Modulation of spectral power and of phase resetting of EEG contributes differentially to the generation of auditory event-related potentials

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Nowadays, the mechanisms involved in the genesis of event-related potentials (ERPs) are a matter of debate among neuroscientists. Specifically, the debate lies in whether ERPs arise due to the contribution of a fixed-polarity and fixed-latency superimposed neuronal activity to background electroencephalographic oscillations (evoked model) and/or due to a partial phase synchronization of the ongoing EEG (oscillatory model). The participation of the two mechanisms can be explored by the spectral power modulation and phase coherence of scalp EEG rhythms, respectively. However, an important limitation underlies their measurement: the fact that an added neural activity will be relatively phase-locked to stimulus, thus enhancing both spectral power and phase synchrony measures and making the contribution of each mechanism less clear-cut. This would not be relevant in the case that an increase in phase concentration was not accompanied by any concurrent spectral power modulation, thus opening the way to an oscillatory-based explanation.

We computed event-related spectral power modulations and phase coherence to an auditory repeated-stimulus presentation paradigm with tone intensity far from threshold (90 dB SPL), in which N1 decreases its amplitude (N1 gating) as an attenuation brain process. Our data indicate that evoked and oscillatory activity could contribute together to the non-attenuated N1, while N1 to repeated stimuli could be explained by partial phase concentration of scalp EEG activity without concurrent power increase. Therefore, our results show that both increased spectral power and partial phase resetting contribute differentially to different ERPs. Moreover, they show that certain ERPs could arise through reorganization of the phase of ongoing scalp EEG activity only.
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Introduction

Event-related potentials, ERPs, with their magnetic counterpart event-related fields, ERFs, are a useful and extended non-invasive window for the study of fast (sub-second time order) cerebral processes. ERPs involve searching for event-locked regularities of brain dynamics, averaging multiple time intervals that share the same experimental conditions and, thus, reducing trial-to-trial time-locked response variability.

However, in spite of the importance of the topic, at present, there is no consensus explanation of how electromagnetic event-locked brain activity occurs. At the poles of a controversy, two alternative theories are now competing as explanations of the genesis of ERPs. One is the classic view, also known as the evoked model, whereby the ERP arises as a fixed-polarity and fixed-latency superimposed neuronal contribution to the background electroencephalogram (EEG) (Hillyard, 1985; Vaughan and Arezzo, 1988; Schroeder et al., 1995; Mäkinen et al., 2004). The other view, known as the oscillatory model, argues that ERP reflects an event-locked increase in phase concentration of EEG ongoing oscillations (Sayers et al., 1974; Basar, 1980; Brandt et al., 1991; Makeig et al., 2002; Kruglikov and Schiff, 2003). Finally, recent theoretical studies (David et al., 2005) have proposed that ERP characteristics (phase resetting and power enhancement) could be a consequence of the level of activity of the neural networks involved in their generation.

However, as ERPs were habitually the result of averaging numerous event-locked EEG epochs, it is not feasible to find whether what constructed the ERPs was an evoked or an oscillatory mechanism, or a combination of the two (Penny et al., 2002). Therefore, in the search for the mechanisms of ERP production, recent research has applied time-frequency method analysis to single EEG epochs/trials before averaging them (Tallon-Baudry et al., 1996; Rodriguez et al., 1999; Yardonova and Kolev, 1998; Makeig et al., 2002).

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In single trials, time-frequency methods determine a super-imposed neural contribution in the latency range of the ERP by computing changes in the power spectrum in comparison with the pre-event activity (Makeig, 1993). In addition, an event-locked modification of the phase reorganization of EEG oscillations could be detected well by a transient change in inter-trial phase coherence (Makeig et al., 2002). However, current phase and spectral power measurements did not provide unambiguous evidence of evoked or oscillatory contribution to the ERP when concurrent modulation of the two mechanisms was involved (Yeung et al., 2004; Mäkinen et al., 2004). Thus, evoked responses would be relatively phase-locked to stimulus presentation, and so enhanced phase coherence measurements could be due (in some degree) to an evoked component (Klimesch, 1999). Nonetheless, in the absence of any spectral power contribution, the participation of the evoked mechanism in ERP generation can be clearly discarded, so opening the way to an oscillatory-based explanation (Makeig et al., 2004a).

Since it is usual to encounter modulation of both spectral power and phase coherence effects in most ERP trial-by-trial studies (Gruber et al., 2005; Klimesch et al., 2004), and given the limitations of available methods for unambiguously separating evoked and oscillatory contributions to ERPs, our proposal for surmounting these problems is to adopt another strategy based on examining the effects of the manipulation of the putative generation mechanisms of ERPs. This involves exploring the experimental conditions under which a parameter of the ERP (i.e. amplitude) could be modulated by the stimulation paradigm and thus enabling differential behavior in spectral power and phase coherency to a sole ERP variation to be observed.

Therefore, auditory tone stimuli, presented at a brief time interval, provide different ERPs with a physically identical incoming stimulus, with the second and subsequent responses showing less amplitude than the first response (Näätänen, 1992). This provides a useful experimental situation of amplitude modulation of an ERP response, also called "gating" (Boutros et al., 1999). This phenomenon was initially attributed to an inherent property of the generator cells in the auditory cortex (i.e. refractoriness). However, increasing evidence has appeared that N1 amplitude reduction could underlie more active behavior by the brain. This approach, described in the works of Loveless et al. (1989, 1996) and McEvoy et al. (1997), states that N1 attenuation implies an active inhibitory mechanism of those neural populations that respond to N1. Sable et al. (2004) posited that the first tone in each train would cause transient excitation of the N1 generators, resulting in a large N1, and that, later, these activations would spread to neurons that feedback on the N1 generators to inhibit them. Another study (Pantev et al., 2004) showed the implications of lateral inhibition in non-primary areas for the auditory N1 attenuation process. This study showed that reduced N1 amplitude was linked to inhibition mediated by lateral connections in non-primary auditory cortex. Nevertheless, N1 brain attenuation could not rule out the involvement of various neuronal populations not located in the auditory temporal areas, such as those in frontal areas. Thus, in Sable et al. (2004), it has been proposed that frontal lobe could participate in this feedback circuitry. In addition, it has been suggested that the lack of N1 suppression in disorders such as schizophrenia could underlie a deficit in this circuitry (Ford et al., 2001). In addition, pre-attentive sensory perception studies have suggested that, when two identical stimuli are presented in a short time interval, the amplitude of the N1 wave of auditory ERPs to the

second stimulus and the 2–8 Hz frequency contribution of phase coherence are both reduced (Jansen et al., 2003).

The aim of this study was to analyze changes in the involvement of event-locked spectral power and phase coherency of EEG rhythms in auditory N1 amplitude reduction with repeated stimulation. We searched for the possibility that evoked and oscillatory mechanisms behaved differently as a function of N1 amplitude parameter decrease, which would provide new insight into ERP genesis.

Materials and methods

Subjects

16 right-handed healthy subjects (23–30 years of age; seven female) participated in the study. Subjects had no history of head injury, neurological disease, audiological problems, severe medical illness or drug abuse. After complete description of the study to the subjects, their written informed consent was obtained. The experiment complied with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Stimuli and procedure

Pure sinusoidal tones were generated by a Neurosoft Sound program and delivered binaurally through headphones by the Stim Interface System (Neuroscan Inc). 4 blocks of 50 stimuli trains consisting of two types of auditory stimulus were presented to the subjects. Stimuli were a 75 ms (standard) and 25 ms (deviant) 1000 Hz sinusoidal tone burst, both 90 dB sound pressure level and 10 ms rise/fall. Stimulation trains had three tones (namely S1: first, S2: second and S3: third tone), with the first two always standard, while the third was randomly standard ($P = 0.5$) or deviant ($P = 0.5$). Intra-train interval was 584 ms and inter-train interval was 30 s. Participants sat in a comfortable chair in a dimly lit and electrically and acoustically shielded booth. During the EEG recording, each subject was instructed to perform an irrelevant visual task (reading) to ignore the auditory stimuli and to avoid extra eye movements and blinking.

Electrophysiological recording

EEG activity was recorded by a 32-channel Synamps amplifier (Neuroscan Inc). EEG data were recorded from 30 Ag–AgCl electrodes at the scalp, following the 10–20 position system (FP1, OZ, FP2, F7, F3, FZ, F4, F8, T3, C3, CZ, C4, T4, T5, P3, PZ, P4, T6) with 10 additional electrodes (FC1, FC2, FT3, FT4, M1, M2, IM1, IM2, TP3, TP4, CP1, CP2), with input impedance of <5 kΩ. An electrode attached to the tip of the nose served as a reference. Ocular movements (EOG) were recorded from two electrodes at the outer canthus of each eye. A single ground electrode was attached at AFz. Sample frequency was 500 Hz. EEG and EOG were amplified within a 0.1–70 Hz band-pass and notch-filtered at 50 Hz. In this study, only EEG activity from Fz, C3, Cz, C4 and Pz was analyzed.

Event-related potential data analysis

Only those stimuli trains containing three standard tones were analyzed in this study. Deviant stimuli responses will be

described elsewhere. ERPs were obtained off-line by averaging 3000 ms EEG epochs, which included 1000 ms pre-stimulus as a baseline period and S1, S2 and S3 responses. Epochs that exceeded ±100 μV in EEG and/or EOG were excluded automatically. No digital off-line band-pass filter was used for ERP extraction. A total of 1173 trials were obtained for the analysis, in which each subject contributed with 71 ± 17 trials (mean ± SEM).

Auditory N1 was identified as the largest negative component between the 80 and 180 ms time window of the ERPs to the three standard sounds. The P3 component was measured, after S1 response, as the most positive peak in the 250–450 ms time window range. In each case, the baseline-to-peak value was taken as the magnitude (μV) of the response.

One-way analysis of variance (ANOVA) was carried out on mean amplitude measurements of N1 ERP at all the electrode locations with respect to the pre-stimuli baseline (1000 ms). N1 reduction to repeated stimuli was assessed by the N1 amplitude decrease after repeated incoming stimuli. Repeated-measures ANOVA was calculated, in which the factors Electrode (Fz, C3, Cz, C4 and Pz) × Condition (N1 to S1, S2 or S3) to the N1 peak values were compared. P values were calculated by using the Greenhouse–Geisser correction when appropriate. Post hoc comparisons by Student's t test for paired samples were made to N1 peak values (S1, S2 and S3) within each electrode when the within-subject Condition factor was statistically significant.

Event-related spectral power modulation and inter-trial phase coherence analysis

Trial-by-trial event-related spectral power modulation and event-locked phase concentration of the EEG rhythms were studied by EEGLAB v4.5 toolbox (Delorme and Makeig, 2004) under Matlab v7.0 (Mathworks, Natick, MA). Trial-by-trial time-frequency analysis used Hanning-windowed sinusoidal wavelets, for which the cycle number linearly increases with frequency, from a minimum of 2 cycles for 3.9 Hz to 13 cycles for 48.8 Hz. Significance levels were computed by bootstrap distributions, extracted at random from baseline data epochs and applied 200 times.

Event-related spectral power changes were analyzed by the event-related spectral perturbation (ERSP) index (1),

$$ERSP(f,t) = \frac{1}{n} \sum_{k=1}^{n} (F_k(f,t))^2 \qquad (1)$$

where, for n trials, $F_k(f,t)$ is the spectral estimate of trial k at frequency f and time t. ERSP shows mean time-frequency points across the input epochs, where higher or lower spectral power differs from mean power during the 1000 ms pre-stimulus baseline period of the same epochs (Makeig, 1993). Event-locked phase concentration was computed by the event-related inter-trial coherence (ITC) index (2), analogous to the "phase-locking index" (Tallon-Baudry et al., 1996),

$$ITC(f,t) = \frac{1}{n} \left| \sum_{k=1}^{n} \frac{F_k(f,t)}{|F_k(f,t)|} \right| \qquad (2)$$

where $||$ represents the complex norm. ITC measures the consistency across trials of EEG spectral phase at each frequency

and latency window. ITC measurement takes values from 0 to 1, with values near to 1 meaning near-perfect EEG phase coherence across trials. Phase coherency significance was performed, as for ERSP, using the bootstrap comparison method extracted from random baseline data. Frequency-to-frequency mean ITC and ERSP were also plotted without bootstrap significance, leading to the observation of each ERSP and ITC frequency distribution without any significant restriction.

To find whether ERSP and ITC results obtained by the general trial-by-trial analysis could be affected by inter-individual variability in the ERPs, those frequencies that resulted significant in the previous analysis (general trial-by-trial analysis) were computed to each subject and electrode location. Subsequently, subject-to-subject and frequency-to-frequency ERSP and ITC peak values in the N1 latency range were compared to determine whether ITC and ERSP obtained after S1, S2 and S3 stimuli were significantly different from each other. The non-parametric Wilcoxon Matched-Pairs Signed-Rank test was used in this analysis to avoid false assumptions about data distribution.

Results

Event-related potentials

All tones (S1, S2 and S3) elicited significant N1 ERP to all electrode locations studied ($P < 0.001$). Fig. 1 depicts the grand average of ERP waveforms to each stimulus across 16 subjects at all electrodes analyzed.

N1 attenuation was measured by N1 decreased amplitude across each electrode ($F(2,15) = 105.9$, $P < 0.0001$) in which a main Electrode × Condition interaction effect was observed ($F(8,15) = 5.26$, $P < 0.001$). This suggested that decreased N1 amplitude was not equivalent at all electrode locations. Post hoc
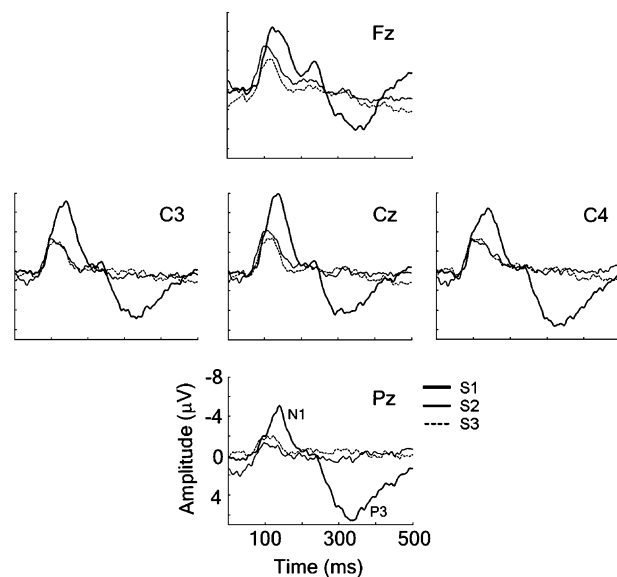

Fig. 1. The grand mean of ERPs in response to the first (S1), second (S2) and third stimulus (S3) at all electrodes analyzed allowed observation the lower N1 amplitude to S2 and S3 than to S1 response, due to repeated incoming stimulation. In addition, a prominent P3 component appeared after the S1 stimulus, but not after the S2 and S3 responses. Stimuli were delivered at 0 ms.

Table 1
Comparison between N1 S1, S2 and S3 peak amplitudes using Student's t test for paired samples (**$P < 0.001$, *$P < 0.01$)

($t(15)$ values)	Fz	C3	Cz	C4	Pz
S1 vs. S2	−6.09**	−5.99**	−5.11**	−5.07**	−6.09**
S1 vs. S3	−3.97**	−6.26**	−4.99**	−4.39*	−3.97**
S2 vs. S3	2.63	−0.23	−0.94	0.00	1.45

comparisons were made at each repetition of N1 peak value (S1, S2 and S3) and electrode position, to observe that N1 amplitude decrease depends on repetition. While N1 to S1 was higher than N1 to S2 and S3, no significant differences were encountered between N1 amplitudes to S2 and to S3. These results are extended to all electrode locations. Table 1 summarizes all comparisons.

Repeated-measures ANOVA (Electrode × Condition) was also computed for N1 latencies. Although N1 latencies showed no repetition ($F(2,15) = 0.49$, $P < 0.1$) or electrode ($F(4,15) = 0.35$, $P < 0.1$) effect, a main significant Electrode × Condition interaction was observed ($F(8,15) = 19.71$, $P < 0.001$), which, consistent with N1 amplitude analysis, suggested that N1 latencies, when the repetition factor was considered, were not equivalent at all electrode locations.

Event-related spectral power change and event-locked phase coherency

Figs. 2a–c depict the grand mean ERP, the ERSP and the ITC results of the global trial-by-trial analysis (1173 trials) to S1, S2 and S3 responses at Cz. S1 responses showed significant 3.9–15.6 Hz ERSP ($P < 0.001$), whereas no significant modulation of ERSP was found for S2 and S3 responses in the 3.9–48.8 Hz frequency band (Fig. 2b). However, time-frequency analysis showed significant ITC values in the 3.9 to 15.6 Hz frequencies for each stimulus response (S1, S2 and S3) ($P < 0.001$) (Fig. 2c). Moreover, enhanced 3.9–5.8 Hz ERSP and ITC were found in the P3 component interval range ($P < 0.001$, both) to S1 stimuli. In addition, ERSP was not significant to either S2 or S3 after the same analysis was computed with $P < 0.05$ for all frequencies, thus confirming that these results were not due to high statistical restrictions (see Figs. 2d and e for raw data analysis). The same results were found at the other electrode locations.

Our results, when the same analysis was applied to each of the 16 subjects individually, showed that ERSP and ITC behavior for the S1, S2 and S3 responses corresponded to the behavior found with the global analysis (all subject trials), that is, S1 enhanced spectral power modulation ($P < 0.001$) and event-locked phase coherency ($P < 0.001$), while both S2 and S3 stimuli responses showed only increased phase coherency contributions to the N1 responses ($P < 0.001$) (see Fig. 3a for an example of a subject analysis). These results were extended to all electrodes analyzed, in which each N1 ERP appeared after each stimulus. In addition, event-locked phase coherency contribution to N1 production was validated when no clear N1 ERP to the S2 and S3 stimuli was observed in the Pz electrode and thus no clearly significant ITC values within the same latency window were shown (Figs. 3a and b).

However, since possible inter-individual peak dominant frequency differences could mix up likely ERSP modulations when averaging together all the subject trials (Klimesch, 1999), we
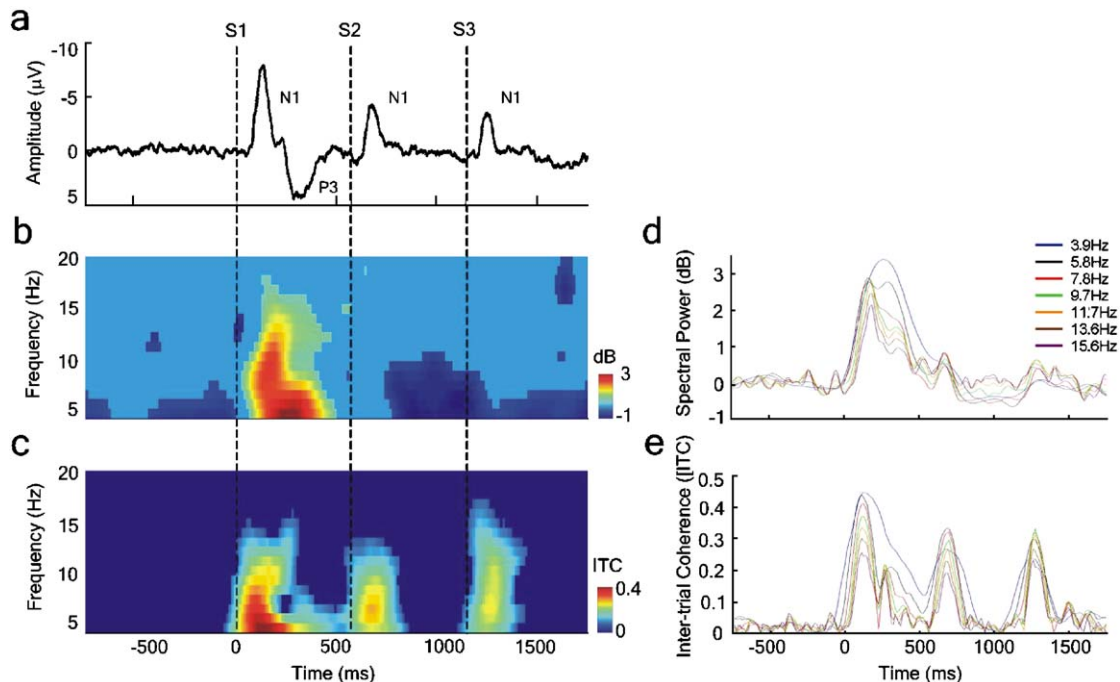

Fig. 2. (a) ERP average over all the subjects' pooled trials ($n = 1173$) in response to the first (S1), second (S2) and third (S3) stimulus at Cz electrode. ERSP (b) and ITC (c) analysis for 3.9–20 Hz frequency range responses after S1, S2 and S3. No significant ERSP and ITC were found in the 20–48.8 Hz frequency range. Colored areas show ERSP and ITC that are statistically significant ($P < 0.001$) compared with the baseline. Black dotted lines show the onset of S1, S2 and S3 stimuli presentation. Raw frequency-to-frequency decomposition of the ERSP (d) and ITC (e) analysis for 3.9–15.6 Hz frequency range with no bootstrap computation shows that, whereas S1 response enhanced ERSP and ITC, S2 and S3 responses only did so for ITC.
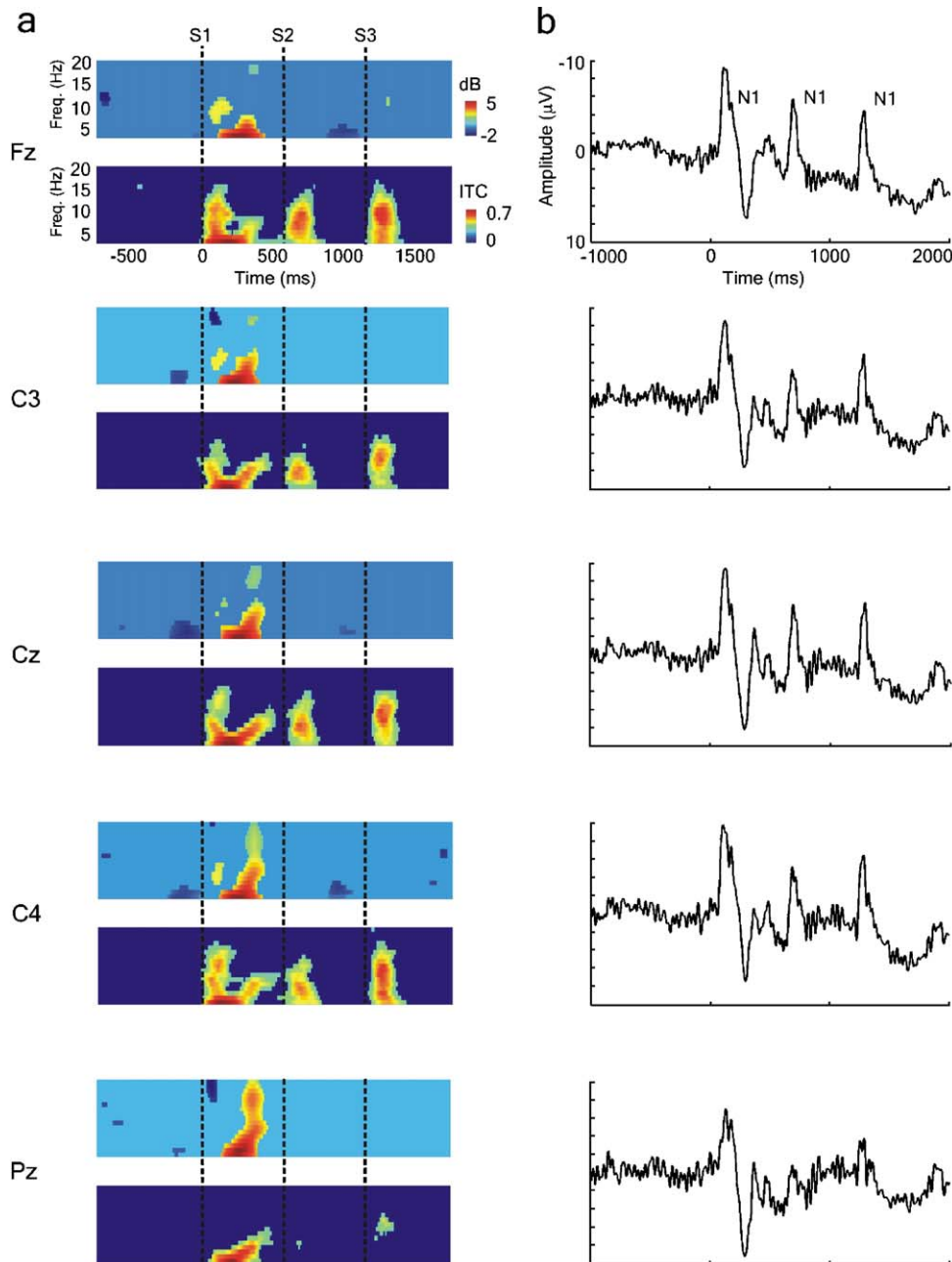
Fig. 3. (a) Time-frequency analysis (ERSP and ITC) to one subject at all electrode locations. For each electrode, top panels show those ERSP values that resulted significant on comparison of the time period after S1, S2 and S3 stimuli with the baseline period ($P < 0.001$). Bottom panels show those EEG frequencies that showed significant event-locked phase synchrony after each stimulus onset than baseline ($P < 0.001$). (b) ERP grand average over 87 trials containing S1, S2 and S3 responses. Whereas S1 ERSP and ITC are significant, for S2 and S3 responses only ITC remained as an ERP production mechanism. Furthermore, Pz results show that, while ERP to S1 showed both ERSP and ITC, no clear S2 response was found in the ERP plot and thus expressed no ERSP and ITC significant values. Dotted lines show the onset of S1, S2 and S3 stimuli presentation.

conducted additional time-frequency analysis after clustering those subjects for whom the dominant frequency during the baseline period coincided within 6–8 Hz (2 subjects), 8–10 Hz (9 subjects) and 10–12 Hz (7 subjects). ERSP and ITC results, separately analyzed for each dominant frequency group, corresponded with results for all subject trials computed together ($P < 0.001$ in all cases).

Subject-to-subject ERSP contributions to N1 to S1 were greater than S2 and S3 ERSP for 3.9 to 15.6 Hz frequency band at all electrode locations. Specifically, the low-frequency range (3.9 to 9.7 Hz) appeared to be most consistent after sequential Bonferroni adjustment was applied to the comparisons. No differences in ERSP were found at any electrode location on comparison of N1 elicited by S2 and S3. Further, significantly lower ITC values were encountered with 3.9 to 15.6 Hz oscillatory EEG rhythms to S2 and S3 than with S1 response at N1 interval range. As with ERSP, after Bonferroni correction, most ITC comparisons remained significant for lower frequencies. ITC values for the repeated

Table 2
Wilcoxon matched-pairs signed-ranks test results on comparison of event-related spectral perturbation (ERSP) and inter-trial coherence (ITC) among the three stimuli (S1, S2 and S3) at the N1 responses latency peak

	Fz			C3			Cz			C4			Pz		
	S1 Vs S2	S1 Vs S3	S2 Vs S3	S1 Vs S2	S1 Vs S3	S2 Vs S3	S1 Vs S2	S1 Vs S3	S2 Vs S3	S1 Vs S2	S1 Vs S3	S2 Vs S3	S1 Vs S2	S1 Vs S3	S2 Vs S3
ERSP															
3.9 Hz	+++	+++	−	+++	+++	−	++	+++	−	+++	+++	−	+++	+	−
5.8 Hz	++	+++	−	+++	+++	−	+++	+++	−	+++	+++	−	+++	+++	−
7.8 Hz	++	+	−	+++	+++	−	+++	++	−	+++	+++	−	+	+	−
9.7 Hz	+	+	−	+++	++	−	+++	++	−	+++	+++	−	+	+	−
11.7 Hz	+	+	−	+++	+	−	+++	++	−	+++	+++	−			
13.6 Hz	+	+	−	+	+	−	+++	++	−	+	+	−			
15.6 Hz	−	+	−	+	+	−	++	++	−	+	+++	−			
ITC															
3.9 Hz	+++	+	−	+++	+++	−	+++	+++	−	+++	+++	−	+	+++	−
5.8 Hz	+++	+++	−	+++	+++	−	++	++	−	+	+++	−	+	+++	−
7.8 Hz	+	+	−	+++	+++	−	++	++	−	+++	+++	−	+	+	−
9.7 Hz	+	+	−	+++	+	−	++	+	−	+	+	−	+	+	−
11.7 Hz	+++	+	−	+	+	−	+	+	−	+++	+	−			
13.6 Hz	+++	+	−	+	+	−	+	+	−	+	+	−			
15.6 Hz	+	+	−	+	+	−	−	−	−	+	+	−			

Comparisons were made with those frequencies that were significant after computing time-frequency at the global (1173 trials) trial-by-trial analysis (+++: $P < 0.0001$, ++: $P < 0.001$, +: $P < 0.01$ and −: $P > 0.01$). Those comparisons still significant after sequential Bonferroni adjustment are colored grey.

stimuli responses (S2 and S3) showed no significant differences between them (see Table 2).

Discussion

Due to the ambiguous interpretation of experimental results in terms of proposed ERP genesis models (evoked vs. oscillatory) given by the available time-frequency methods (Yeung et al., 2004; Mäkinen et al., 2004), our study explored the possibility of each generation mechanism behaving independently as a function of the amplitude modulation of a specific ERP component (auditory N1 during a tone repetition paradigm).

Our findings on S1 stimulus responses showed a clear N1, where both spectral power (3.9–15.6 Hz) and phase coherence (3.9–15.6 Hz) were enhanced in the N1 latency range. In addition, the long-lasting time interval of 30 s immediately preceding the S1 stimulus strongly supports the view that, for this stimulus, only N1 production mechanisms are being analyzed with no interference of any attenuation effects from previous stimuli presentation (Nelson and Lassman, 1968). In this case, finding the spectral power enlargement on S1 response ensured that an evoked mechanism held up the appearance of ERP whereas, as argued in the introduction, increased inter-trial coherence could have occurred due to enhanced transient EEG synchrony and/or fixed-latency and fixed-polarity added neural response, without guaranteeing the amount of the contribution of either mechanism.

In the present study, reduced N1 responses to incoming S2 and S3 stimuli, which were physically identical to S1 and presented at a short interval of approximately 500 ms, could be explained by a similar degree of phase reorganization (3.9–15.6 Hz), whereas spectral power modulation was absent, opening the way to an oscillatory-based explanation (Makeig et al., 2004a). The basic logic is that increased phase coherence in the absence of power modulation provides support for the oscillatory model. Subsequently, partial phase concentration of ongoing EEG activity becomes the most likely mechanism for explaining the generation of N1 to repeated stimuli observed in scalp EEG in this case, and hence, giving support to the oscillatory model not just in theoretical terms.

Otherwise, it could be argued that both inter-subject N1 latency variability (Makeig, 1993) and differences in the individual EEG ongoing dominant frequency (Klimesch, 1999) could mix up or mask some ERSP modulation after averaging all the subjects' pooled trials. However, these likely inter-subject differences cannot explain the lack of spectral power contribution to the S2 and S3 responses, because this phenomenon also occurred in individuals and after clustering subjects, depending on their ongoing EEG dominant oscillations. Otherwise, it should be noted that finding no ERSP in the EEG scalp data after S2 and S3 stimuli could not completely rule out the occurrence of an evoked response. A flat scalp ERSP (mean = 0) could be the result of an evoked response brought about by a spectral power increase and, simultaneously, a spectral power decrease due to an event-related desynchronization (ERD) (Pfurtscheller, 1977), exactly balanced at the same times and frequencies. However, the coincidence of the intensity of these opposed effects at each frequency and time frame, analyzed after both S2 and S3 stimuli responses, seems unlikely.

On the other hand, there are a diminishing inter-trial coherence measures between S2 and S3 relative to the S1 stimulus (see Table 2). This could confirm previous work on gating of N1 (Jansen et al., 2003), if interpreted as produced by decreased event-locked phase reorganization in attenuated N1 responses. Nonetheless, this is to some extent inconclusive and, as mentioned above, is due to the non-feasibility of distinguishing between evoked and oscillatory contributions when both spectral power and phase coherence contributions are simultaneously present in the analysis.

Moreover, our S1 results show that an "extra" neural process (in terms of evoked and/or oscillatory activity) plays a key role in the higher N1 amplitude of S1 rather than S2 and S3 stimuli (see Fig. 1). This additional neural contribution might underlie some aspects of the novelty of the stimulus supported by the subsequent prominent P3 component, observed after S1 only, and broadly related to attention mechanisms (Picton, 1992). Further, the time-frequency analysis of P3 component showed that, as in N1 response to S1, both spectral power and phase coherency increase would underlie its generation, which corroborates previous auditory (Yardonova and Kolev, 1998) and visual (Makeig et al., 2004b) results. On the basis of this "extra" neural activity underlying N1 to S1, ERP studies suggested that "attention switching" can be elicited by stimulus onsets (regardless of repetition/change), in particular if they appear after long "silent" intervals (Folk et al., 1992). Although it has been suggested that auditory N1 reflects a transient detector system of incoming stimuli, mostly located in bilateral supratemporal areas (Näätänen, 1992), it has also been posited that N1 could trigger an attention-capturing signal for conscious perception of the stimulus (Näätänen, 1990, 1992) facilitating sensory and motor responses to the eliciting stimulus (Näätänen and Picton, 1987), which could be performed by frontal sources (Giard et al., 1994). Given this, S1 to N1 could incorporate an extra function when compared with

attenuated N1 to S2 and S3, corresponding to the aforementioned attention-switching process. Under this assumption, although N1 to S1 could imply synchrony mechanisms of its basic supratemporal neural generators, other brain structures responsible for the "attention switching" mechanism (i.e. frontal sources) might respond differently (i.e. increasing their firing rate), so supporting the enhanced power contribution found. An alternative explanation arose when we take into account that those neural networks involved in the S1 response, also corresponding with the ones involved in S2 and S3, responded with different mechanisms due to the neural network state influenced by the previous sudden S1 entrance. Thus, novelty detection related to S1 response could generate transient responses that would change the activity level of the neural networks involved (David et al., 2005), modifying their behavior in front of S2 and S3. However, these proposals could not be verified with our results. One way of doing so would be to study the dynamics (in terms of evoked/oscillatory) of each neural source involved in the ERP generation (Makeig et al., 2002, 2004b; Grau et al., in preparation).

In line with previous studies (Makeig et al., 2002; Klimesch et al., 2004; Gruber et al., 2005), our results show that the EEG phase synchrony mechanism of ERP generation is a multi-frequency phenomenon. This could be explained by the assumption that event-locked phase concentration may be covered in transiently co-activated neural networks, supported by different neural assemblies with distinct oscillatory patterns (Salinas and Sejnowski, 2001; Varela et al., 2001). Moreover, recent findings support the view that statistically independent components from several anatomically distinct areas might contribute to ERP production (Jung et al., 2001; Makeig et al., 2002; Anemuller et al., 2003; Marco-Pallarés et al., 2005). The present results suggest that one line for future studies to follow would be to consider whether each structure contributed to the ERP with various putative mechanisms (i.e. evoked, oscillatory or both), which is consistent with the suggestion that each of them could encode distinct characteristics of stimulus-related information (Shah et al., 2004). However, whether either mechanism has a special processing role needs further investigation.

Despite a large number of studies and the interest of the topic, physiological mechanisms that could explain entirely the oscillatory model have still to be established (Buzsáki and Draguhn, 2004; David et al., 2005). However, recent studies have opened up some choices that could help advance in the clarification of this topic. On the one hand, in Huxter et al. (2003), hippocampal single unit recordings of neuronal activity in rats have demonstrated that the phase of the theta activity could be changed because of external factors (i.e. animal's location and speed of movement). On the other hand, Siapas et al. (2005) recently found that theta synchrony between neurons from the medial prefrontal cortex (mPFC) and hippocampus was not necessarily linked to a change in firing rates of mPFC neurons. These authors suggested that the apparent absence of theta power in mPFC could be explained by the characteristics of connections between hippocampus and mPFC. Thus, it was hypothesized that mPFC phase-locking could be due to the modulation of pyramidal cell excitability by a mPFC inhibitory network based on lateral interneurons, which would be imperceptible at a macroscopic scale (such as EEG) due to random geometric order and their relatively small size. A similar approach could help explain changes in neuronal coupling without a concomitant increase in spectral power in the present study. Finally, another approach is based on theoretical models that have showed that oscillatory phase resetting could appear without the concurrence of power enhancement depending on the strength of implied neural network activity (David et al., 2005).

While these findings clearly support the view that oscillatory activity is mainly responsible for certain ERP generation, they also make clear that amplitude and phase modulations could operate together in the brain, as recently indicated by brain signal simulation (David et al., 2005). Hence, event-related EEG phenomena could be understood as a time-frequency spectral state space where evoked and oscillatory aspects could coexist simultaneously (Makeig et al., 2004a).

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