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Effects of mnemonic load on cortical activity during visual working memory: Linking ongoing brain activity with evoked responses

Tjeerd W. Boonstra [a,b,c,*], Tamara Y. Powell [a,b,d], Saeid Mehrkanoon [a,b], Michael Breakspear [a,b,d,e]

[a] School of Psychiatry, University of New South Wales, Sydney, Australia
[b] Black Dog Institute, Sydney, Australia
[c] Research Institute MOVE, VU University Amsterdam, The Netherlands
[d] Queensland Institute of Medical Research, Brisbane, Australia
[e] Royal Brisbane and Women's Hospital, Brisbane, Australia

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ABSTRACT

The mechanisms generating task-locked changes in cortical potentials remain poorly understood, despite a wealth of research. It has recently been proposed that ongoing brain oscillations are not symmetric, so that task-related amplitude modulations generate a baseline shift that does not average out, leading to slow event-related potentials. We test this hypothesis using multivariate methods to formally assess the co-variation between task-related evoked potentials and spectral changes in scalp EEG during a visual working memory task, which is known to elicit both evoked and sustained cortical activities across broadly distributed cortical regions. 64-channel EEG data were acquired from eight healthy human subjects who completed a visuo-spatial associative working memory task as memory load was parametrically increased from easy to hard. As anticipated, evoked activity showed a complex but robust spatio-temporal waveform maximally expressed bilaterally in the parieto-occipital and anterior midline regions, showing robust effects of memory load that were specific to the stage of the working memory trial. Similarly, memory load was associated with robust spectral changes in the theta and alpha range, throughout encoding in posterior regions and through maintenance and retrieval in anterior regions, consistent with the additional resources required for decision making in prefrontal cortex. Analysis of the relationship between event-related changes in slow potentials and cortical rhythms, using partial least squares, is indeed consistent with the notion that the former make a causal contribution to the latter.

1. Introduction

The relationship between ongoing activity and evoked responses has been a matter of debate for several decades. Two alternative mechanisms (additive activity and phase reset) have been widely debated as possible mechanisms for the generation of evoked responses (Boonstra et al., 2006; Fell et al., 2004; Makeig et al., 2004; Mäkinen et al., 2005; Sayers et al., 1974). In the classic additive model, afferent activity is linearly added to ongoing brain activity – which is treated as noise – and can be hence extracted by averaging across trials, suppressing the contribution from background activity that is not phase-locked to the stimulus. In contrast, the phase-reset model states that a stimulus induces a partial alignment of the phases of ongoing brain oscillations. Accordingly, averaging these phase-aligned oscillations over trials will result in an ERP. Although both models suggest opposing mechanisms for the generation of ERPs, they appear difficult to distinguish in experimental data (e.g., Ritter and Becker, 2009).

Recently, a third generative mechanism for event-related potentials has been proposed. Ongoing brain oscillations may not be symmetric: the peaks and troughs may have a different magnitude such that oscillations have a non-zero mean. Changes in the amplitude of ongoing oscillations will therefore result in a baseline shift that will not average out (Mazaheri and Jensen, 2008; Nikulin et al., 2007, 2010). This model implies that slow event-related responses are created as a direct consequence of amplitude modulations in brain oscillations. Indeed, a recent study showed that the cognitive modulations of alpha power and event-related responses were strongly correlated over subjects (van Dijk et al., 2010). Whereas the additive and phase-resetting models focus on early evoked components, the amplitude asymmetry model particularly focuses on late occurring components. Asymmetric alpha activity may result from an asymmetry of the intracellular currents that propagate forward and backward down the dendrites (Mazaheri and Jensen, 2010). Indeed, EEG and MEG signals are generally thought to result from these dendritic currents in pyramidal cells (Hamalainen et al., 1993). Mazaheri and Jensen (2010) point out that amplitude asymmetry can thus easily arise from physiological models of oscillatory activity and posit that amplitude asymmetry may in fact be the norm and amplitude symmetry the exception.

* Corresponding author at: School of Psychiatry, Black Dog Institute Building, Hospital Road, Randwick, NSW 2031, Australia. Tel.: +61 2 9382 8375; fax: +61 2 9382 8208.
E-mail address: t.boonstra@unsw.edu.au (T.W. Boonstra).

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Multivariate analysis techniques are particularly suitable to disambiguate the contribution of these alternative mechanisms underlying event-related potentials (Turi et al., 2012). The causal link between amplitude modulations and event-related responses will manifest itself as consistent correlations across channels. The redundant information can be exploited by multivariate techniques to reliably quantify these relationships. In this paper we directly test the predicted correlations between amplitude modulations in ongoing brain oscillations and slow event-related responses using partial least squares (PLS). PLS is a regression technique that captures the covariance structure between two multidimensional data sets into orthogonal modes (McIntosh and Lobaugh, 2004). We use the event-related changes in the amplitude of oscillations at different frequencies as multivariate contrast, or latent variable, to predict the observed event-related potentials. In particular, we investigate the correlations between the experimental changes in both event-related activities to test the hypothesis of asymmetric amplitude modulations.

We acquired scalp EEG from healthy participants performing a visual working memory (VWM) task across three levels of difficulty by parametrically increasing mnemonic load. Visual working memory is a key cognitive process that involves active encoding, retention and retrieval of information in distributed cortical networks. Stimulus encoding occurs principally in posterior cortical regions, whereas strategy, working memory and decision making derive from prefrontal cortex (Kochan et al., 2011). The variety of processes and regions underlying VWM hence appeals as an attractive paradigm in which to study traditional ERPs, event-related spectral changes, and their relationship (Freunberger et al., 2009, 2011; Mitchell and Cusack, 2011). We decomposed event-related data into raw potentials and their spectra and studied the effect of memory load in each domain separately. Finally, we used partial least squares to study patterns of co-variation across scalp regions and frequency content.

2. Materials and methods

2.1. Participants

Eight healthy volunteers (four females, mean age 24.9, SD 4.0) with no history of neurological or psychiatric disorders, participated as paid volunteers in this study. Informed consent was given in accordance with the National Health and Medical Research Council guidelines and the Human Research Ethics Committee of The University of New South Wales.

2.2. Experimental design

Subjects were seated in a light and sound attenuated room and completed an event-related visual working memory (VWM) paradigm that manipulated mnemonic load in a parametric manner. Individual trials had a duration of 24 s, broken into 4 segments of 6 s duration (Fig. 1, top row): A fixation cross was shown from 0 to 6 s ('fixation'); An encoding stimulus was shown from 6 to 12 s ('encoding'); then a fixation cross from 12 to 18 s ('retention'); and finally a retrieval stimulus ('retrieval'). Each stimulus (encoding and retrieval) consisted of a combination of target pictures and nondescript background fillers on a background. Subjects were requested to press the right button during retrieval if one or more of the pictures that appeared during encoding re-appeared in the same location on the grid, or press the left button if not. We used a library of images from the public domain that do not lend themselves easily to verbal naming. Picture stimuli consisted of abstract, multi-colored designs obtained from an online database (Barbeau, E.J.: http://cerco.ups-tlse.fr/~barbeau/, accessed November 2005). Images and locations were randomized to ensure an even presentation of true and false outcomes. By manipulating the ratio of target pictures to background fillers, *memory load* was parametrically increased from easy (1 target, 5 fillers) to medium (3 targets, 3 fillers) and hard (5 targets, 1 filler) while keeping the visual load and visual scan path constant. The retrieval stimulus consisted of the same number of target pictures and background fillers as the encoding stimulus. Subjects undertook 24 trials of each level of difficulty with a total of 72 trials.

2.3. Data acquisition

Scalp EEG data were acquired from 64 channels using BrainAmp MR Plus amplifiers (Brain Products, Munich, Germany, hardware bandpass filter 0.1–250 Hz, resolution 0.1 μV, range +/− 3.3 mV) and custom electrode caps (Easy Cap, Falk Minnow Services, Herrsching–Breitbrunn, Germany) arranged according to the international 10–20 system. All data were referenced against an electrode centered on the midline between Fz and Cz and sampled at 5 kHz. Electrode impedances were kept below 5 kΩ. The electrooculogram and two electrocardiogram channels were also recorded. Responses were recorded with custom-made response buttons, which subjects had to press with the left or right index finger. All EEG channels were re-referenced to their mean signal and artifact correction was performed using independent component analysis (Jung et al., 2000). Subsequently, EEG data were low-pass filtered at 35 Hz and down sampled to 2 kHz for further analysis.

2.4. Data analysis

Task-related EEG activity was characterized by conventional ERP analysis to investigate time-locked changes in scalp voltage, and by time-frequency decomposition to assess changes in oscillatory power that reflect event-related synchronization (ERS) and desynchronization (ERD) of a cortical population (Neuper and Pfurtscheller, 2001; Pfurtscheller and Lopes da Silva, 1999). Partial least squares (PLS) analysis was then used to investigate whether changes in oscillatory power co-vary with changes in evoked responses. If ongoing brain oscillations have a non-zero mean, changes in oscillatory power will result in a DC shift in the ERPs, hence predicting correlations between both types of responses.

ERPs were calculated using stimulus onset times as event-defining indices. A baseline period of 750–250 ms prior to the presentation of the first fixation cross was used. Trials were averaged separately for each condition. Oscillatory power was estimated using short-time Fourier transform with a sliding time window (0.5 s Hamming window, 20 ms time step). Windowed data were Fourier transformed and the power spectral densities were averaged across trials. The spectra were then baseline-corrected using data in the time window of 750–250 ms before target onset. To normalize for inter-subject variance, oscillatory power was expressed as the percentage of baseline. Baseline power spectra were averaged over all conditions resulting in a single reference power spectrum for each subject and channel (cf. Manganotti et al., 1998).

2.5. Multivariate analysis

Multivariate techniques such as principal component analysis (PCA) have been commonly used to assess changes in event-related EEG activity (Barry et al., 2011; Boonstra et al., 2005, 2007; Kayser and Tenke, 2003; Spencer et al., 2001). Here we use partial least squares to investigate the covariance structure between multi-channel ERPs and changes in oscillatory power across channels. PLS is a regression technique, which decomposes the original data into orthogonal modes that account for that part of the covariance structure that correlates with a specified design matrix or contrast (Langdon et al., 2011; Lobaugh et al., 2001; McIntosh and Lobaugh, 2004). According to the amplitude asymmetry model, amplitude modulations in brain oscillations directly generate slow event-related responses. Event-related amplitude modulations are therefore used as latent variables to predict the observed event-related