rate verbally the stimulus magnitude by a numerical scale ranging from 0 (no sensation) to 10 (pain tolerance threshold). In this scale, the subjective evaluation was 1 for sensory threshold, 2 for strong sensory (just before of painful threshold), 3 for painful threshold, 4 for slight pain, 5 for intermediate pain, 6 for moderate pain, and so on up to 10. For the present experiments, the galvanic stimulation was delivered at level 2 (strong sensory but not painful) in the non-painful recording blocks and at level 6 (moderate pain) in the painful recording blocks. At the end of each block subjects verbally confirmed the subjective evaluation of the stimulus intensity across the blocks, by defining the control stimulation as "strong but non-painful" and the experimental stimulation as "painful". To minimize the effects of stress and fatigue, we could not test the effects due to different intensity levels in the range of non-painful stimuli (Backer et al., 1999).

2.4. EEG recordings

The EEG data were continuously recorded (bandpass: 0.01–100 Hz, sampling rate: 256 Hz; EB-Neuro Be-plus©, Firenze, Italy) from 56 scalp electrodes (cap) positioned over the whole scalp according to a 10–10 system. Fig. 2 shows the EEG electrode montage. The electrical reference was located between the AFz and Fz electrodes, and the ground electrode was located between the Pz and Oz electrodes. The electrode impedance was kept below 5 KOhm. Simultaneously, bipolar electro-oculographic data were recorded to monitor blinking and eye movements (EOG; bandpass: 0.1–100 Hz; sampling rate: 256 Hz).

2.5. Preliminary EEG data analysis

The EEG and EOG data were segmented into single trials of 8 s duration, each trial lasting from −5 to +3 s with respect to the reference time (i.e. onset of the target visual stimuli when the electrical stimulation was applied). Data epochs showing instrumental, ocular, and muscular artifacts were identified and automatically eliminated by a computerized procedure using EEG and EOG signals as input (Moretti et al., 2003). The EEG data affected by ocular artifacts were corrected with an autoregressive method (Moretti et al., 2003). Finally, two expert electroencephalographists (C.D.P and N.M.) manually confirmed the automatic selection and correction of the EEG single trials, with special attention to residual contamination of the EEG epochs due to eye movements and blinking. Therefore, only the EEG single trials totally free from artifacts were considered for the subsequent analyses. These EEG epochs were referred to common average reference for further analyses.

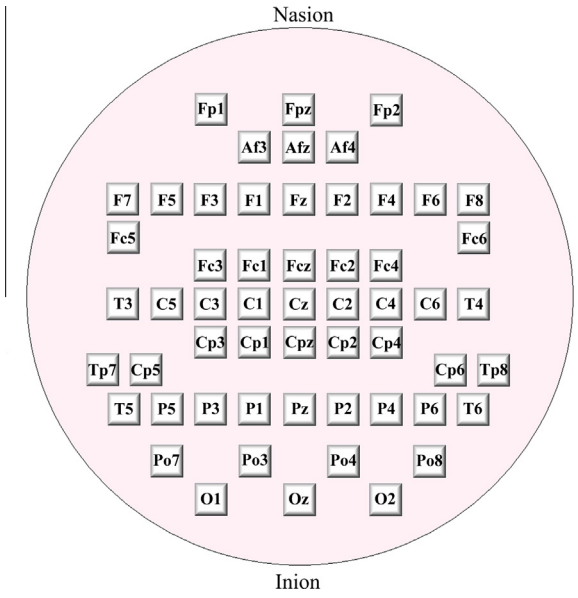

Fig. 2. Electroencephalographic (EEG) electrode montage.

For the Low-hypnotizability group, the mean number of the artifact-free EEG single trials was of 79 (±6 SE) for the No-Pain condition, and 78 (±5 SE) for the Pain condition. For the High-hypnotizability group, the mean number of the artifact-free EEG single trials was of 84 (±3 SE) for the No-Pain condition, and 81 (±6 SE) for the Pain condition. An ANOVA using the factors Group (Low-hypnotizability, High-hypnotizability) and Condition (Pain, No-Pain) served to compare the amount of artifact-free EEG single trials for the two groups and two conditions. No statistically significant difference was found ($p > 0.5$).

2.6. Somatosensory evoked potentials (SEPs)

For the two conditions (No-Pain, Pain), the artifact-free EEG single trials were averaged with respect to the onset of the target visual stimuli associated with electrical stimulation (zerotime), in order to generate two classes of somatosensory evoked potentials (SEPs). The first class was constituted by EEG single trials related to the painful electrical stimulation, while the second class was formed by EEG single trials related to the non-painful electrical stimulation. The component typically reflecting cortical responses at the electrical stimulation is the vertex N1–P2 complex (Chudler and Dong, 1983; Chen, 1993; Chen et al., 1998a,b; Bromm and Lorenz, 1998), defined as the amplitude difference between main negative (N1) and positive (P2) peaks. The amplitude of N1 and P2 peak was calculated with reference to a baseline taken in a pre-stimulus period from 1 s before to the warning stimulus. Firstly, to evaluate the latency of N1 and P2 peaks, the reference latency at Cz electrode was measured in line with our previous reference studies (Babiloni et al., 2001, 2004a,b, 2006, 2007, 2008) showing that vertex N1–P2 complex has central scalp distribution that is maximal at midline central scalp sites. The N1 peak latency was defined as the instant showing the maximum amplitude of the negative SEPs in the range from +100 to +150 at Cz electrode. The P2 peak latency was defined as the instant showing the maximum amplitude of the positive SEPs in the range from +150 to +250 at Cz electrode. Secondly, to analyze the spatial distribution of N1 and P2 peaks, the N1 and P2 peaks amplitude was automatically measured for each experimental condition at each of the 56 electrodes.

2.7. Topographic maps of the vertex N1–P2 complex

For illustrative purpose, the amplitude of the vertex N1–P2 complex in the Low-hypnotizability and High-hypnotizability groups was depicted as topographical voltage maps (256 hues) based on all electrodes of the montage. This was done for the two conditions (No-Pain, Pain).

2.8. Statistical analysis

The following three statistical sessions were performed.

The first session aimed at verifying the quality of the EEG experiments in that the amplitude of the vertex N1–P2 complex was expected higher in painful (Pain) than non-painful (No-Pain) stimulations. To this aim, the amplitude of the vertex N1–P2 complex from enrolled subjects was used as an input for an ANOVA design. Mauchley's test evaluated the sphericity assumption, and the correction of the degrees of freedom was made by Greenhouse–Geisser procedure. Duncan test was used for post hoc test comparisons ($p < 0.05$). The ANOVA used the factors Condition (No-Pain, Pain), and Electrode (Fz, C3, Cz, C4, Pz). Of note, the electrodes of interest were those roughly overlaying primary sensorimotor cortex of both sides (C3, C4) and midline areas (Fz, Cz, Pz). The working hypothesis would be confirmed by the following two statistical results: (i) a statistical ANOVA effect including the factor Condition ($p < 0.05$); (ii) a post hoc test indicating statistically significant differences of the vertex N1–P2 complex amplitude with the patterns Pain > No-Pain (Duncan test, $p < 0.05$).

The second session tested the working hypothesis that the cortical activity related to painful and/or non-painful stimuli was lower in High-hypnotizability compared to Low-hypnotizability subjects. To this aim, the amplitude of the vertex N1–P2 complex from High-hypnotizability and Low-hypnotizability subjects was used as an input for an ANOVA design using age and gender as covariates. The ANOVA used the factors Group (Low-hypnotizability, High-hypnotizability), Condition (No-Pain, Pain), and Electrode (Fz, C3, Cz, C4, Pz). The working hypothesis would be confirmed by the following two statistical results: (i) a statistical ANOVA effect including the factor Group ($p < 0.05$); (ii) a post hoc test indicating statistically significant differences of the vertex N1–P2 complex amplitude with the patterns High-hypnotizability < Low-hypnotizability (Duncan test, $p < 0.05$).

The third session tested the working hypothesis that the cortical activity related to painful and/or non-painful stimuli was related to hypnotizability level. To this aim, we performed a correlation analysis (Pearson test, $p < 0.05$) between the amplitude of the vertex N1–P2 complex and the Stanford Hypnotic Susceptibility Scale (SHSS) in all enrolled subjects as a single group. This correlation was computed for the two conditions (No-Pain, Pain) and for the five electrodes (Fz, C3, Cz, C4, Pz).

3. Results

3.1. Pain vs. No-Pain

Fig. 3 shows grand average waveforms (N = 16) of the SEPs computed from the electrodes of interest (Fz, C3, Cz, C4, Pz) in the non-painful (No-Pain) and painful (Pain) stimulations. The electrodes of interest were those roughly overlaying primary sensorimotor cortex of both sides (C3, C4) and midline areas (Fz, Cz, Pz). As a sign of data reliability, standard components of the SEPs were observed after the electrical stimulation, namely the vertex N1–P2 complex. This complex was more represented at scalp vertex (Cz electrode site; vertex potential). Furthermore, it was stronger in amplitude in the Pain compared to No-Pain conditions.

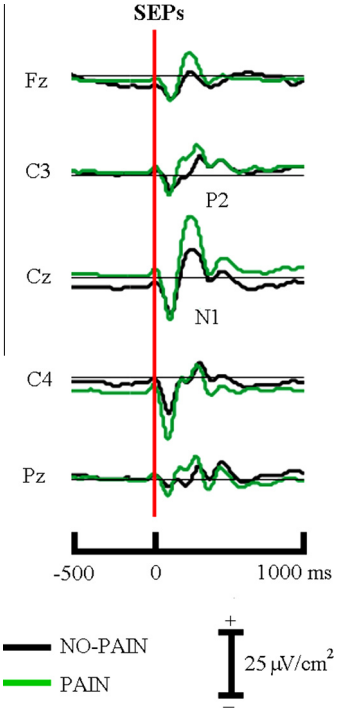

Fig. 3. Grand average waveforms (N = 16) of the somatosensory evoked potentials (SEPs) computed from the scalp electrode sites of interest (Fz, C3, Cz, C4, Pz) in the non-painful (No-Pain) and in the painful (Pain) electrical stimulation.

Table 1
Mean (±standard error, SE) of N1 and P2 peak latencies recorded at Cz electrode for No-Pain and Pain conditions.

Latency	No-pain	Pain
N1	108 (±8)	117 (±6)
P2	220 (±14)	202 (±10)

Table 1 reports the mean (±SE) of N1 and P2 peak latencies for No-Pain and Pain conditions. Furthermore, Fig. 4 shows the spatial distribution of the vertex N1–P2 complex for the No-Pain and Pain conditions. As expected, this complex was more represented at scalp vertex and was stronger for the Pain compared to No-Pain conditions.

The ANOVA for the evaluation of the quality of the EEG experiments (i.e. the amplitude of the vertex N1–P2 complex was expected higher in Pain than No-Pain conditions) showed a statistically significant interaction ($F(4,60) = 2.93$; $p < 0.02$; see Fig. 5) between the factors Condition (No-Pain, Pain) and Electrode (Fz, C3, Cz, C4, Pz). Duncan post hoc testing indicated that the amplitude of the vertex N1–P2 complex was higher in the Pain than in the No-Pain conditions at Fz ($p = 0.0003$), C3 ($p = 0.00008$), Cz ($p = 0.00003$), C4 ($p = 0.0002$), and Pz ($p = 0.00004$) electrodes. The present results confirmed the quality of our EEG experiment.

3.2. Low-hypnotizability vs. High-hypnotizability

Fig. 6 shows grand average waveforms (N = 8) of the SEPs computed from the electrodes of interest (Fz, C3, Cz, C4, Pz) in the non-painful (No-Pain) and painful (Pain) stimulations for Low-hypnotizability and High-hypnotizability groups. For both conditions (No-Pain, Pain), the amplitude of the vertex N1–P2 complex was lower in the High-hypnotizability compared to Low-hypnotizability subjects at C3, Cz, C4 and Pz electrodes.

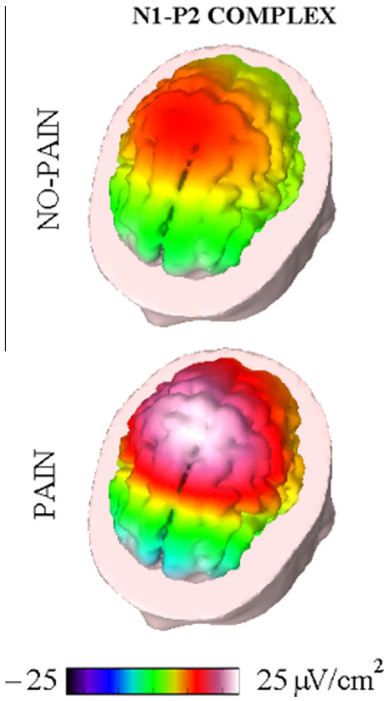

Fig. 4. Spatial distribution of the vertex N1–P2 complex for the No-Pain and Pain conditions. Color scale indicates voltage (μV) with 256 hues. The maximal voltage value of the vertex N1–P2 complex is reported under the maps.

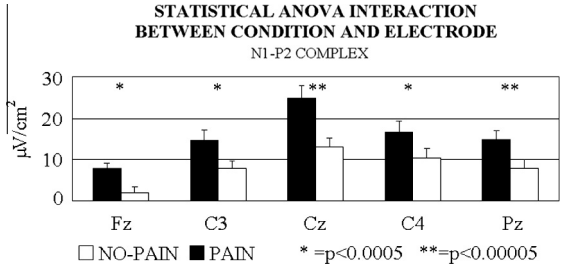

Fig. 5. Across subjects' means (±standard error, SE) of the N1–P2 complex amplitude illustrating a statistical ANOVA interaction between the factors condition (No-Pain, Pain), and electrode (Fz, C3, Cz, C4, Pz).

Table 2 reports the mean (±SE) of N1 and P2 peak latencies for No-Pain and Pain conditions in the Low-hypnotizability and High-hypnotizability groups. Furthermore, Fig. 7 shows the spatial distribution of the vertex N1–P2 complex for the No-Pain and Pain conditions in the Low-hypnotizability and in the High-hypnotizability subjects. This complex was lower in amplitude in the Low-hypnotizability compared to the High-hypnotizability subjects for both conditions (No-Pain, Pain).

The ANOVA for the evaluation of the first working hypothesis (i.e. amplitude difference of the vertex N1–P2 complex between Low-hypnotizability vs. High-hypnotizability groups) showed a statistically significant interaction ($F(4,56) = 2.64$; $p < 0.04$; see Fig. 8) between the factors Group (Low-hypnotizability, High-hypnotizability) and Electrode (Fz, C3, Cz, C4, Pz). Duncan post hoc testing indicated that regardless the factor Condition, the amplitude of the vertex N1–P2 complex was lower in the High-hypnotizability than in the Low-hypnotizability subjects at C3 ($p = 0.00007$), Cz ($p = 0.00003$), C4 ($p = 0.0003$), and Pz ($p = 0.01$) electrodes. The present results confirmed the working hypothesis of a decrease of cortical activity related to painful and/or non-painful stimuli in the High-hypnotizability compared to the Low-hypnotizability subjects.

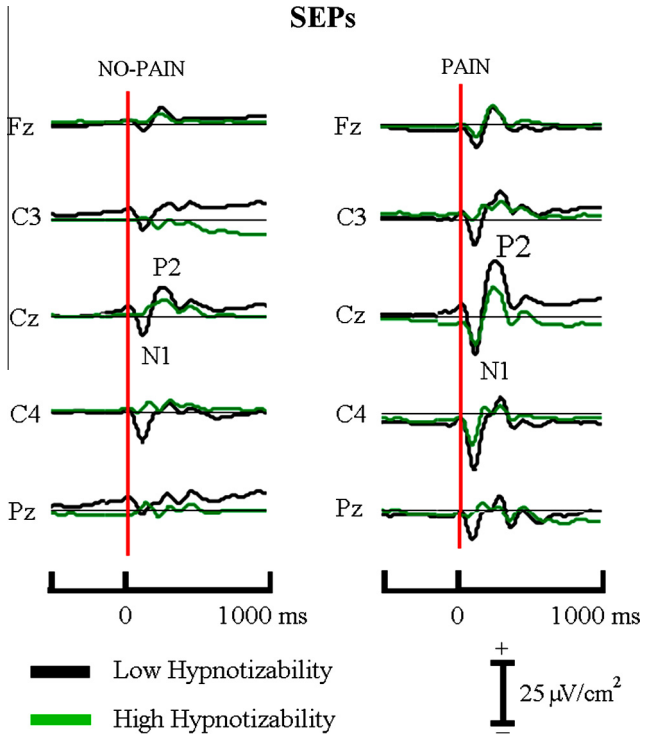

Fig. 6. Grand average waveforms (N = 16) of the SEPs computed from the scalp electrode sites of interest (Fz, C3, Cz, C4, Pz) for the No-Pain and Pain conditions in the Low-hypnotizability and in the High-hypnotizability group.

Table 2
Mean (±standard error, SE) of N1 and P2 peak latencies recorded at Cz for the Pain and No-Pain conditions in the Low-hypnotizability and in the High-hypnotizability group.

Latencies (ms)	Low-hypnotizability		High-hypnotizability	
	No-Pain	Pain	No-Pain	Pain
N1	112 (±4)	115 (±10)	104 (±16)	119 (±8)
P2	215 (±18)	200 (±12)	225 (±23)	204 (±18)

Finally, the amplitude of the vertex N1–P2 complex for the two conditions (No-Pain, Pain) and for the five electrodes (Fz, C3, Cz, C4, Pz) was correlated with the Stanford Hypnotic Susceptibility Scale (SHSS; Pearson test, $p < 0.05$). SHSS showed a statistically significant negative correlation with amplitude of the vertex N1–P2 complex at C3 ($r = -0.5$, $p = 0.04$) and Cz ($r = -0.5$, $p = 0.04$) electrodes only for No-Pain conditions (see Fig. 9).

4. Discussion

In the present study, we tested the hypothesis that EEG cortical activity associated to non-painful and painful stimuli was related to the level of hypnotizability in the condition of waking state (no hypnotic procedure). In particular, we verified that compared to subjects with low hypnotizability, subjects with high hypnotizability was characterized by an amplitude modulation of N1–P2 complex related to electrical non-painful and painful stimuli.

We report that N1–P2 complex was more represented at scalp vertex (Cz electrode site) and was stronger in the painful compared to the non-painful condition, in line with previous EEG evidence showing a typical negative-positive peak complex 100–300 ms following an electrical painful stimulus, which is typically highest in amplitude at scalp vertex (Chudler and Dong, 1983; Chen, 1993;

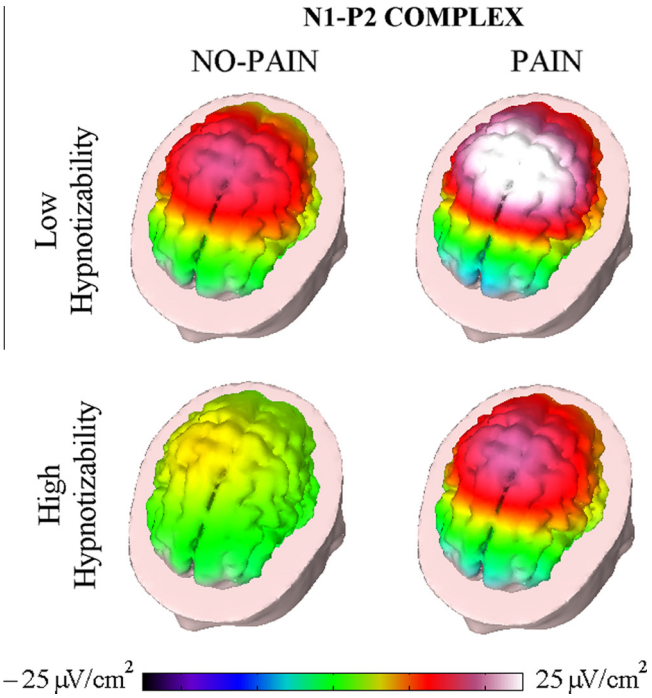

Fig. 7. Spatial distribution of the vertex N1–P2 complex for the No-Pain and Pain conditions in the Low-hypnotizability and High-hypnotizability groups. Color scale indicates voltage (μV) with 256 hues. The maximal voltage value of the vertex N1–P2 complex is reported under the maps.

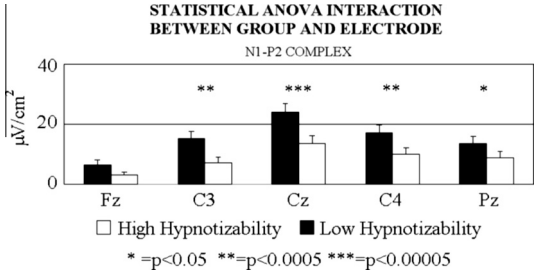

Fig. 8. Across subjects' means (±standard error, SE) of the vertex N1–P2 complex amplitude illustrating a statistical ANOVA interaction between the factors Group (Low-hypnotizability, High-hypnotizability), and electrode (Fz, C3, Cz, C4, Pz).

Chen et al., 1998a,b; Bromm and Lorenz, 1998). The specificity of this effect was suggested by the significant correlation among the vertex potential amplitude, pain magnitude, and analgesics administration ($p < 0.05$). The negative-positive peak complex would roughly model the event-related response of midfrontal and cingulate cortex, deeply involved in the attentional and affective aspects of the cortical information processing (Bromm and Lorenz, 1998; Chen et al., 1998b).

As original results of the present study, we found that N1–P2 complex related to both non-painful and painful stimuli in waking state was lower in amplitude in the subjects with high hypnotizability compared to the subjects with low hypnotizability. This was observed in a large scalp region overlying primary sensorimotor cortex of both hemispheres (C3 and C4 electrodes), as well as centro-parietal midline areas (Cz and Pz electrodes). Furthermore, the level of hypnotizability was negatively related to the amplitude of the N1–P2 complex overlying sensorimotor cortex of left hemisphere (C3 electrode) and central midline area (Cz electrode) only for non-painful stimuli. The present results suggest that in the condition of waking state, there was a reduced cortical activity related to both non-painful and painful stimuli in the subjects with high hypnotizability compared to those with high hypnotizability.

What is the relationship between hypnotizability and cortical activity related to both non-painful and painful stimuli? Human nociception is a multidimensional phenomenon involving separate sensory-discriminative, affective-motivational, and cognitive aspects, which would be subserved by a distributed brain system (Melzack and Casey, 1968; Coghill et al., 1994). Positron emission tomography has revealed that the major brain structures involved in tonic painful information processing are the contralateral insula, anterior cingulate cortex (ACC), the bilateral thalamus and premotor cortex, and the cerebellar vermis (Casey, 1999). Furthermore, the vertex N1–P2 complex is mostly generated by neurons in the anterior cingulate cortex (ACC) and is important for the emotional component of sensation (Bromm and Chen, 1995; Valeriani et al., 1996; Garcia-Larrea, 1998; Garcia-Larrea et al., 2003; Frot et al., 1999). The ACC is part of the limbic system and mainly modulates the affective- emotional component of pain perception (Derbyshire, 2000; Peyron et al., 2000). Therefore, it can be speculated that compared to the subjects with low hypnotizability, the subjects with high hypnotizability are characterized by a reduced activation of ACC areas during non-painful and painful stimuli.

The results of the present study are compatible with previous EEG findings showing that compared to subjects with low hypnotizability, subjects with high hypnotizability were characterized by a stronger reduction of late ERPs potentials related to a electrical or laser painful stimuli in hypnotic (i.e. hypnotic analgesia, hypnotic suggestions of deep relaxation, dissociated imagery, hypnotic obstructive hallucination) compared to waking condition (De Pascalis and Carboni, 1997; Crawford et al., 1998; De Pascalis, 1999; De Pascalis et al., 1998, 1999, 2008; Ray et al., 2002). Furthermore, the present findings extend previous evidence reporting

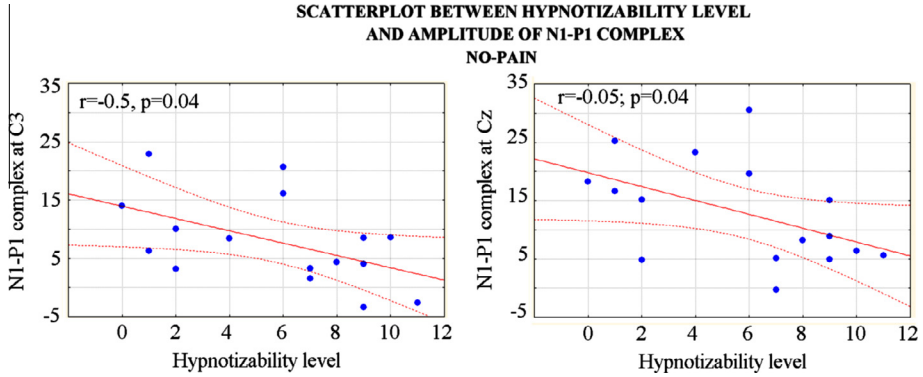

Fig. 9. Scatterplots showing the correlation between the amplitude of vertex N1–P2 complex and the Stanford Hypnotic Susceptibility Scale in all subjects as a single group. The *r*- and *p*-values in the diagram refer to Pearson correlation.

that compared to subjects with low hypnotizability, subjects with high hypnotizability present an amplitude reduction of ERPs components related to auditory, visual, and olfactory stimuli not only in hypnotic state but also in normal waking condition (Barabasz and Lonsdale, 1983; Spiegel et al., 1985; Spiegel and Barabasz, 1988; Crawford et al., 1996; Nordby et al., 1999; Barabasz et al., 1999; Jensen et al., 2001; Gruzelier et al., 2002).

In conclusion, here we tested that the EEG cortical activity associated to non-painful and painful stimuli was related to the level of hypnotizability in condition of waking state (no hypnotic procedure). Results showed that the amplitude of the N1–P2 complex was lower in the subjects with high hypnotizability compared to the subjects with low hypnotizability. This was true in a large scalp region overlying primary sensorimotor cortex of the two hemispheres (C3 and C4 electrodes) and centro-parietal midline (Cz and Pz electrodes) for both non-painful and painful conditions. Furthermore, the level of hypnotizability showed a statistically significant negative correlation with amplitude of the N1–P2 complex at C3 and Cz electrodes only for non-painful stimuli ($p < 0.05$). The present results suggest a relationship between hypnotizability and cortical activity related to both non-painful and painful stimuli in the condition of waking state (no hypnotic procedure).

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