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Auditory Evoked Responses Are Additive to Brain Oscillations

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ABSTRACT

The generation mechanism of stimulus-evoked electro- and magnetoencephalographic (EEG & MEG) responses has remained controversial. One view holds that evoked responses are independent components, additive to ongoing brain activity. The other view holds that evoked responses are generated via stimulus-induced phase reorganization of ongoing brain activity. This issue has been commonly addressed with signal processing techniques that assume a high level of stationarity (i.e., unchanging properties over time) of the measured signal. Here we used signal analysis methods suitable for analyzing non-stationary signals. We found that auditory stimulation leads to a large power increase of the poststimulus signal compared to prestimulus level. Linear superposition of the (time-domain) averaged response and the unaveraged prestimulus signal accounted for 90% of the power increase. Further, we found that auditory stimulation does not lead to a phase-coherent state of ongoing oscillations. Taken together our results show that auditory evoked responses are directly additive to ongoing oscillations and only 10 % of the observed power increases are explained by non-phase-locked brain activity. When examining evoked brain activity with methods providing simultaneous frequency and time information, emphasizing temporal accuracy is likely to provide more accurate descriptions of non-stationary processes of the human brain.

KEY WORDS

Auditory, Evoked responses, Electroencephalography, Magnetoencephalography, Ongoing oscillations, Phase estimation, Spectral estimation, Stationarity.

INTRODUCTION

The neural underpinnings of human sensory and cognitive processes can be non-invasively explored with MEG and EEG through stimulus-evoked brain responses. The human brain, however, displays ongoing oscillatory signals in MEG and EEG even without sensory stimulation. One possibility is that evoked responses are the result of stimulus-induced phase synchronization of ongoing oscillations [Sayers, 1974] [Makeig, 2002] [Jansen, 2003] [Klimesch, 2004]. The alternative possibility is that evoked responses are separate from and additive to ongoing oscillations. The examination of this issue is intimately tied to the methodology used for the analysis. Most established signal analysis methods are based on the theory of statistical signal processing [e.g. Hayes, 1996], where signals are commonly assumed to be stationary (i.e., their statistical properties do not change over time). Recent methods such as wavelet and short-time Fourier transforms (FTs) are well suited for the analysis of quasistationary signals such as ongoing brain oscillations which are approximately stationary over some short time window. However, when these methods are applied to transient brain responses - which (by definition) are neither stationary nor quasistationary - misinterpretations may result.

FT-based spectral analysis tools are widely available and they have been used for examining whether EEG or MEG signal power is affected by sensory stimulation. However, the results of the analysis are affected by how the data is preprocessed (e.g., in terms of the length of the analyzed time window, the weighting window, etc.). Further, although FT-based spectral estimation provides accurate analysis of stationary signals only, negative results have been used as evidence of the absence of additive components to ongoing brain oscillations [Sayers, 1974] [Makeig, 2002]. It is, however, possible to measure the power of a signal with minimal *a priori* assumptions and without spectral estimation; the power of a signal is defined as its integrated squared magnitude and filtering can be used to focus on the frequency band of interest. Here we evaluated the effect of auditory stimulation on MEG power with this method and examined the averaged auditory responses as an explanatory factor of the power changes.

The question of the generation of evoked responses has also been approached through measuring intertrial coherence (ITC), i.e., the phase distribution of MEG or EEG signals over trials [Makeig, 2002]. This analysis method focuses on narrow frequency bands and specific brain rhythms. The principle of time-frequency uncertainty [Gabor, 1946] [Gröchenig, 2001], however, dictates that with narrow frequency bands events accurately localized in time become dispersed and affect the power and phase of the signal far from their actual latency of occurrence, thus distorting the results. We have previously introduced a method for evaluating ITC without requiring strict limiting of the frequency band [Mäkinen, Submitted] and the issue is further elaborated on here.

METHODS

Ten healthy human subjects were studied with their informed and written consent. The study was approved by the Ethical Committee of Helsinki University Central Hospital. The measurements were carried out in a magnetically shielded room with a 306-sensor MEG device (Vectorview, Elekta Neuromag Oy, Finland). The subjects watched a silent film and were under instruction to ignore the auditory stimuli. The stimuli were 750-Hz tones of 50-ms duration with 5-ms linear onset and offset ramps. The stimuli were adjusted to 80 dB (sound pressure level, A-weighted) and presented 800 times using an onset-to-onset interstimulus interval of 1200 ms. The data were collected using a sampling rate of 600 Hz and a pass-band of 0.03–200 Hz. The data were divided into 1200-ms epochs (starting 400 ms before stimulus onset) and epochs coinciding with >100 μV EOG amplitudes were excluded from analysis. Epochs were also rejected if their mean variance over all sensors (1-200 Hz band) exceeded two standard deviations (SD; calculated over all trials).

For each subject, data was analyzed using the sensor which displayed the N100m response of largest amplitude. The data was filtered with Chebyshev type-II filters optimized for maximal steepness of transition from pass-band to stop-band. Stop-band attenuation was set to 40 dB and two-way zero-phase filtering was employed. The signal was band-limited to 4–40 Hz for the examination of ITC, which was evaluated as the SD of signal amplitudes over trials calculated at each time point of the epoch. The mean of the –400...0 ms prestimulus values was used as the baseline SD and the mean of values over 75…125 ms was used as the SD of the N100m. Signal power was calculated from the unaveraged data

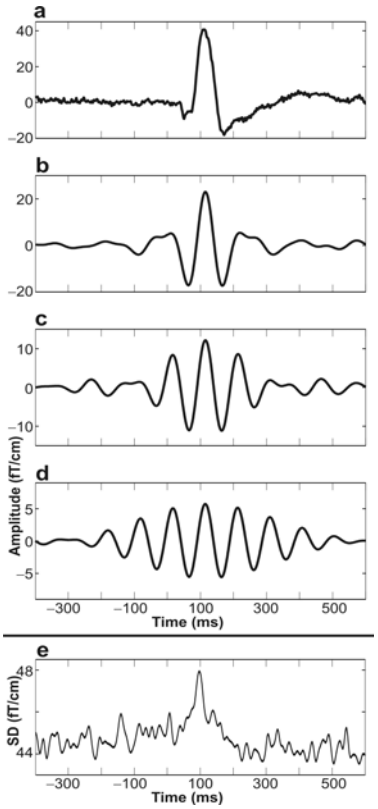

Figure 1. The grand-averaged auditory MEG response **a**) unfiltered or limited to **b**) 6–14 Hz **c**) 8–12 Hz **d**) 9-11 Hz pass-bands and **e**) the trial-to-trial amplitude variance over time.

(4–40 Hz pass-band) as the mean of the squared signal in 250-ms pre- and poststimulus time windows. The same frequency band and time windows were used with the superposition of averaged responses to the unaveraged prestimulus data. Statistical significance was evaluated with t-tests.

RESULTS

Auditory stimulation elicited a prominent N100m response peaking around 100 ms from stimulus onset (Fig. 1a; unfiltered data). The response was sharp and well localized in time thus resembling an impulse response, which has energy at all frequencies. When the frequency band of the response is limited the response inevitably spreads in time (Fig. 1b-d). Narrow-band filters and wavelets are often used in the analysis of signal phase and ITC. Yet, as demonstrated in Fig. 1b-d, although the unfiltered signal is a transient deflection it determines the phase of the oscillatory response manufactured by the filtering. Therefore, to analyze the ITC properly one must use a sufficiently wide frequency band in which case the ITC evaluation can be performed through analysis of the intertrial amplitude variance over time. To elaborate, a stimulus-induced phase coherent state of oscillation is analogous to an amplitude coherent state and can be seen as a reduction of the trial-to-trial amplitude variance compared to baseline. However, we observed an increase of 5 % ($t[9] = 2.9$, $P < 0.01$) in the amplitude variance at the latency of N100m (Fig. 1e). Thus, the ongoing oscillations are not in a coherent state at this latency.

Auditory stimulation increased the poststimulus signal power of the unaveraged data in the 4–40 Hz frequency band by 27 % ($t[9] = 3.4$, $P < 0.01$) and a direct linear superposition of the averaged response and the unaveraged prestimulus data, separately carried out for each subject, accounted for 90% of the power increases.

DISCUSSION

Here we observed that no phase synchronization of ongoing oscillations accompanies the emergence of auditory evoked responses in MEG, corroborating our previous results obtained with spatially filtered data [Mäkinen, Submitted]. The slightly increased incoherence of amplitude is explained by the trial-to-trial amplitude variance of the N100m response which is additive to that of the ongoing oscillations. Analysis of signal power, based directly on the definition of signal energy, revealed prominent power increases produced by auditory stimulation. Only 10 % of these increases were explained by changes in non-phase-locked brain responses. Thus, 90 % of the auditory evoked processes are accounted for by the waveform observed with stimulus time-locked averaging being additive to ongoing oscillations.

Methods intended for analyzing stationary periodic data (e.g. narrow-band filters) will unavoidably provide inaccurate results on non-stationary signals such as evoked responses. More generally, signals generated by the brain have both time and frequency aspects and, depending on the emphasis of the analysis, very different descriptions can be obtained from the same data. For example, wavelets with a high temporal resolution yield information on the properties of each evoked response, whereas wavelets with high frequency resolution reflect the temporal distribution of different evoked responses [Mäkinen, In press]. The question whether a signal yields more meaningful information in the frequency (i.e. rate) or time domain is important for analysis of EEG and MEG data but might also hold the key for understanding the neural code on the single-cell level.

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