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Dissociation of the functional relevance of different pre-stimulus oscillatory activity for memory formation

Neda Salari, Michael Rose *

Department of Systems Neuroscience, University Medical Center Hamburg Eppendorf, Martinistr. 52, 20246 Hamburg, Germany

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ABSTRACT

The state of a neural assembly preceding an incoming stimulus modulates the processing of that subsequently presented stimuli. For human memory formation, the role of oscillatory brain activity within different frequency ranges has been discussed but a more functional relation could not be established. In the present Experiment I, an increase of pre-stimulus theta- (3–7 Hz) and beta- (13–17 Hz) band oscillations during encoding for later remembered stimuli was observed. To establish a more direct functional relation, we adopted a novel brain–computer-interface (BCI) method to selectively detect oscillatory activity in real-time combined with an adaptive stimulus presentation at different levels of activity. Therefore, in the second experiment the BCI was used to present the visual stimuli with a high temporal resolution directly within defined brain states of beta- or theta-band activity. The quality of the subsequent processing of the stimuli was assessed at the behavioral level with a surprise recognition task. Results revealed a variation of memory performance in direct relation to the amount of pre-stimulus beta- but not theta-band oscillations, suggesting a functional relevance of beta-band oscillations for memory encoding. Thus, the BCI method enabled a more functional differentiation of the effective role of ongoing oscillatory activity.

Introduction

A relevant amount of the variability of human task performance can be attributed to intrinsic fluctuations of neural activity prior to actual task processing (van Dijk et al., 2008; Fox et al., 2007; Hesselmann et al., 2008a,b; Linkenkaer-Hansen et al., 2004; Romei et al., 2010). Even for memory formation recent studies reported the relevant role of ongoing activity prior to the stimulus presentation for the successful encoding of that stimulus into memory (Addante et al., 2011; Galli et al., 2012a; Guderian et al., 2009; Otten et al., 2010; Park and Rugg, 2010; Adcock et al., 2006). The nature of pre-stimulus activity during memory encoding was more precisely characterized in an MEG study that related the memory effect to theta band oscillations (3–7 Hz) and reported to locate the origin of a part of this activity within the Medial Temporal Lobe (MTL) (Guderian et al., 2009). The possible relevance of pre-stimulus theta activity within the hippocampus for learning was also demonstrated in animal studies showing increased conditioning effects during states of high theta-band amplitudes within the hippocampus (Berry and Thompson, 1978; Griffin et al., 2004; Seager et al., 2002). The results further indicate that pre-stimulus activity reflects additional processes that are independent from post-stimulus processing and may contribute important neural prerequisites for the formation of memory.

Interestingly, intracranial electrophysiological recordings directly within the MTL of human volunteers during the encoding of verbal material revealed that differences in the pre-stimulus period between later remembered and forgotten words were not restricted to the theta-band (Merkow et al., 2014) but were accompanied by effects over a large range of different frequencies including alpha- (8–12 Hz), beta- (13–17 Hz) and also gamma-band (around 40 Hz) (Fell et al., 2011). Modulations of oscillatory activity within the beta- and gamma-band were reported to predict successful long-term retrieval in other studies (Osipova et al., 2006; Staudigl et al., 2012) and it was proposed that desynchronization effects in the alpha- and beta-band contribute equally to memory formation (Hanslmayr et al., 2012). However, it remains unclear whether all of these observed oscillatory activities actually play important functional roles for memory encoding or whether activities in some of the frequency bands can be regarded as a simple byproduct of neuronal processing without a causal role.

Here we aimed to establish a method for a functional dissociation of the role of different neural oscillations for the formation of memory using a brain–computer interface (BCI) that allows the presentation of stimuli within well described and online estimated brain states. The BCI estimates the individual variance in the selected frequency ranges and compares the actual value in real-time to the distribution of the values. At predefined thresholds the BCI then initiates the presentation of a stimulus and therefore ensures a processing directly embedded in

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* Corresponding author at: Department of Systems Neuroscience, University Medical Center Hamburg Eppendorf, Martinistrasse 52, D-20246 Hamburg, Germany. Fax: +49 40 7410 59955.

E-mail address: rose@uke.uni-hamburg.de (M. Rose).

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the desired state of the brain dynamics. This adaptive presentation method can be used to test the functional relevance of spontaneous occurring modulations of ongoing neural activity in different frequency bands for behavior without external stimulation.

The majority of studies that examined pre-stimulus memory effects used verbal material and cue-stimuli that precedes the presentation of the actual stimulus and therefore enables the participants to prepare voluntarily for the upcoming stimulus processing. Therefore, the pre-stimulus activity which overlaps with cue evoked activity can be regarded in part as post-cue processing. Furthermore, the voluntarily established preparatory state is highly specific for the task set, instructions and expected processing demands as demonstrated by the fact that the effect is modulated by reward and processing resources (Galli et al., 2012b; Gruber and Otten, 2010). It remains an open question whether also spontaneous fluctuations without a cue presentation can establish systematic pre-stimulus effects and affects the formation of memory. This pre-stimulus activity that is not evoked by an external cue stimulus plays an important role for other cognitive processes like attention (Coste et al., 2011) and perception (Hesselmann et al., 2008a; Linkenkaer-Hansen et al., 2004) (Hanslmayr et al., 2007; Wyart and Tallon-Baudry, 2009) Therefore, in our first experiment we presented images of objects with an unpredictable timing, without a cue and without an instruction that evoked a specific memory related strategy. We then assessed the pre-stimulus oscillatory activity during encoding of images that dissociates between later remembered and forgotten stimuli. The results revealed significant effects in the pre-stimulus period for the theta and beta bands over the temporal and frontal cortex but this analysis cannot dissociate the functional role of the different oscillatory activity for the formation of memory. The second experiment aimed to test the functional relation of the observed oscillatory activity at both frequency bands more directly using the BCI method.

Therefore, in the second experiment the BCI was used to present the same stimuli with a high temporal resolution directly within modulated brain states of beta- or theta-band activity at identical frequencies and at identical locations as observed in the first experiment. The quality of the subsequent processing of the stimuli was assessed at the behavioral level with a surprise recognition task after the object encoding task and can be assigned to the distinct states of high beta or theta pre-stimulus activity. Due to the unexpected recognition task the volunteers were not aware about the memory test and were not able to voluntarily prepare a memory related processing strategy.

The adaptive stimulation in direct temporal relation to the manipulation of the ongoing activity allows an estimation of the immediate consequences for behavior. The online detection of different brain states combined with the adaptive stimulation resulted in clearly dissociable effects for the subsequent information processing and allows a more direct functional characterization of ongoing oscillatory activity at different frequencies.

Materials and methods

Volunteers

In Experiment I 15 volunteers were recruited (mean age 31 years, range 25–36, 6 females). Volunteers were paid, and gave written informed consent. In Experiment II 28 new volunteers participated (mean age 29 years, range 25–35, 10 females). 14 randomly selected volunteers participated in the experiment based on adaptive stimulation during different beta-band states (beta-band group) and the other 14 participants were assigned to the experiment based on adaptive stimulation during different theta-band states (theta-band group). All volunteers were right-handed with normal or corrected-to-normal vision. The study was approved by the Ethics Committee of the German Psychology Association.

Data collection

The volunteers were placed in an electrically shielded and sound attenuated cabin 1 m in front of a screen. EEG was measured from 61 active electrodes at standard locations (Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T7, T8, P7, P8, Fz, Cz, Pz, Oz, FC1, FC2, CP1, CP2, FC5, FC6, CP5, CP6, F1, F2, C1, C2, P1, P2, AF3, AF4, FC3, FC4, CP3, CP4, PO3, PO4, F5, F6, C5, C6, P5, P6, AF7, AF8, FT7, FT8, TP7, TP8, PO7, PO8, Fpz, AFz, CPz, POz, FCz) (ActiCap, Brain Products, Gilching, Germany) and all channels were referenced to Cz, but offline re-referenced to a common average and electrode Cz was included (resulting in 62 EEG channels). In addition, we recorded vertical and horizontal EOG from above versus below the left eye (supraorbital VEOGS and infraorbital VEOGI) and from the outer canthi of the eyes (left HEOGL, right HEOGR), for detecting eye movements. Electrode resistance was kept below 20 kΩ. EEG and EOG were amplified using a 0.03 Hz high-pass filter (= 5 s time constant, 50 Hz notch filter and 1000 Hz high cutoff filter) and A/D converted at 250 Hz sampling rate.

Behavioral procedure

For all experiments 120 different images (size 336 × 252 pixels; 24-bit color depth) were selected from an internal database of natural scenes and object images.

Images were selected on the basis of the results from a behavioral pilot study ($n = 12$). In this study 240 images were presented and the encoding and recognition performance was compared. For the present experiments 120 images were selected based on different criteria. First, all images were selected that were identified as living or non-living from all subjects with a maximal reaction time of 2000 ms. Second, an equal number of images were selected representing the living or non-living category. Third, only one exemplar from an object was selected for the final stimulus pool (i.e., only one image with a cup). In the majority of images (88%) a dominant object was present (i.e., a bird or a cup) and 15 images show scenes (i.e., trees or buildings). All used scenes have an unambiguous assignment to a living or non-living category, since no scenes were used with objects from both categories. In the instruction part of the experiment the participants were instructed to rate all natural images (like a bird or trees) as living and all constructed images (like a cup or a building) as non-living. Recognition rate and encoding speed were not different between the categories.

Overall, 80 images were shown during the encoding in Experiment I and 40 additional images were used for the recognition memory task after the encoding task. Each image was shown for 2 s (size: 6.8 × 5.1° visual angle) and the participant had to indicate the category of the actual image by a button press (living, non-living) and the next image was presented after a random interval of 2–10 s. Stimulus presentation and behavioral response collection was accomplished using the software 'Presentation' (version 14.6, **http://www.neurobs.com**) for Experiment I and adaptive presentation was accomplished in the BCI module using customized software.

Recognition memory task

After the encoding task a short distraction task was performed by the volunteers to avoid an active rehearsal of the last presented images. Therefore, the volunteers were asked to do a simple arithmetic task for about 10 min (aloud counting back from 113 in steps of 5). After the distraction task an identical surprise recognition task was presented in all experiments, which entailed the presentation of the 80 previously seen images with 40 new images. The images were presented in a randomized order while the participant had to judge images as 'previously seen' or 'new'. Each image was shown for 2 s and the next image was shown after 2–4 s.