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A novel mechanism for evoked responses in the human brain

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Abstract

Magnetoencephalographic and electroencephalographic evoked responses are primary real-time objective measures of cognitive and perceptual processes in the human brain. Two mechanisms (additive activity and phase reset) have been debated and considered as the only possible explanations for evoked responses. Here we present theoretical and empirical evidence of a third mechanism contributing to the generation of evoked responses. Interestingly, this mechanism can be deduced entirely from the characteristics of spontaneous oscillations in the absence of stimuli. We show that the amplitude fluctuations of neuronal α oscillations at rest are associated with changes in the mean value of ongoing activity in magnetoencephalography, a phenomenon that we term baseline shifts associated with α oscillations. When stimuli modulate the amplitude of α oscillations, baseline shifts become the basis of a novel mechanism for the generation of evoked responses; the averaging of several trials leads to a cancellation of the oscillatory component but the baseline shift remains, which gives rise to an evoked response. We propose that the presence of baseline shifts associated with α oscillations can be explained by the asymmetric flow of inward and outward neuronal currents related to the generation of α oscillations. Our findings are relevant to the vast majority of electroencephalographic and magnetoencephalographic studies involving perceptual, cognitive and motor activity.

Introduction

Evoked responses (ERs) in magnetoencephalography (MEG) and electroencephalography are an important source of information about real-time neuronal processing in non-invasive studies of the human brain. Two different mechanisms for the genesis of ERs have been put forward, i.e. ERs may be additive to ongoing oscillations (Shah *et al.*, 2004; Mäkinen *et al.*, 2005; Mazaheri & Jensen, 2006) or they may result from a phase resetting of ongoing oscillations (Sayers *et al.*, 1974; Makeig *et al.*, 2002; Fell *et al.*, 2004; Hanslmayr *et al.*, 2007).

Here we present theoretical and empirical evidence of a third mechanism contributing to the generation of ERs. It is based on two prerequisites: (i) ongoing magnetoencephalographic/electroencephalographic oscillations are amplitude modulated by stimuli or tasks and (ii) oscillatory signals should have a non-zero mean, so that the mean amplitude of ongoing activity is modulated concurrently with the amplitude of oscillations. We denote the modulation of the mean amplitude of ongoing activity as 'baseline shift'. Whereas the oscillatory pattern disappears in the averaging of several trials because of phase cancellation, the associated baseline shift remains, leading to the appearance of ERs (Fig. 1A and B). Figure 1C and D illustrates the scenario of non-phase-locked oscillations with zero mean; opposite phases cancel out and no ERs are present after the averaging procedure.

The first prerequisite has been demonstrated in practically all experimental tasks, especially for α oscillations (Klimesch, 1999; Pfurtscheller & Lopes da Silva, 1999). To demonstrate the second prerequisite we show a systematic association of α oscillation amplitude with baseline shifts in data recorded at rest with no specific stimuli (Experiment 1). Secondly, we show empirical evidence that stimulus-induced amplitude changes of ongoing α oscillations indeed contribute to ERs as predicted from the first experiment. Baseline shifts associated with α oscillations are expected to contribute to ERs in many different experimental paradigms.

Materials and methods

Subjects and conditions

Eight healthy subjects (six males and two females; 20–34 years old; no history of neurological or psychiatric disorders) were measured with a 306-channel MEG system (Vectorview, Elekta Neuromag Oy, Helsinki, Finland) consisting of 204 planar gradiometers and 102 magnetometers; only the data from the gradiometers were used for the analysis. The signals were sampled at 900 Hz and digitized off-line to

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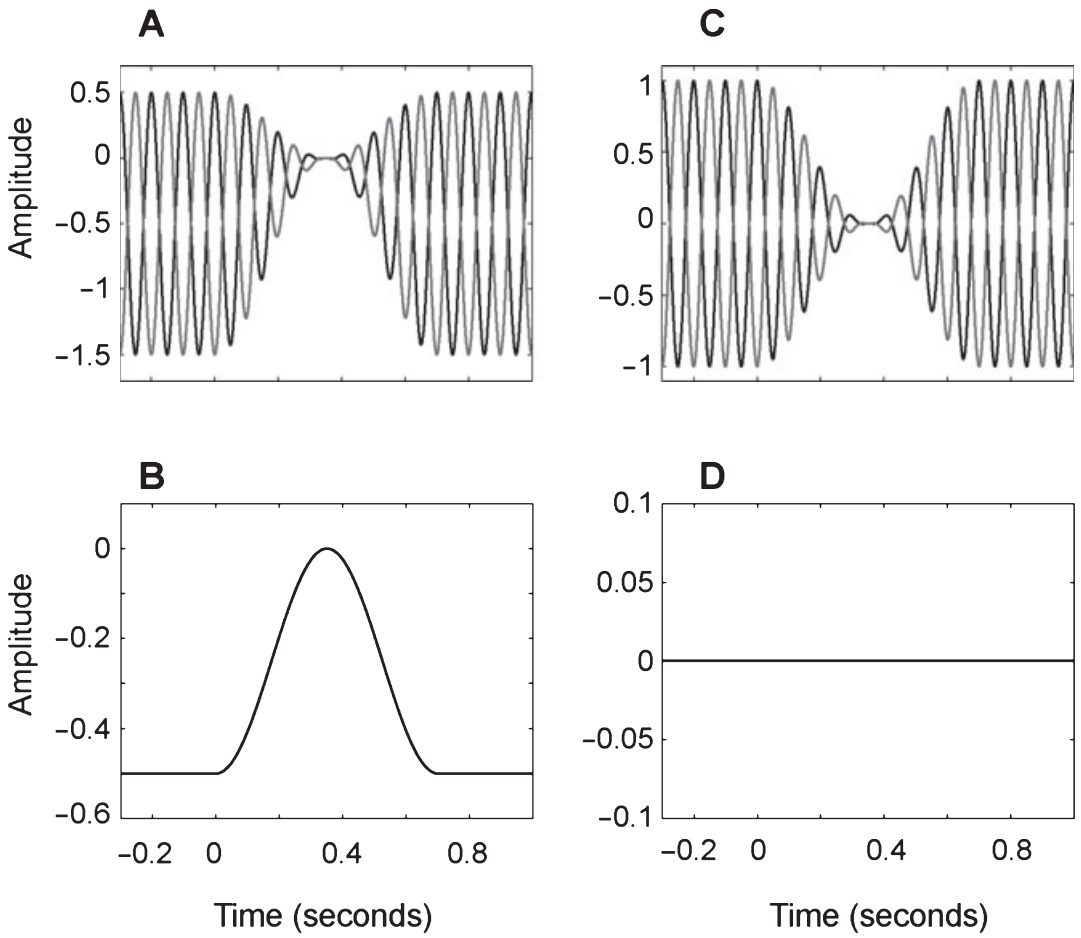


FIG. 1. Illustration of the mechanism for generation of evoked responses through an amplitude modulation of non-zero mean ongoing oscillations. (A) For simplicity only two trials in antiphase (in black and grey) are shown. Each trial consists of an amplitude-modulated 10-Hz cosine: A(t) [cos(2π f t) − 0.5], where A(t) is a modulating signal, $f = 10$ Hz and t is time. (B) Averaging of trials leads to a recovery of A(t) × offset, where offset is −0.5 in the current example. This curve shows a baseline shift, which constitutes an evoked response (ER). It should be emphasized that, in this scenario, ERs are not additive to the ongoing oscillations but result from the amplitude modulation of ongoing oscillations with non-zero mean. (C and D) As in A and B but offset is 0 and thus there is no ER after the averaging procedure.

300 Hz with the pass-band 0.1–100 Hz. In Experiment 1, the rest condition, the subjects were instructed to keep their eyes closed and sit still for 20 min. In Experiment 2, the stimulation condition, the left median nerve was stimulated at the wrist with an interstimulus interval of 3 s while the subjects had their eyes closed for 20 min; the intensity was sufficient to evoke a thumb twitch. The protocol was approved by the Ethics Committee of the Department of Radiology of the Helsinki University Central Hospital. An informed consent was obtained from the subjects. The study conforms to the code of ethics of the World Medical Associations.

Independent component analysis

The main challenge in the detection of a baseline shift related to a change in the amplitude of α oscillations in the absence of a stimulus (Experiment 1) is due to the fact that magnetoencephalographic recordings contain large-amplitude low-frequency fluctuations of a noisy origin. High-pass filtering is not a solution because it would not only filter out unwanted low-frequency noise but also the low-frequency baseline shifts. Independent component analysis (ICA) was used in order to remove low-frequency noise and extract components with the strongest α activity in the rest condition (Experiment 1). For magnetoencephalographic and electroencephalographic recordings, a linear decomposition used in ICA is a reasonable approach as the recorded signals represent a linear superposition of electromagnetic sources (Makeig *et al.*, 1997; Vigario *et al.*, 2000; Ziehe *et al.*, 2000). The measured signals can then be modelled as a linear combination of component vectors: $X = AS$ where X is the matrix with the recorded MEG, S are estimated independent components (ICs) and A is the mixing matrix. ICA provides a decomposition such that for N channels the data are explained as a superposition of N components. Each component is characterized by a (temporally fixed) spatial pattern and a (spatially fixed) time-course. One can regard the time-course as the activity of a specific source somewhere within the brain and the topography as the field/potential of that source with unit amplitude. Hence, if we display the time-course and topography, e.g. in Figs 2A and 3C and D, respectively, we display the two aspects (temporal and spatial) of one specific component.

The ICA approach used in the present study consists of a two-step procedure. First we used the temporal decorrelation source separation (TDSEP) algorithm (Ziehe *et al.*, 2000) in order to extract components with strong oscillatory activity in the 8–13 Hz frequency range. TDSEP is based on the idea of exploiting distinctive spectral/temporal characteristics of the sources via simultaneous diagonalization of covariance matrices with different time delays $\tau = 0, 1 \ldots 50$ samples in the present study. Ten ICs with the strongest contribution to the

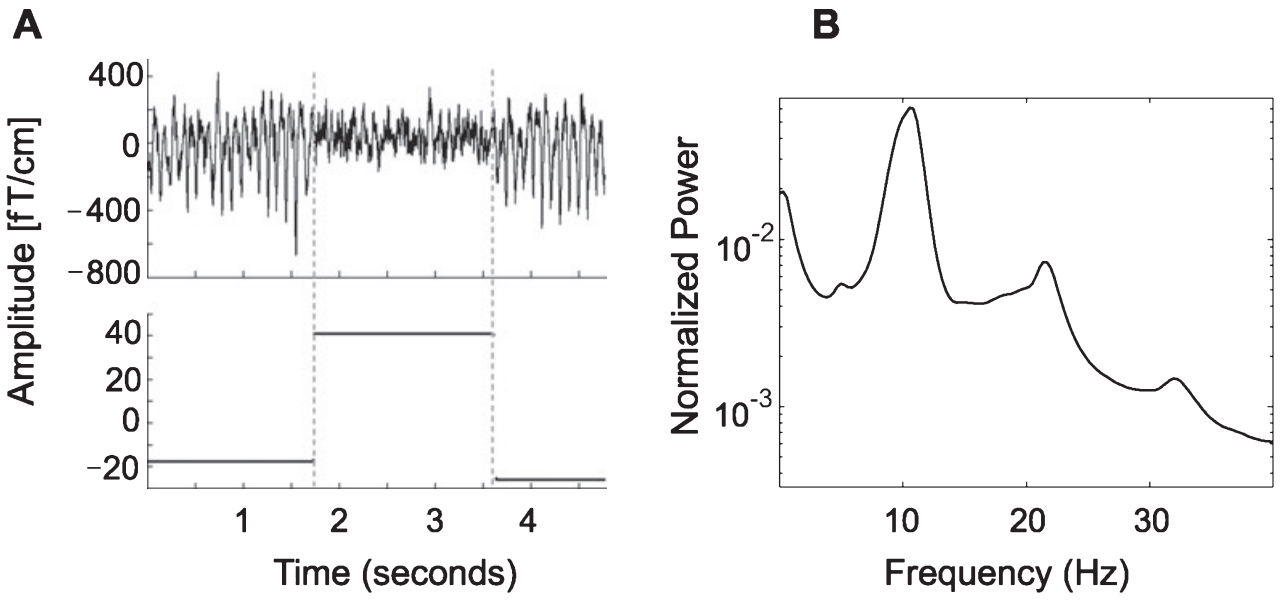


FIG. 2. Baseline shifts in ongoing oscillations. (A) Upper trace: spatially filtered (with independent component analysis) broadband signal from a channel above the right sensorimotor area during rest; lower trace: the mean values in three time intervals. Clearly, there are baseline shifts in the ongoing activity associated with α oscillations changing from large to small and back to large amplitude. If many epochs with similar amplitude dynamics are averaged, oscillatory patterns would disappear whereas the baseline shifts would remain leading to the appearance of an evoked response. (B) Grand average of normalized spectra from all independent components in all subjects. Vertical axis is logarithmic.

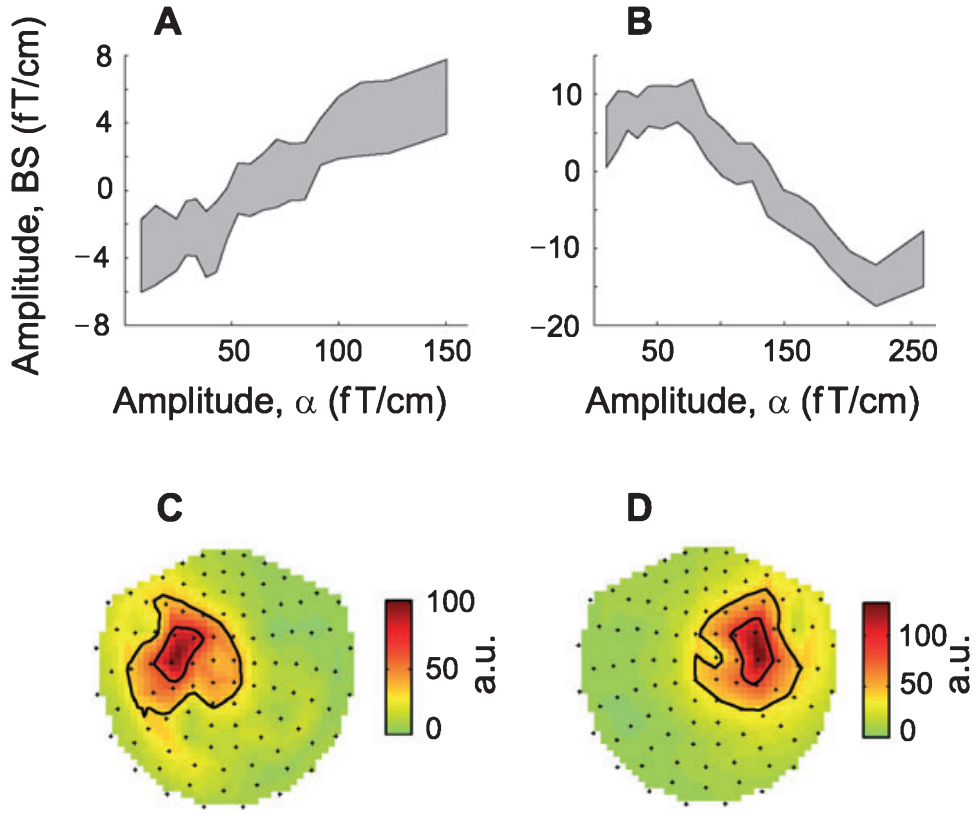


FIG. 3. An example of a relationship between the amplitude of α oscillations and baseline shifts (BS) in the rest condition. (A and B) 95% confidence interval for the relationship between α oscillations and baseline shifts calculated for 20-min signals (recorded at rest) in the channels above the left and right sensorimotor areas, respectively. (C and D) The topography of independent components related to A and B, respectively. The mapped values represent vector sums of the elements in the mixing matrix for each pair of orthogonal gradiometers. a.u., arbitrary units. Data from one subject.

α-frequency range were selected. For these components the ratio was calculated between the largest powers in the frequency ranges of 8–13 and 0–2 Hz. Only components with a ratio >0.8 (approx. seven components on average) were selected for further analysis in order to prevent a contribution of sources with large low-frequency oscillations in the subsequent analysis. A smaller ratio would lead to a more

dominant influence of the residual low-frequency noise, whereas a larger ratio would prevent many ICs entering into the subsequent FastICA analysis. The ratio of 0.8 represented a reasonable compromise between these two factors.

In the second step we used FastICA (Hyvärinen & Oja, 1997) for further decomposition of the selected subspaces. The main idea behind this is the observation that second-order methods, like TDSEP, are in principle only designed to separate components of different spectra. Therefore, it is expected that the α components found by TDSEP might still be a mixture of the true independent generators of α oscillations. A further decomposition of sources of the same spectra would thus require an exploitation of higher-order statistics, e.g. kurtosis, which was used as a contrast function in FastICA.

Blind source separation methods can be based on two different assumptions: either (i) source activities have a non-Gaussian distribution or (ii) the spectra of different sources are different. Therefore, one can expect that a suitable combination of methods based on these principles is of advantage if the data indeed have both properties, which is the case for real electroencephalographic or magnetoencephalographic data. Our method of first applying TDSEP, which separates sources with different spectra, and then applying FastICA, which separates non-Gaussian distributed sources, is such a combination. Importantly, the order matters and our decision not to combine both principles in a single step was driven by the needs of this specific problem. As FastICA (like any higher-order ICA method) is very sensitive to outlier samples, we first estimated a subspace of α activity, which is essentially free of outliers but cannot be reliably reduced further into single components because the spectra might be quite similar. Applying FastICA only to this subspace provides a reliable estimation of the individual components (note that it is not necessary that the components have different distributions as long as they are non-Gaussian), whereas at the same time outliers cannot re-enter the components.

Alpha oscillations were used in the present study because they have the largest signal-to-noise ratio in the spontaneous neuronal MEG/electroencephalography. It is plausible, however, that neuronal oscillations in other frequency bands (theta, beta and gamma) are also associated with baseline shifts.

Relationship between the amplitude of α oscillations and baseline shifts

The amplitude envelope (the modulus of an analytic signal) of α oscillations was extracted with band-pass filtering and the Hilbert transform. The filters (Butterworth filter, fourth order) were centred at the peak frequency of α oscillations separately for each IC and the width of the filter was 3 Hz. Baseline shifts were obtained by low-pass filtering the ICs with a 3-Hz cut-off frequency. Thus, the transformation of the *j*-th IC yielded two vectors $V_{j\alpha}$ and V_{jBS} that represent the time-courses of the instantaneous amplitude of α oscillations and baseline shifts, respectively. The values in each $V_{j\alpha}$ were sorted into 20 bins using 5-percentile amplitude steps. Samples in V_{jBS} were also sorted into 20 bins but according to the sorting of samples in $V_{j\alpha}$. The values in each of the bins were averaged for $V_{j\alpha}$ and V_{jBS}. A least-squares line was then fitted to capture the dependency between the amplitude of α oscillations and baseline shifts. In order to estimate the significance of the obtained slope, *b*, a bootstrap procedure was used. Each original $V_{j\alpha}$ and V_{jBS} was split into 20 non-overlapping segments of equal length and the new bootstrap sequences were created by random resampling from these segments with replacement. The order of segments was, however, identical in $V_{j\alpha}$ and V_{jBS} but these two vectors were different in each bootstrap sequence because of random selection of the segments. For each newly obtained $V_{j\alpha}$ and V_{jBS} the least-squares lines were determined. Altogether 200 bootstrap sequences were produced yielding 200 estimates of the slope *b*. The *P*-value for the slope was calculated according to:

$$P = 1 - erf\left(\frac{r}{\sqrt{2}}\right),$$

where $r = \left|\frac{\bar{b}}{\sigma_b}\right|$, and *erf* is the error function defined by:

$$erf(x) = \frac{2}{\sqrt{\pi}}\int_o^x \exp(-t^2)\,dt$$

The statistical evaluation was made for each IC thus leading to multiple testing in each subject. The Bonferroni correction was used to compensate for multiple tests. The corrected *P*-value was fixed at 0.05.

Evaluation of the amplitude dynamics of α oscillations and evoked responses in stimulation condition

For each gradiometer in the stimulation session the reactivity of α oscillations was evaluated using band-pass filtering and Hilbert transform as described above. Somatosensory evoked fields (SEFs) were also calculated. The number of epochs for each subject exceeded 300. Principal component analysis (PCA) was also performed on the averaged SEFs and on averaged stimulus-induced changes in the amplitude of α oscillations (phenomena also known in the literature as event-related desynchronization and synchronization). The reason for using PCA was to find long-latency components (200–600 ms) in SEFs that would have considerable overlap in time and space with the PCA components representing attenuation of sensorimotor oscillations caused by the median nerve stimulation. PCA was performed on the averaged data instead of ICA because ICA requires a large amount of data for a reasonable decomposition, which is only available for the raw data.

1 : 2 phase synchronization

If ϕ_α and ϕ_β are the phases of α and β oscillations, then the phase difference $\phi_{2\alpha-\beta}$ between 2α and β oscillations can be defined as:

$$\phi_{2\alpha-\beta} = 2\phi_\alpha - \phi_\beta$$

The cyclic relative phase (Rosenblum *et al.*, 2001) $\psi_{2\alpha-\beta}$ is defined as:

$$\psi_{2\alpha-\beta} = \phi_{2\alpha-\beta} \bmod (2\pi)$$

For each IC the peak in the distribution of $\psi_{2\alpha-\beta}$ is then obtained representing a phase shift between 2α and β oscillations. The band-pass filters for β oscillations were defined with cut-off frequencies $2\alpha_{peak} \pm 1.5$ Hz, where α_{peak} is the peak frequency of α oscillations from a given IC. The phases for both α and β oscillations were extracted using the Hilbert transform.

Results

Relationship between the amplitude of α oscillations and baseline shifts

Figure 2A shows a fragment of ongoing oscillations (spatially filtered with ICA) during eyes-closed rest (Experiment 1) from a planar gradiometer above the right sensorimotor region. The mean values of

periods with and without α oscillations are different thus creating baseline shifts, which in turn constitute a basis for ER. Subjects had on average three ICs (range one to eight) with a significant linear trend between the amplitude of α oscillations and baseline shifts. These ICs had a spatial distribution over the occipito-parietal areas in seven subjects and over the central areas in four subjects. Figure 3A and B shows the relationship between the amplitude of α oscillations and baseline shifts for two ICs. The corresponding spatial distributions of the ICs are presented in Fig. 3C and D. This relationship between α oscillations and baseline shift observed in the rest condition suggests that stimulus- or task-induced changes in the amplitude of α oscillations should also be accompanied by a baseline shift. Amplitude changes in ongoing activity that are related to baseline shifts will not average out to zero, contrary to the oscillatory part of α rhythm, which would disappear with increasing number of averaged epochs. Thus, the amplitude modulation of ongoing α oscillations may lead to the appearance of an ER.

Baseline shifts move toward the peaky part of α oscillations

The spectrum of the extracted ICs (Experiment 1) contained peaks in α and β frequency ranges (Fig. 2B), which is consistent with the 'comb-shaped' signals. The exact direction of the pointed part of these oscillations depends on the phase shift between the 2α oscillations and their harmonic in the β frequency range because comb-like signals can be represented as a sum of 10- and 20-Hz cosines with a specific phase shift. If this phase shift is in the proximity of 0 radians the sharp deflections in the oscillations are pointing upward (Fig. 4A), whereas the phases close to π (–π) radians are associated with the sharp deflections pointing downwards (Fig. 4B). The dominant phase shift is determined from the histograms of the cyclic relative phase (Fig. 4C and D). If the slope of the line, characterizing the relationship between α oscillations and baseline shifts, depends on the shape of the signal, one should observe a correspondence between the sign of the slope and the phase shift between 2α and β oscillations. Figure 5 shows that

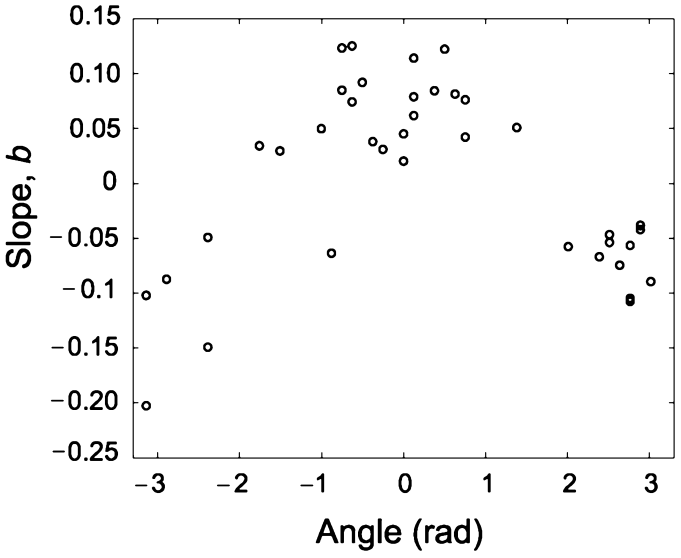


FIG. 5. The phase difference between 2α and β oscillations determines whether α oscillation amplitudes and baseline shifts are positively or negatively correlated. The data are for independent components from eight subjects.

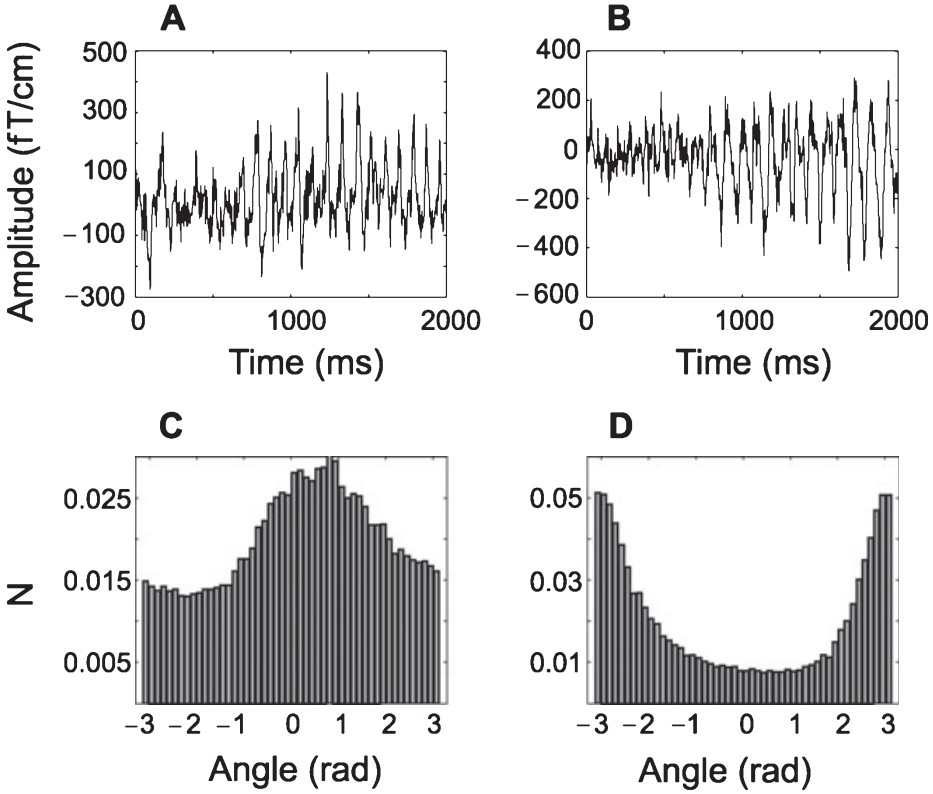
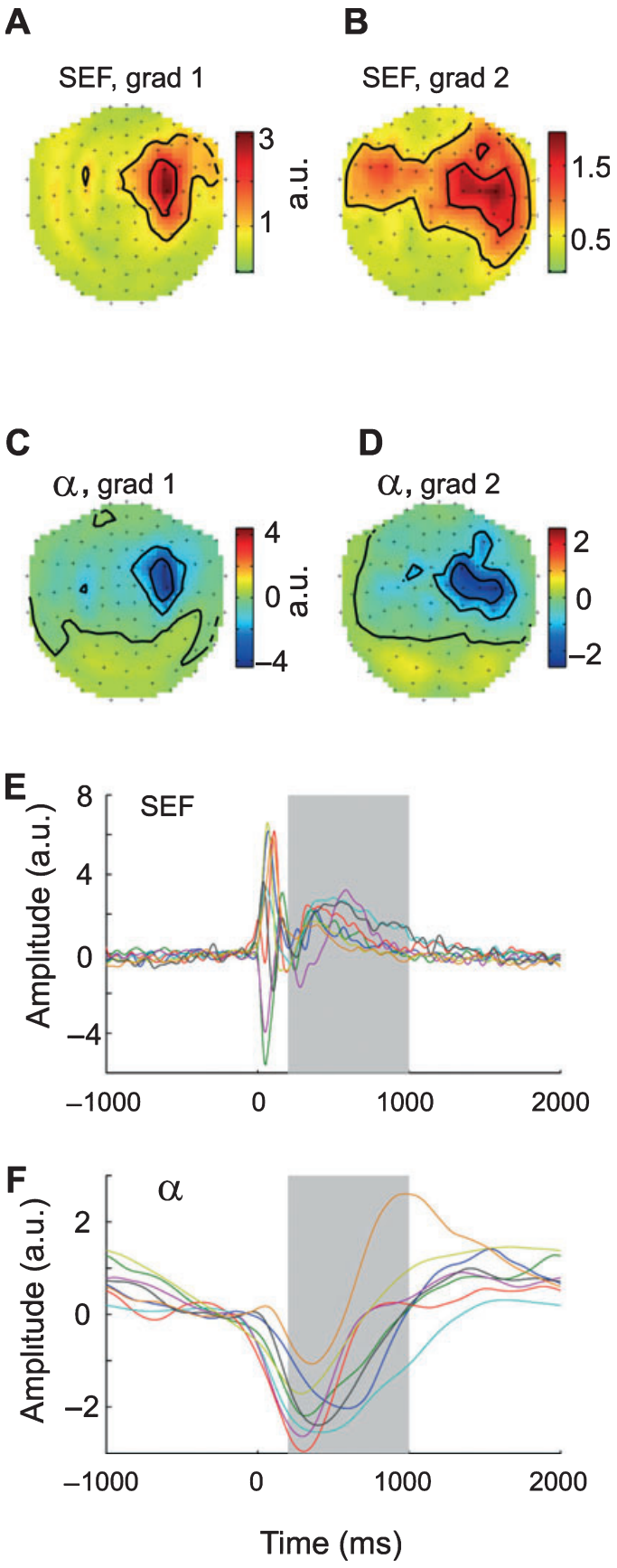


FIG. 4. The shape of α oscillations depends on the phase difference between 2α and β oscillations. (A and B) Fragments of spontaneous oscillations from two independent components. (C and D) Normalized histograms representing the distribution of phase difference between 2α and β oscillations, corresponding to the signals depicted in A and B, respectively.



the slope of the least-squares lines indeed depends on the phase shift between 2α and β oscillations, indicating that the baseline shifts are positively correlated with α oscillation amplitudes for phase differences between −1.5 and 1.5 radians, whereas the baseline shifts are negatively correlated with α oscillations if the absolute value of the phase difference is > 2 radians. In other words, the baseline shift tends to move toward the peaky part of α oscillations.

Evoked responses and the event-related changes in the amplitude of sensorimotor α oscillations to median nerve stimulation

The main prediction following from the existence of a relationship between α oscillations and baseline shifts is that the amplitude modulation of ongoing α oscillations should lead to the generation of ER.

In Experiment 2 with median nerve stimulation we identified a clear late SEF component in all subjects, which coincided in time with the pronounced attenuation of sensorimotor α oscillations caused by the median nerve stimulation. The spatial patterns of PCA components (related to SEFs) containing a late deflection at about 300–600 ms are shown as a grand average in Fig. 6A and B and spatial patterns of PCA components related to the amplitude attenuation of α oscillations, induced by the median nerve stimulation, are displayed in Fig. 6C and D. The individual time-series traces corresponding to the spatial components of SEFs and of α oscillation attenuation are shown in Fig. 6E and F, respectively. The largest amplitude of the late SEF component and the largest attenuation of α oscillations had similar spatial distribution and were primarily localized over the right sensorimotor area (contralateral to the stimulated median nerve).

Discussion

The results of the present study show that ongoing α oscillations have a non-zero mean and the amplitude modulation of α oscillations is therefore associated with baseline shifts in broadband ongoing activity. Figure 1 provides a theoretical basis for the generation of ERs through the amplitude modulation of α oscillations with non-zero mean. From the relationship between α oscillation amplitudes and the baseline shift, which was obtained in experiments without stimuli, it naturally follows that a stimulus-evoked transient change in the amplitude of α oscillations directly translates into a shift in the baseline, generating an ER. To verify this theoretical prediction, the second experiment employed median nerve stimulation. Indeed, we

FIG. 6. Principal component analysis of somatosensory evoked fields and attenuation of α oscillations induced by the median nerve stimulation. (A and B) Two sets of orthogonal gradiometers showing grand average (across all subjects) spatial topographies of principal components related to the late somatosensory response at about 250–600 ms. As we are interested in the magnitude of the late responses rather than their phase, spatial topographies were rectified before the averaging. Grad 1 and grad 2 represent two sets of gradiometers measuring two different planar (i.e. tangential to the inner dewar surface) derivatives of the radial field component. (E) Time-course of individual components for somatosensory evoked fields (SEFs) (one curve for each subject). These individual curves were normalized to have a unity variance. For visualization purposes the curves are plotted with late SEF component pointing upward. (C and D) Gradiometers as in A and B but the grand average topographies are for the amplitude dynamics of α oscillations induced by median nerve stimulation. Negative values and positive values correspond to attenuation and enhancement of α oscillations, respectively. (F) The time-courses of individual components (one curve for each subject). a.u., arbitrary units.

observed a low-frequency late component that matched the spatial topography and temporal profile of the amplitude-attenuated sensorimotor α-band oscillations. The fact that baseline shifts have been demonstrated for spontaneous α oscillations implies that they should influence the generation of any ER regardless of modality or nature of the task when modulation of these oscillations is present. In this respect, one should mention that virtually all experiments involving sensory stimulation, motor or cognitive activity lead to the amplitude changes of α oscillations. Contrary to the classical additive mechanism of ERs, which treats ongoing neuronal oscillations as noise that cancels out during the averaging of several trials, the amplitude dynamics of α oscillations play a pivotal role in the generation of ERs via the baseline shifts associated with α oscillations.

Spatial aspects of the relationship between α oscillations and baseline shifts

Intracortical recordings in humans show that α oscillations have a spatial structure on a millimetre scale, as revealed by a rapidly decaying coherence between the neighbouring electrodes (Bullock *et al.*, 1995). MEG and electroencephalography have relatively low spatial resolution and the sensors therefore detect neuronal oscillations originating from multiple neuronal populations with potentially different phases, which inevitably attenuate magnetic fields or electric potentials of α oscillations. Interestingly, however, the associated baseline shift does not necessarily attenuate because it only depends on the amplitude of the oscillations and not the phase. Therefore, it may even be possible to record ERs based on the baseline shifts associated with α oscillations without actually detecting significant changes in the amplitude of macroscopic α oscillations. Thus, the baseline shifts associated with α oscillations might be captured in the measured signals only partially because of the superposition of multiple sources of α oscillations in the MEG sensors. The detection of a baseline shift also depends on how well low-frequency noise can be removed with spatial filtering. Extracted ICs are still likely to contain residual low-frequency noise leading to an underestimation of the relationship between α oscillations and baseline shifts. Also, a more complete evaluation of baseline shifts associated with spontaneous neuronal oscillations would require DC recordings.

It has been pointed out previously in experiments with functional magnetic resonance imaging (fMRI; Brookes *et al.*, 2005) that if the drop in the amplitude of α oscillations corresponded mainly to a phase desynchronization of α sources then one would not observe a strong modulation of fMRI signals related to the amplitude modulation of α oscillations, whereas a significant change in the number of neurons, participating in the generation of α oscillations, would lead to a modulation of fMRI signals, which has been observed in a number of studies (Singh *et al.*, 2002; Moosmann *et al.*, 2003; Feige *et al.*, 2004). Thus, baseline shifts are likely to reflect changes in the number of neurons participating in the generation of α oscillations.

Neurophysiological explanation for the presence of baseline shifts

The most commonly accepted theory for the genesis of α oscillations states that they are generated as a result of interactions between the thalamus and cortex (Lopes da Silva *et al.*, 1980; Bouyer *et al.*, 1983; Steriade & Llinas, 1988; Hughes *et al.*, 2004). Rhythmic activity originates in the thalamus and then thalamocortical neurones project to the cortex evoking excitatory postsynaptic potentials (EPSPs) in the pyramidal cells. These EPSPs are largely generated through glutamate synapses (Salt *et al.*, 1995; Krukowski & Miller, 2001), which are associated with strong inward currents. Thalamocortical synapses are mostly located on the dendrites close to the soma of the pyramidal cells (Creutzfeldt, 1995; Douglas *et al.*, 2004) and, because of such asymmetric placement, the inward EPSP currents should flow toward and along the apical dendrites. However, the repolarization of the membrane potential is associated with the outward currents flowing in different directions because potassium channels (primarily responsible for repolarization) are uniformly distributed across the soma and apical dendrite (Bekkers, 2000; Benhassine & Berger, 2005). Therefore, currents related to EPSP and repolarization are unlikely to produce magnetic fields that counterbalance each other when summated over a few α oscillations periods. Consequently, α oscillations should be associated with non-zero mean magnetic fields and electric potentials.

The EPSPs usually have a rapidly rising phase and much slower falling phase (McCormick, 2004), which relates to the dynamics of different trans-membrane currents, thus leading to rhythmic but not strictly sinusoidal magnetoencephalographic or electroencephalographic activity during α oscillations. As baseline shift is also associated with the succession of postsynaptic potentials, one would expect to see a certain correspondence between the shape of α oscillations and the direction of the baseline shift. In agreement with this prediction, we observed a correspondence between the shape of α oscillations (reflected in the phase difference between 2α and β oscillations) and the baseline shifts. Negative or positive slopes of the relationship between α oscillations and baseline shift probably relate to the fact that neuronal oscillations reflect activity of a dipolar generator and, depending on the position of the sensors with respect to the sources of α oscillations, the slope can be either positive or negative.

Baseline shifts and evoked responses

The spatial topographies of PCA components with a late SEF and components with attenuation of sensorimotor α oscillations were very similar and so were the temporal profiles of these components (Fig. 6). Taken together, these results provide strong support for the idea that the baseline shifts associated with α oscillations can contribute to the generation of ERs. A precise correspondence between the time-courses of ERs and the amplitude dynamics of α oscillations is hardly achievable because ERs usually represent a mixture of components from different sources, which is likely to obscure the contribution of the baseline shifts especially in the early latency range ($< \sim$300 ms). Moreover, analysing the amplitude dynamics of α oscillations requires a narrow band-pass filtering, which gives rise to temporal smoothing, whereas ERs based on the baseline shifts associated with α oscillations may have a steep onset if the change in α amplitude is abrupt (Fig. 2).

The observation that the amplitude modulation of α oscillations usually overlaps in time and space with ERs suggests that the baseline shifts commonly contribute to ERs. In some paradigms the correspondence between the amplitude dynamics of α oscillations and ERs is especially pronounced, e.g. for movement-related responses (Toro *et al.*, 1994; Feige *et al.*, 1996; Babiloni *et al.*, 1999; Stancak *et al.*, 2000; Bai *et al.*, 2005) and contingent negative variation (Magnani *et al.*, 1998; Bender *et al.*, 2004). A recent magnetoencephalographic study also demonstrated a remarkable similarity between the time-courses of a sustained visual ER and α rhythm attenuation in the visual cortex (Brookes *et al.*, 2005). Most of the frequency content of the baseline shifts associated with α oscillations is expected to be below α frequencies and depends on the temporal profile of modulation of

α oscillations. However, if the attenuation of spontaneous α oscillations is very steep then even early evoked components can have a contribution from an additional offset produced by the baseline shifts.

Although a modulation of α oscillations in many cortical areas is not considered unusual, a broad cortical distribution of ERs to the stimuli is not expected as ERs are traditionally associated with the neuronal events restricted to specific cortical areas. In a recent magnetoencephalographic study (Bauer *et al.*, 2006), tactile stimuli were shown to produce ERs in the occipital areas, which would be counterintuitive to the conventional understanding of where tactile information is processed. However, the novel mechanism suggests that ERs can be broadly distributed because of the spatially generalized modulation of ongoing oscillations, which is also present in the occipital areas.

Understanding the neuronal mechanisms that contribute to the waveform of ERs is of fundamental interest to a broad range of fields in the neurosciences and the novel mechanism has some intriguing consequences for the interpretation of ERs. Whereas ERs that are generated through an additive mechanism imply that specific neuronal activations have taken place, the baseline shifts associated with α oscillations imply that ERs may be created through the same mechanisms that cause amplitude modulation of ongoing α oscillations. Thus, the transient suppression of α and any other neuronal activity could also be the cause of ERs. In general, ERs are likely to be generated through a mixture of different processes and, whereas the major part of ERs might stem from the additive mechanism, the baseline shifts that are produced by amplitude dynamics of α oscillations will contribute additionally to the ERs.

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Abbreviations

EPSP, excitatory postsynaptic potential; ER, evoked response; IC, independent component; ICA, independent component analysis; MEG, magnetoencephalography; PCA, principal component analysis; SEF, somatosensory evoked field; TDSEP, temporal decorrelation source separation.

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