

Functional Features of Nociceptive-Induced Suppression of Alpha Band Electroencephalographic Oscillations

Li Hu,^{*} Weiwei Peng,[†] Elia Valentini,^{‡,§} Zhiguo Zhang,[¶] and Yong Hu[†]

^{*}Key Laboratory of Cognition and Personality (Ministry of Education) and School of Psychology, Southwest University, Chongqing, China.

[†]Department of Orthopaedics and Traumatology, The University of Hong Kong, Pokfulam, Hong Kong, China.

[‡]Psychology Department, Sapienza University of Rome, Rome, Italy.

[§]Santa Lucia Foundation, Scientific Institute for Research, Hospitalization and Health Care, Rome, Italy.

[¶]Department of Electrical and Electronic Engineering, The University of Hong Kong, Pokfulam, Hong Kong, China.

Abstract: Nociceptive stimuli can induce a transient suppression of electroencephalographic oscillations in the alpha frequency band (ie, alpha event-related desynchronization, α -ERD). Here we investigated whether α -ERD could be functionally distinguished in 2 temporally and spatially segregated subcomponents as suggested by previous studies. In addition, we tested whether the degree of dependence of nociceptive-induced α -ERD magnitude on the prestimulus α -power would have been larger than the degree of dependence on the poststimulus α -power. Our findings confirmed the dissociation between a sensory-related α -ERD maximally distributed over contralateral central electrodes, and a task-related α -ERD (possibly affected by motor-related activity), maximally distributed at posterior parietal and occipital electrodes. The cortical sources of these activities were estimated to be located at the level of sensorimotor and bilateral occipital cortices, respectively. Importantly, the time course of the α -ERD revealed that functional segregation emerged only at late latencies (400 to 750 ms) whereas topographic similarity was observed at earlier latencies (250 to 350 ms). Furthermore, the nociceptive-induced α -ERD magnitude was significantly more dependent on prestimulus than poststimulus α -power. Altogether these findings provide direct evidence that the nociceptive-induced α -ERD reflects the summation of sensory-related and task-related cortical processes, and that prestimulus fluctuations can remarkably influence the non-phase-locked nociceptive α -ERD.

Perspective: Present results extend the functional understanding of α -oscillation suppression during pain perception and demonstrate the influence of prestimulus variability on this cortical phenomenon. This work has the potential to guide pain clinicians in a more accurate interpretation on physiological and psychological modulations of α -oscillations.

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Key words: Pain, intra-epidermal stimulation, event-related desynchronization, α -oscillation, prestimulus α -power, electroencephalography.

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Address reprint requests to Dr. Yong Hu, Department of Orthopaedics and Traumatology, The University of Hong Kong, Duchess of Kent Children's Hospital, 12 Sandy Bay Road, Pokfulam, Hong Kong, China. E-mail: yhud@hkucc.hku.hk

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Sensory stimuli can elicit transient changes in ongoing electroencephalography (EEG), which can be distinguished between phase-locked event-related potentials (ERPs) and non-phase-locked modulations of spontaneous EEG oscillations.^{45,54} These modulations are characterized by either transient enhancement (event-related synchronization, ERS) or transient suppression (event-related desynchronization, ERD) of the EEG power.^{43,56} The functional significance of ERS and ERD differs according to the frequency band within which they occur. For example, ERD in the alpha band (α -ERD, frequencies ranging from 8 to 13 Hz) has been hypothesized to reflect cortical activation or disinhibition,^{43,45,54,67} while ERS in the gamma band (frequencies ranging from 30 to 100 Hz) has been

hypothesized to play a crucial role in cortical integration and perception.^{16,38,62,63,68}

Among the modulations of EEG oscillations, the α -ERD has been observed not only during the elaboration of stimuli belonging to different sensory modalities (eg, visual and auditory; ie, sensory-related α -ERD),^{9,48,60,67} but also during various mental tasks (eg, working memory processes; ie, task-related α -ERD).^{19,28,30,64} In particular, some authors recently hinted to the coexistence of both sensory-related α -ERD and task-related α -ERD during pain.^{43,55,56} These scholars reported that nociceptive-induced α -ERD over the contralateral sensorimotor cortex^{1,51} may reflect the exogenous activation of the primary somatosensory cortex⁵⁵ and its contributions to pain processing.^{51,58} In contrast, other authors reported a widespread suppression of α -oscillation at the level of posterior parietal and occipital regions following nociceptive stimulation,^{43,46,56} which was hypothesized to reflect endogenous task-related cortical processing.²³ It is important to note that some of the reported modulations^{1,4,15,56,60} have been expressed as a function of the poststimulus α -power as compared to the prestimulus α -power (ie, baseline correction procedure). This procedure is classically accepted (in fact, desired) to provide a theoretically noise-free reference cortical signal. Crucially, this assumption does not always hold true, and it has actually been reported that the α -power preceding either sensory stimulation or cognitive operations can dramatically influence the subsequent neural responses (eg, α -ERD),^{39,55,60} thus reflecting the fluctuations in subjects' mental states (eg, attention and vigilance).^{15,18,33}

Here we investigated these multiple features of the nociceptive-induced α -ERD (sensory-related, task-related, and state-dependent) in an attempt to provide a functional characterization of their distinct electrophysiological features. A 64-channel EEG set-up was used to record event-related brain responses during a classical oddball task, whereby subjects were required to detect and respond to low-probability nociceptive target events intermingled in a series of high-probability nociceptive nontarget events. This task allowed us to explore whether the posterior parietal and occipital α -ERD would have been preferentially associated with the top-down endogenous voluntary orienting of attention toward task-relevant nociceptive stimuli (ie, targets) while the sensorimotor α -ERD would have been rather associated with the bottom-up exogenous involuntary orienting of attention to salient nociceptive stimuli, regardless of their task relevance (ie, nontarget). In addition, we tested the hypothesis that the degree of dependence of nociceptive-induced α -ERD magnitude on the prestimulus α -power would have been larger than the degree of dependence on the poststimulus α -power, regardless of the experimental condition.

Methods

Subjects

Eighteen healthy right-handed volunteers (9 females) with a mean age of 22 years (range, 19–29 years) participated in the study. All subjects gave written informed consent before participation, and the study was approved by

the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster.

Nociceptive Stimulation

Intra-epidermal electrical stimuli were constant-current square electric pulses of .5-ms duration delivered through a stainless steel concentric bipolar needle electrode consisting of a needle cathode (length: .1 mm; diameter: .2 mm) surrounded by a cylindrical anode (diameter: 1.4 mm).^{25,26} The stimuli were delivered to the medial and lateral side of the left hand dorsum, and the stimulus intensity was twice the individual perceptual threshold, previously proved to be able to preferentially activate the A δ nonnociceptive fibers without coactivation of the fast-conducting A β fibers.⁴⁴

Experimental Procedure

Subjects were seated in a comfortable chair in a lighted, shielded room and were instructed to relax and equally attend all the sensory stimuli prior to experiment start. Nociceptive stimuli were administered in 2 separated blocks. In 1 block, target and nontarget stimuli were randomly delivered to the medial and lateral side of the left hand dorsum according to a probability rate of 1:4. In the other block, the stimulus sites of target and nontarget stimuli were reversed, and they were randomly presented with the same probability rate used in the previous block (1:4). Each block consisted of 200 stimuli, and interstimulus intervals were randomly varied between 2,500 and 3,000 ms. The subjects were required to respond as fast and accurately as possible to the predefined target stimuli by pressing the response button upon their detection, using their right index finger. The order of the blocks was counterbalanced across subjects. Prior to data collection in each block, the subjects were repeatedly presented with 20 stimuli to familiarize them with the task.

Behavioral Data Analysis

In the target condition, trials without any response and those with reaction times shorter than 200 ms or longer than 1,000 ms were considered as error trials,⁷ while in the nontarget condition, trials with any response were considered as error trials. The percentage of error trials across all trials (both target and nontarget conditions) was defined as error rate. As a result, 71 ± 3 (out of 80) and 304 ± 9 (out of 320) trials were obtained for the target and nontarget conditions, respectively. To rule out any statistical bias due to different size of trials in the 2 conditions, trials with the same number as in the target condition were randomly selected from the nontarget condition in each subject. Results are reported as mean $\pm$ standard error of mean (SEM). Statistical differences were considered significant at $P < .05$.

EEG Recording

The EEG data were recorded using a 64-channel Brain Products system (Brain Products GmbH, Munich, Germany; pass band, .01–100 Hz; sampling rate, 500 Hz) using a standard EEG cap based on the extended 10–20 system. The left mastoid was used as the reference channel, and all channel impedances were kept lower than 10 k Ω . To monitor ocular movements and eye blinks, electro-oculographic signals were simultaneously recorded from 4 surface electrodes:

1 pair placed over the upper and lower eyelids, and the other pair placed 1 cm lateral to the outer corner of the left and right orbits.

EEG Data Analysis

Preprocessing

EEG data were preprocessed using EEGLAB,¹⁰ an open source toolbox running under the MATLAB environment. Continuous EEG data were low-pass filtered at 30 Hz. EEG epochs were segmented in 1,500-ms time window (prestimulus 500 ms and poststimulus 1,000 ms), and baseline corrected using the prestimulus time interval. Trials contaminated by eye blinks and movements were corrected using an independent component analysis algorithm.^{10,27,37} In all datasets, independent components with a large electro-oculographic channel contribution and a frontal scalp distribution were removed. After independent component analysis and an additional baseline correction (−500 to 0 ms), EEG trials were re-referenced to the bilateral mastoid electrodes.

Time-Frequency Analysis

The whole procedure to calculate the magnitude of α -ERD consisted of the following 4 steps.

Calculation of Time-Frequency Representations. Continuous Morlet wavelet transform (MWT) was used to estimate the time-frequency representations (TFRs) of single-trial EEG responses.⁴⁵ The MWT adapts the width of its window of analysis as a function of frequency, and thereby offers an optimal compromise for time-frequency resolution,⁴⁵ apt to disclose both phase-locked and non-phase-locked modulations of EEG signal. The parameters of central frequency and restriction of the MWT were 5 and .15, respectively. TFRs between 1 and 30 Hz in intervals of .5 Hz were computed.

Baseline Correction. For each estimated frequency, TFRs were baseline corrected using the prestimulus interval (−400 to −100 ms), according to the formula $ER(t,f)\% = [F(t,f) - R(f)]/R(f)$, where $F(t,f)$ is the signal power at a given time t and at a given frequency f , and $R(f)$ is the signal power of the frequency f averaged within the reference interval.⁵⁴ Across-trial averaging of the TFRs was displayed in a spectrogram of the average EEG oscillation magnitude as a function of time and frequency. This time-frequency map was used to identify phase- and non-phase-locked nociceptive-related EEG activity for each subject in both target and nontarget conditions. Single-subject TFRs were subsequently averaged across subjects to obtain group-level average TFR.

Definition of Time-Frequency Region of Interest (TF-ROI). According to previous reports,^{9,43,55} the group-level grand average TFR showed prominent nociceptive-induced suppressions of cortical activity in the alpha band (8–13 Hz) within a time window ranging between 200 and 800 ms poststimulus. Therefore, the α -ERD TF-ROI was defined according to such a temporal-spectral window (8–13 Hz, 200–800 ms).

Measurement of α -ERD Magnitude. Within the TF-ROI, time-frequency pixels were sorted according to the

ER% values, and 20% time-frequency pixels with the lowest ER% values were selected. The α -ERD was estimated by computing the mean of the selected 20% time-frequency pixels for each subject at 3 different spatial regions of interest (sROIs), namely the 1) posterior parietal and occipital electrodes (P1 + Pz + P2 + PO3 + POz + PO4)/6; 2) contralateral central electrodes (FC4 + FC6 + C4 + C6 + CP4 + CP6)/6; and 3) ipsilateral central electrodes (FC3 + FC5 + C3 + C5 + CP3 + CP5)/6. Note that the definition of sROIs was based on the distribution of electrodes displaying the lowest ER% values within the defined TF-ROI. Within these 3 sROIs, the top 20% summary measure reflected the lower ER% values, thus avoiding the noise introduced by including all points of the spectrogram, some of which may display little or no response. This approach has the potential to disclose condition-specific effects and has been successfully used in several studies.^{23,24,41}

α -ERD Source Localization

To estimate the neural sources of α -ERD scalp topographies, an EEG source reconstruction approach was adopted. First, a standardized Boundary Element Method, provided by the eConnectome,²¹ served as a first approximation for the subjects' head and brain model.⁴⁰ As the EEG source reconstruction is an ill-posed problem (ie, infinite different source configurations could explain a given scalp topography distribution equally well), a priori assumptions are necessary to constrain the space of the feasible solutions and thus contribute to finding a unique solution for the EEG source reconstruction. The minimum norm provides a unique solution, in which 1 combination of neural sources can have the lowest overall intensity while exactly fitting the scalp data. However, such a constraint way (assumption) that the overall intensity should be as low as possible may not be always physiologically plausible. This algorithm favors weak and localized sources, which are normally superficially distributed, because less activity is required at superficial neural sources to determine a certain scalp distribution.⁴⁰ Therefore, to compensate for the bias of the minimum norm solution, a lead field weighted minimum norm, based on the norm of the columns of the lead field matrix,²⁰ was adopted in the present study. To achieve the calculation of the lead field weighted minimum norm algorithm, a common method of source reconstruction regularization was adopted (Tikhonov regularization⁶⁵). Finally, 3-dimensional visualization of the brain activity of α -ERD at source space was displayed based on the standard MNI brain (from the Montreal Neurological Institute).

Comparison of α -ERD Between Target and Nontarget Conditions

We compared the α -ERD magnitudes between target and nontarget conditions with paired 2-sample t-test on the previously defined sROIs (posterior parietal and occipital electrodes, contralateral central electrodes, and ipsilateral central electrodes).

Series of 11 scalp topographies of α -ERD magnitude were plotted by spline interpolation at intervals of 50 ms, in a time window ranging from 250 to 750 ms, for

both target and nontarget conditions. Global dissimilarity (GD) for all time points was computed to describe the topographic resemblance between target and nontarget conditions. GD is an index to show topographic differences between conditions regardless of the relative strength.^{8,29,36,47} Such an index is obtained by calculating the square root of the mean squared differences between all corresponding electrodes after 2 given scalp topographies have been recalculated against the average reference and normalized to unitary strength (ie, divided by its own global field power).³⁶ The GD index is inversely related to the spatial correlation between 2 scalp topographies and varies from 0 (map homogeneity) to 2 (map inversion).⁸

Dependence of α -ERD on Prestimulus and Poststimulus α -Power

The baseline corrected α -ERD is associated with the power variance belonging to both prestimulus and poststimulus α -activity, as detailed by the previously illustrated formula, $ER(t,f)\% = [F(t,f) - R(f)]/R(f)$. However, to the best of the authors' knowledge, there is no available information detailing to what extent the α -ERD magnitude would depend more on the prestimulus or poststimulus α -power. To test for the degree of such dependency, single trials were sorted according to the magnitude of α -ERD in each subject, and the entire amount of trials was divided into 7 bins for both target and nontarget conditions, respectively. The number of trials was identical in different bins. Note that after baseline correction, α -ERD magnitude was calculated within the poststimulus TF-ROI (8–13 Hz, 200–800 ms) at (P1 + Pz + P2 + PO3 + POz + PO4)/6 in the target condition, and at (FC4 + FC6 + C4 + C6 + CP4 + CP6)/6 in the nontarget condition, respectively. For each bin, prestimulus α -power was calculated by averaging the spectral power (without baseline correction) within the prestimulus TF-ROI (8–13 Hz, –400 to –100 ms) at (P1 + Pz + P2 + PO3 + POz + PO4)/6 in both target and nontarget conditions, while poststimulus α -power was calculated by averaging the spectral power (without baseline correction) within the poststimulus TF-ROI (8–13 Hz, 200–800 ms) at (P1 + Pz + P2 + PO3 + POz + PO4)/6 in the target condition, and at (FC4 + FC6 + C4 + C6 + CP4 + CP6)/6 in the nontarget condition, respectively.

The α -ERD magnitude and prestimulus and poststimulus α -power were normalized (between 0 and 1) for each subject and each condition. To test the dependence of α -ERD magnitude on prestimulus and poststimulus α -power, prestimulus and poststimulus α -power at different magnitude bins (bin1-bin7) were compared using 7-level, 1-way repeated-measures analysis of variance (ANOVA) (each level a different bin) with a statistical significance level of $P < .05$. Mauchly's test was applied to assess violations of sphericity.⁵⁹ If the assumption of sphericity was violated ($P < .05$), the degrees of freedom were adjusted ($\epsilon < .75$, Greenhouse-Geisser correction; $\epsilon > .75$, Huynh and Feldt correction).¹⁷ When the main effect of the ANOVA was significant, post hoc Tukey pairwise comparisons were performed.

Furthermore, a multiple linear regression model was employed to quantitatively measure the level of depen-

dence of α -ERD magnitude (the dependent variable) on prestimulus and poststimulus α -power (the independent variable). According to the calculation of baseline corrected TFR (ie, $ER(t,f) = F(t,f)/R(f) - 1$), a linear relationship between α -ERD and prestimulus and poststimulus α -power can be established according to the formula $\ln(\alpha\text{-ERD} + 1) = \ln(\text{poststimulus } \alpha\text{-power}) - \ln(\text{prestimulus } \alpha\text{-power})$. Therefore, for each subject and each bin, the common logarithm ($\ln$) of 3 variables (α -ERD magnitude + 1, prestimulus and poststimulus α -power) was calculated and subsequently standardized by subtracting the mean values and dividing by the standard deviations. Such standardization allowed us to evaluate the importance of these explanatory variables in determining the variance of the dependent variable (α -ERD), by comparing the absolute values of the standardized regression coefficients. The resultant linear regression model can be written as:

$$y = \beta_1 x_1 + \beta_2 x_2 + \varepsilon$$

where y is the standardized value of $\ln(\alpha\text{-ERD} + 1)$; x_1 and x_2 are the standardized values of $\ln(\text{prestimulus } \alpha\text{-power})$ and $\ln(\text{poststimulus } \alpha\text{-power})$, respectively; β_1 and β_2 are coefficients that weight the fit of x_1 and x_2 to the data y ; and ε is the residual error of the fitted model. For each subject, the coefficients β_1 and β_2 were calculated by ordinary least squares. The absolute values of β_1 and β_2 across all subjects were compared using paired 2-sample t-test for the target and nontarget conditions, respectively.

Results

Behavioral Results

Mean reaction times to the target stimuli were 501 ± 19 ms. The error rate for both target and nontarget conditions was $5\% \pm 1\%$.

Comparison of α -ERD Between Target and Nontarget Conditions

Fig 1 displays the grand average TFRs for target and nontarget conditions (top panels), which were measured at posterior parietal and occipital electrodes and contralateral central electrodes, respectively. Scalp topographies of α -ERD measured at the poststimulus TF-ROI (8–13 Hz, 200–800 ms) displayed a peak of activity at the posterior parietal and occipital electrodes (around Pz and POz) in the target condition, whereas a peak of activity at the contralateral central electrodes in the nontarget condition was observed (around C4 and C6) (Fig 1, top panels). The estimated sources of these local maxima corresponded to the bilateral occipital cortices in the target condition and the contralateral sensorimotor cortex in the nontarget condition (Fig 1, bottom right and bottom left panels, respectively).

The paired 2-sample t-test revealed a significant difference between target and nontarget conditions at the posterior parietal and occipital sROI (-83.08 ± 21.86 versus -40.74 ± 17.52 ER%; $t = -3.73$; $P = .002$; Fig 2, left panel) and at the ipsilateral central sROI (-40.68 ± 8.28 versus

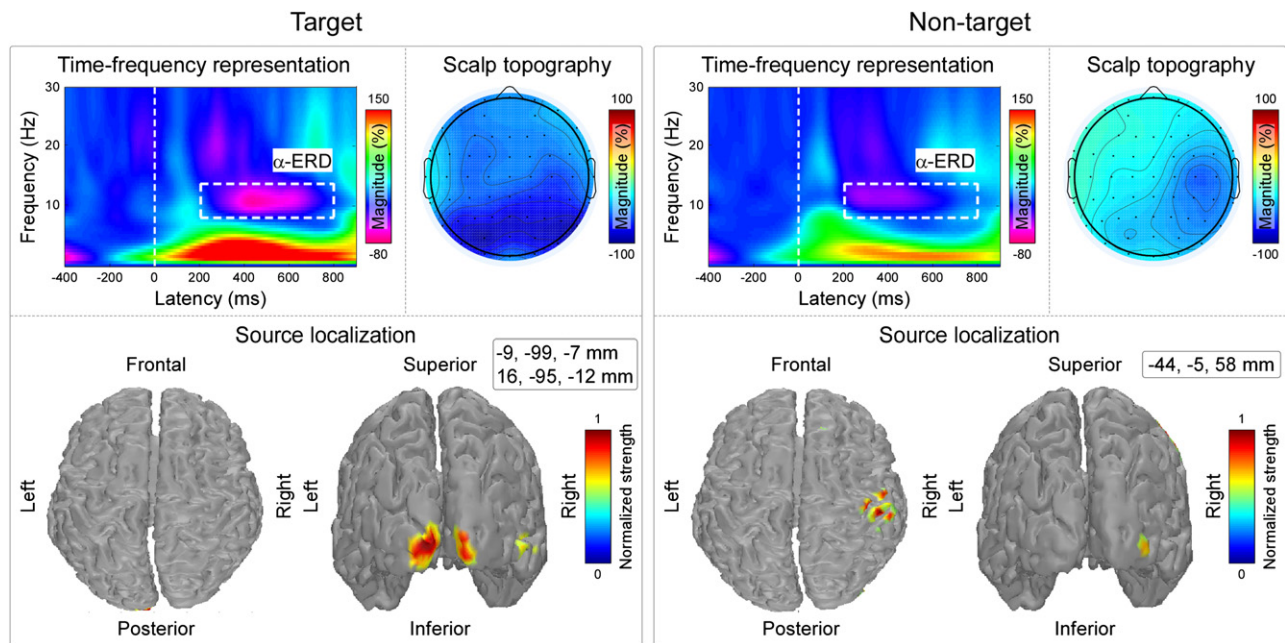


Figure 1. Grand average time-frequency distributions, scalp topographies, and estimated sources of α -ERD in the target and non-target conditions. Top panel: Group-level TFRs and scalp topographies of the α -ERD in the target (posterior parietal and occipital regions) and non-target condition (contralateral central regions). For group-level TFRs, X-axis represents latency (ms); Y-axis represents frequency (Hz); and color scale represents baseline corrected oscillatory magnitude (ER%). Scalp topographies show a different localization of the "top 20%" α -ERD magnitude within the poststimulus ROIs (white rectangles); that is, a peak of activity at the posterior parietal and occipital electrodes in the target condition, versus a peak of activity at the contralateral central electrodes in the non-target condition. Bottom panel: α -ERD estimated sources. Talairach coordinates (x, y, z) of α -ERD sources are -9, -99, -7 mm and 16, -95, -12 mm in the target condition, and -44, -5, 58 mm in the non-target condition, respectively.

-20.88 ± 6.58 ER%; $t = -2.05$; $P = .02$; Fig 2, right panel), whereas no significant difference was detected at the contralateral central sROI (-62.44 ± 13.96 versus -51.49 ± 12.32 ER%; $t = -.95$; $P = .35$; Fig 2, central panel).

The grand average TFRs and α -ERD waveforms measured at (P1 + Pz + P2 + PO3 + POz + PO4)/6 in the target condition and those at (FC4 + FC6 + C4 + C6 + CP4 + CP6)/6 in the non-target condition are displayed in Fig 3. Series of 11 scalp topographies were computed (latency: 250–750 ms, plotting every 50 ms) in both target and non-target conditions.

α -ERD scalp topography displayed a similar pattern for both target and non-target conditions at early la-

tencies (250–350 ms), whereas it showed a clear dissociation between target and non-target conditions at late latencies (400–750 ms). Indeed, α -ERD peaked at posterior parietal and occipital regions (around Pz and POz) in the target condition, whereas it peaked at contralateral central regions (around C4 and C6) in the non-target condition at these late latencies.

The computation of the GD index between the α -ERD scalp topographies in the target and non-target conditions (Fig 4) disclosed a time-varying trend of increasing dissimilarity. Indeed, α -ERD scalp topographies between

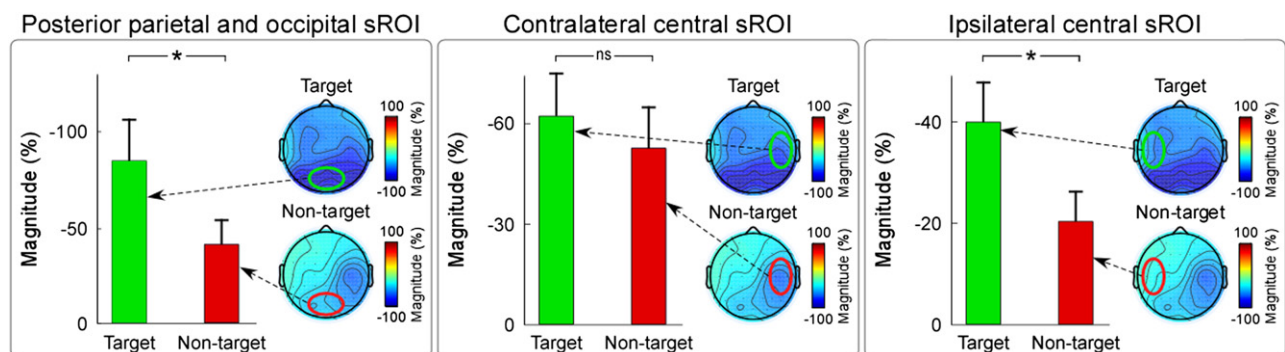


Figure 2. Comparison of α -ERD magnitudes between the target and non-target conditions across the 3 sROIs. α -ERD magnitudes between target and non-target conditions were compared in the following 3 regions: 1) posterior parietal and occipital regions measured at (P1 + Pz + P2 + PO3 + POz + PO4)/6 (marked in circles in the left panel); 2) contralateral central regions measured at (FC4 + FC6 + C4 + C6 + CP4 + CP6)/6 (marked in circles in the middle panel); and 3) ipsilateral central regions measured at (FC3 + FC5 + C3 + C5 + CP3 + CP5)/6 (marked in circles in the right panel). Values are displayed in green and red for target and non-target conditions, respectively. Error bars represent, for each condition, $\pm$ SEM across subjects. Asterisk (*) indicates a significant difference ($P < .05$, paired 2-sample t-test).

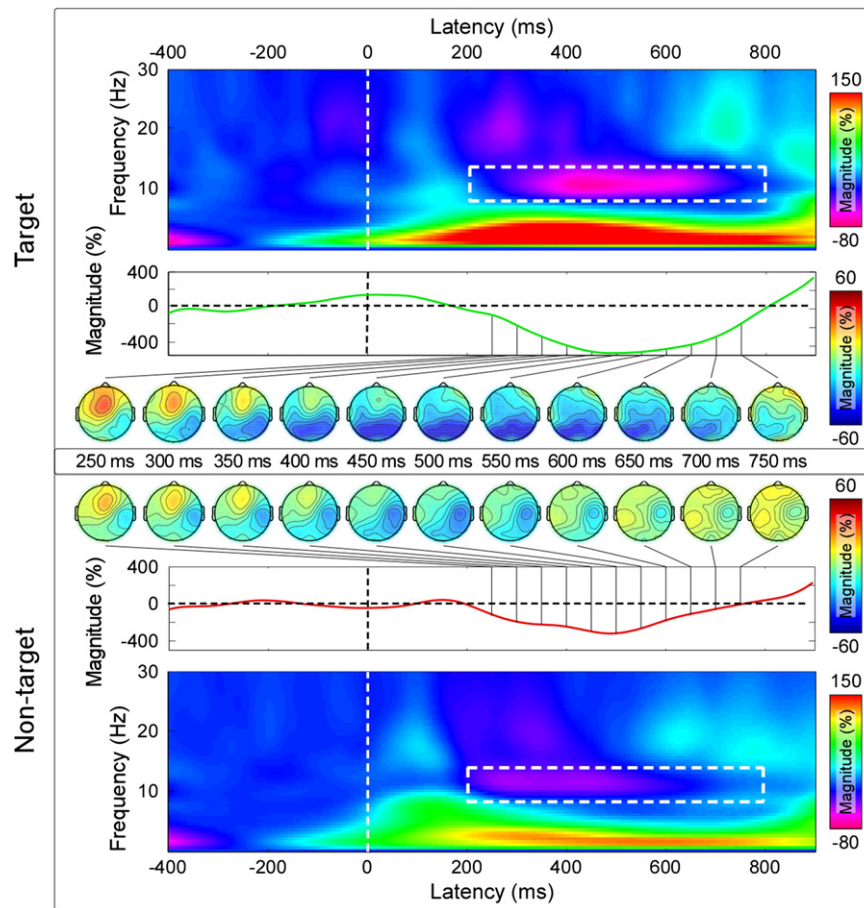


Figure 3. Time varying scalp topographies of α -ERD in target and nontarget conditions. Grand average TFRs and α -ERD waveforms are measured at (P1 + Pz + P2 + PO3 + POz + PO4)/6 in the target condition and at (FC4 + FC6 + C4 + C6 + CP4 + CP6)/6 in the nontarget condition. For group-level TFRs, X-axis represents latency (ms); Y-axis represents frequency (Hz); and color scale represents baseline corrected oscillatory magnitude (ER%). For group-level α -ERD waveforms, X-axis represents latency (ms); Y-axis represents α -ERD magnitude (ER%). Series of 11 scalp topographies are displayed in steps of 50-ms interval from 250–750 ms for both target and nontarget conditions. Note that the α -ERD magnitudes from 250 to 350 ms show similar scalp topographies during both target and nontarget conditions. Conversely, the α -ERD scalp topographies from 400–750 ms are different between target and nontarget conditions, peaking at posterior parietal and occipital regions in the target condition versus contralateral central regions in the nontarget condition.

target and nontarget conditions progressed from a similar negative amplitude peak at contralateral central electrodes (203 ms and GD value = .034) to a marked difference in the negative amplitude (702 ms and GD value = .35) located at posterior parietal and occipital electrodes in the target condition (larger amplitude) and at contralateral central electrodes in the nontarget condition (lower amplitude), respectively.

Dependence of α -ERD on Prestimulus and Poststimulus α -Power

Across subjects, the normalized α -ERD magnitude and prestimulus and poststimulus α -power in the target and nontarget conditions were summarized in Table 1 and displayed in Fig 5. For the prestimulus α -power in the target and nontarget conditions, Mauchly's test indicated that the assumption of sphericity had been violated (target, $\chi^2 = 47.39$, $P < .001$; nontarget, $\chi^2 = 59.16$, $P < .001$); therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity (target, $\varepsilon = .45$; nontarget, $\varepsilon = .43$). As revealed by 7-level, 1-way

repeated-measures ANOVA, prestimulus α -power in the target and nontarget conditions was significantly different across bins (target, $F(2.45, 41.69) = 16.22$, $P < .001$, partial $\eta^2 = .49$; nontarget, $F(2.33, 39.67) = 18.60$, $P < .001$, partial $\eta^2 = .52$). Post hoc pairwise comparisons analysis to compare the normalized values of prestimulus α -power at different magnitude bins (bin1–bin7) in both target and nontarget conditions were summarized in Table 2. For the poststimulus α -power, there was no significant difference across bins in both target and nontarget conditions ($F(6, 120) = 1.07$, $P = .382$; $F(6, 120) = 1.29$, $P = .269$ for target and nontarget conditions, respectively).

The multiple linear regression analysis highlighted significant larger absolute coefficients of $\ln(\text{prestimulus } \alpha\text{-power})$ (β_1) than those of $\ln(\text{poststimulus } \alpha\text{-power})$ (β_2), in both target and nontarget conditions (target: β_1 versus $\beta_2 = .83 \pm .05$ versus $.39 \pm .03$, $P < .001$, paired 2 sample t-test; nontarget β_1 versus $\beta_2 = .77 \pm .05$ versus $.39 \pm .03$, $P < .001$, paired 2 sample t-test). These results indicated that α -ERD magnitude was significantly more dependent on the prestimulus α -power than the poststimulus α -power in both target and nontarget conditions.

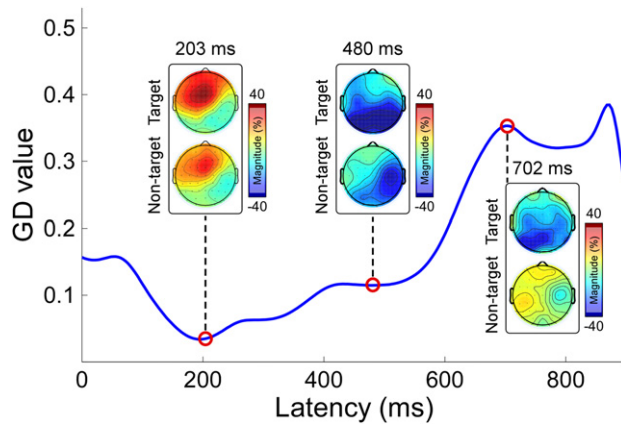


Figure 4. GD values of α -ERD scalp topographies between target and nontarget conditions. X-axis represents latency (ms); Y-axis represents GD value. High GD value indicates that the similarity of the compared scalp topographies is low, and vice versa. The α -ERD scalp topographies between target and nontarget conditions are similarly maximal at the contralateral central region at early latencies (eg, 203 ms). In contrast, the α -ERD scalp topographies are different between target and nontarget conditions at late latencies (eg, 480 and 702 ms).

Discussion

Suppression of α -Oscillation: Sensory- or Task-Related?

By applying a classical oddball paradigm we were able to strengthen the previously reported differentiation between an exogenous sensory-related^{1,51,47,50} and an endogenous task-related^{23,43,46,56} α -ERD during perception of nociceptive stimuli. In fact, our findings confirmed the hypothesis of a coexistence of both sensory-related α -ERD and task-related α -ERD^{43,55,56} (Fig 1). The sensory-related α -ERD (ie, nontarget condition) had a scalp distribution maximal at contralateral central regions and a source estimated at the level of the sensorimotor cortex (Fig 1, left panels), whereas the task-related α -ERD (ie, target condition) had a scalp distribution maximal at posterior parietal and occipital regions and a source estimated at the level of the bilateral occipital cortices (Fig 1, right panels).

It is important to note that preparation, execution, and imagination of movement have been consistently reported to induce α -ERD prominently over contralateral sensorimotor regions.^{53,54} In the present study, the

difference between target and nontarget α -ERD was significant in the central sROI ipsilateral to the nociceptive stimulation (ie, sensorimotor regions contralateral to movement hand; Fig 2, right panel), whereas no significant difference was detected at the central sROI contralateral to the nociceptive stimulation (Fig 2, central panel). This finding supports the notion that if any influence of motor activation would bias the identification of a genuine task-related α -ERD (ie, a side activation associated to the required behavioral response in the target condition), this effect should have been maximally expressed at scalp locations ipsilateral to the stimulated hand rather than at other scalp locations (eg, scalp locations contralateral to the stimulated hand). However, the task-related α -ERD might still be influenced by a motor-related α -ERD due to the inevitable volume conduction of scalp EEG responses. Indeed, the current experimental design does not allow the ruling out of the possible influence of motor processes on the task-related α -ERD.

Interestingly, the time course of the long-lasting suppression of α -oscillation (Fig 3) revealed that a similar topographic pattern could be observed for both target and nontarget conditions at early latencies (250–350 ms; Fig 3, left), whereas a clear dissociation between target and nontarget conditions emerged at late latencies (400–750 ms; Fig 3, right), thus highlighting the temporal function of the topographic differentiation between the sensory-related α -ERD (ie, nontarget condition) and the task-related α -ERD (ie, target condition). This finding was further confirmed by the GD index (Fig 4): the dissimilarity of scalp topographies between target and nontarget conditions increased substantially at around 420 ms and reached a peak at 702 ms. We speculate that the α -ERD at the contralateral central regions in the nontarget condition (250–350 ms) would reflect the early stage of processing of the stimulus features, while the subsequent α -ERD at the occipital regions (400–750 ms) would reflect the allocation of attentional resources required to accomplish the task.

The finding that a time-varying property of the nociceptive α -ERD reflects a functional differentiation between sensorimotor and occipital structures during the processing of nociceptive stimuli is in line with several previous publications.^{1,2,12,22,43,46,55} In fact, the present finding contributes to extend the notion that the nociceptive-induced α -ERD at contralateral sensorimotor

Table 1. Normalized Values of α -ERD Magnitude, Prestimulus α -Power, and Poststimulus α -Power at Different α -ERD Magnitude Bins (Bin1–Bin7) in Both Target and Nontarget Conditions

									ANOVA	
	NORMALIZED VALUES	BIN 1	BIN 2	BIN 3	BIN 4	BIN 5	BIN 6	BIN 7	F	P
Target	α -ERD magnitude	.04 ± .003	.11 ± .008	.16 ± .013	.21 ± .018	.27 ± .024	.36 ± .033	.51 ± .045	—	—
	Prestimulus α -power	.52 ± .033	.45 ± .027	.35 ± .022	.36 ± .028	.33 ± .038	.26 ± .030	.23 ± .032	11.22	<.001
	Poststimulus α -power	.31 ± .041	.32 ± .024	.29 ± .025	.34 ± .027	.36 ± .032	.34 ± .026	.38 ± .029	1.07	.382
Nontarget	α -ERD magnitude	.05 ± .006	.11 ± .011	.16 ± .014	.21 ± .017	.28 ± .021	.36 ± .027	.53 ± .034	—	—
	Prestimulus α -power	.54 ± .027	.44 ± .026	.40 ± .024	.37 ± .021	.30 ± .022	.31 ± .034	.25 ± .038	12.44	<.001
	Poststimulus α -power	.30 ± .036	.32 ± .035	.34 ± .031	.35 ± .024	.33 ± .024	.40 ± .029	.38 ± .030	1.29	.269

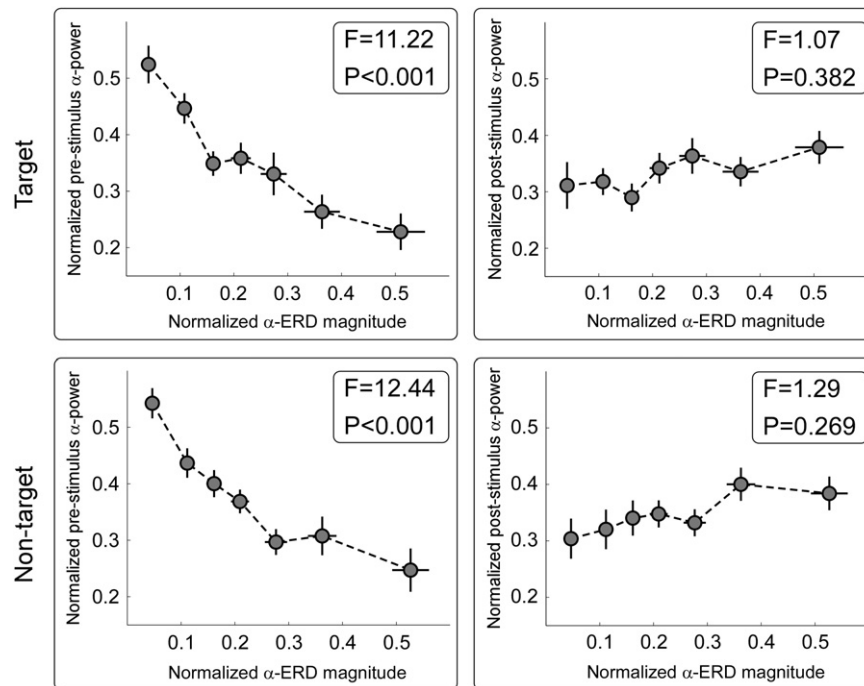


Figure 5. Relationship between α -ERD magnitude and prestimulus and poststimulus α -power in target and nontarget conditions. X-axis represents normalized values of α -ERD magnitude; Y-axis represents normalized values of prestimulus or poststimulus α -power. Each point (marked in gray circle) represents values from 1 magnitude bin. Vertical and horizontal error bars represent, for each bin, the variance across subjects (expressed as SEM). Prestimulus α -power was significantly different across bins of magnitude in both target ($F = 11.22$, $P < .001$) and nontarget ($F = 12.44$, $P < .001$) conditions, whereas poststimulus α -power was not significantly different across bins in both target ($F = 1.07$, $P = .382$) and nontarget ($F = 1.29$, $P = .269$) conditions.

cortex would reflect the processing of the exogenous sensory stimulus,^{49,50,54-56} while its posterior parietal and occipital region counterpart would reflect the endogenous task-related cortical processing.^{12,13,23,43,46}

The latter may be part of a working memory process associated to the task requirements. In other words, it may mediate the maintenance of a current stimulus trace and allow the comparison with formerly processed sensory traces (ie, assess whether a standard or rather a target stimulus was presented).^{5,11,14,57} If any task-relevant change of the sensory stream was detected (ie, detection of a target stimulus), the neural representation of the stimulus environment was updated, and attentional resources were allocated to the novel stimulus so as to prepare and execute the required action to achieve the predefined goal (ie, pressing a button). No update would

take place otherwise if no change in the sensory stream was detected (ie, detection of a nontarget stimulus).

In our opinion such interpretative account is reminiscent of the functional differentiation associated to the event-related P3b in ERPs. Indeed, in analogy with this well-known late phase-locked ERP component, α -band oscillations may be distinguished in specific subcomponents with distinguished functional significance. That is, similarly to the laser-evoked P2a and P2b,^{3,35,63} nociceptive-induced α -band oscillations seem to be characterized by a precise topographic dissimilarity. Interestingly, the P2b (akin to the P3b in the auditory modality⁶) can imply the activation of neural processes related to the detection of the attended events,^{34,57} and its amplitude has been observed to increase gradually with the task-relevance of the target stimuli.^{14,61} Therefore,

Table 2. Post Hoc Pairwise Comparisons Analysis to Compare the Normalized Values of Prestimulus α -Power at Different α -ERD Magnitude Bins (Bin1–Bin7) in Both Target and Nontarget Conditions

TARGET (PRESTIMULUS α -POWER)						NONTARGET (PRESTIMULUS α -POWER)					
Bin 2	.434					.014*					
Bin 3	.003**	.055				.002**	1.00				
Bin 4	.020*	.019*	1.00			.001**	.309	1.00			
Bin 5	.065	.431	1.00	1.00		.000***	.000***	.002**	.023*		
Bin 6	.002**	.003**	.075	.048*	.047*	.004**	.153	.550	.599	1.00	
Bin 7	.001***	.001***	.008**	.007**	.008**	.027*	.001**	.004**	.023*	.028*	1.00
Bin 1											.528

* $P < .05$.

** $P < .01$.

*** $P < .001$.

both the parietal P2b and the parietal-occipital α -band ERD may be interpreted as indexes of endogenous task-related cortical processing. Given the strong association between the P3b and the α -ERD,^{52,57,66,67} future studies may investigate not only if these measures share a similar function but also if they influence one another.

The Influence of Prestimulus α -Oscillation on Poststimulus Neural Responses

By using 2 complementary parametric approaches (1-way ANOVA and multiple linear regression), we showed that the nociceptive-induced α -ERD magnitude was significantly more dependent on the prestimulus than on the poststimulus α -power during both target and nontarget conditions. More specifically, a significant difference between the α -ERD magnitude bins of the prestimulus α -power was found (Fig 5, left panels), whereas no significant difference was observed for the poststimulus α -power bins (Fig 5, right panels). In addition, the multiple linear regression analysis revealed that the absolute coefficients of the prestimulus α -power (β_1) had a significantly larger ability to explain the variations than those modeling the poststimulus α -power (β_2) in both target and nontarget conditions (Table 1 and Table 2). These results indicated that even though the magnitude of the α -ERD was related to the dynamic balance between prestimulus and poststimulus α -power, prestimulus α -power had a greater influence on the resulting α -ERD variance.

Previous studies have indicated that spontaneous α -oscillation could be interpreted as a neural index of the neural networks subserving specific cognitive processing (eg, attention and vigilance).^{32,33,42} Furthermore, several studies demonstrated the impact of prestimulus

variability on poststimulus neural activations.^{1,4,15,31,60} Therefore, the finding that the nociceptive-induced modulation of α -oscillation was strongly influenced by the fluctuation of prestimulus α -power confirms and extends the current knowledge on the role of mental states in determining individual poststimulus brain activity, perception, and behavior.^{31,33,39,55,60}

Clinical and Methodological Remarks

In conclusion, we would like to offer the reader some considerations on the role of α -ERD in clinical pain. Several studies investigated the effects of chronic pain and tonic pain on the spontaneous EEG oscillations.^{2,13,22,49,50} These effects were observed at the posterior parietal and occipital regions in the painful condition as compared to the nonpainful condition. Importantly, even though the induced α -ERD is clearly associated with the processing of the nociceptive input, it must be considered as unspecific to the processing of the sensory aspect contributing to the final perception, and rather associated to supramodal processes, which are required for complex mental operations (eg, pain-coping strategies).⁵⁶

From the methodological point of view, we would like to draw the reader's attention to 2 main suggestions emerging from the present study. First, the α -ERD should be assessed as a temporal-spatial component that covaries with its neural functions. Second, the variability of prestimulus α -power should be considered to explore possible confounds as well as a predictive measure of poststimulus variability of a given mental function. Both these considerations should help researchers to engage in more accurate interpretations of the observed modulations of physiological and/or psychological factors on α -ERD.

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