Phase of electroencephalography theta oscillation during stimulus encoding affects accuracy of memory recall

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Oscillatory activity is a ubiquitous property of brain signals, and yet relatively few studies have investigated how the phase of such ongoing oscillations affects our cognition. One of the main findings in this field is that the phase of electroencephalography (EEG) in the alpha band can affect perception of milliseconds-long stimuli. However, the importance of the phase of EEG for processing more naturalistic stimuli, which have a much longer duration, is still not clear. To address this question here, we presented word–nonword pairs, each of which was visible for 5 s and measured the effect of EEG phase during stimulus onset on later memory recall. The task consisted of an encoding (learning) phase in which 20 novel word–nonword pairs were presented, followed by a test phase in which participants were shown one of the seen words with four target nonwords to choose from. We found that memory recall performance was higher when the words during

encoding were presented at a descending phase of the theta oscillation. This effect was the strongest in the frontal cortex. These results suggest that the phase of ongoing cortical activity can affect memorization of seconds-long stimuli that are an integral part of many daily tasks. *NeuroReport* 30:404–408 Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction

Memory relies on a set of processes that involve encoding, consolidation, and retrieval of information. Encoding is the process of transforming sensory information into a persisting memory trace. Theta oscillations (4–8 Hz), in particular, were reported to contribute to successful encoding. An increase in the peak theta frequency was correlated with an increase in memory performance [1]. Prestimulus thalamic theta power predicted successful and unsuccessful encoding in humans [2]. Between-area phase synchrony in theta frequencies has been reported to be predictive of short-term memory performance [3]. Successful memory formation was linked to tight coordination of spike timing with the local theta oscillation [4]. Short-term memory capacity can be predicted by the theta to gamma cycle length ratio [5]. However, there are emerging evidences that not only the power of electroencephalography (EEG) oscillations but also phase can affect stimulus encoding [6–8].

In this study, we used EEG to test the hypothesis that the phase of theta oscillations might play a role in encoding sensory information and in subsequent memory recall. We recorded the EEG signal over the scalp while human participants performed a word–nonword pair matching experiment. We tested whether stimuli presentation at a particular phase of low-frequency oscillations would affect later recall.

Methods
Participants

Undergraduate students ($n = 18$) were recruited and participated for course credit from a location that will be

identified if the article is published. Participants provided informed written consent. All procedures were in accordance with the Declaration of Helsinki and were approved by the (Author University) Human Subjects Review Committee. Participants reported normal vision and no neurological conditions. Only EEG data from participants who responded correctly at a rate higher than chance (>25% correct) were analyzed. Thus, 11 participants (six female; average age 19.8, SD = 2) contributed toward the data analysis.

Stimuli and procedures

Participants were seated comfortably 57 cm away from a 17-inch LCD monitor, with a refresh rate of 60 Hz. Figure 1 shows the structure of the modified word–nonword pair matching task adapted from [9] using Psychophysics Toolbox version 3. The task consisted of four blocks, each of which was divided into two phases: learning (encoding) and testing. The learning phase included 20 trials. In each trial, a word–nonword pair was presented to the participant for 5 s, followed by a 1 s interstimulus interval. Word–nonword pairs appeared with a white fixation square at the center of the monitor. Each word–nonword pair was comprised of a word and a nonword that were derived from a normative database [10] and the ARC nonword database, respectively [11]. All stimuli were presented on a light gray background. In the self-paced testing phase, the participant was asked to match the word with the nonword in the format of a multiple-choice question as shown in Fig. 1. Twenty word–nonword pairs that were seen previously during the learning phase were

Fig. 1
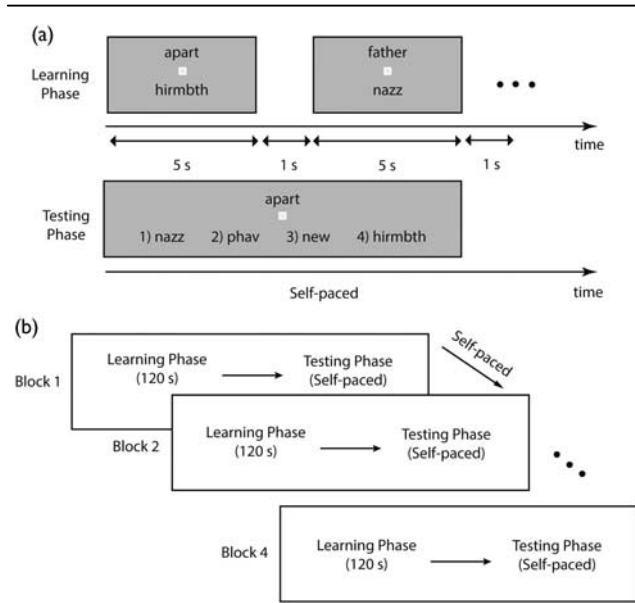
(a) Schematic illustration of the learning and testing phase. (b) Each experiment consisted of four blocks composed of 20 learning and 40 testing trials.

Fig. 2

Average performance of the participants plotted as a function of blocks. The error bars show SEM. The performance is well above the 25% chance level for each block.

presented along with 20 new words. Thus, there were 40 multiple-choice questions in the testing phase.
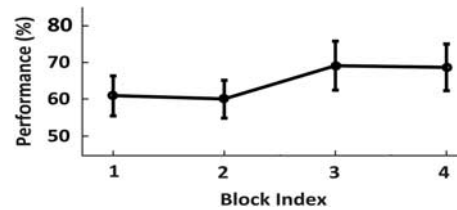
Each participant completed four blocks. Short rest breaks (no > 1 min) were allowed between the blocks. Participants were given verbal instructions before the experiment began and were asked to minimize their eye and body movements.

Electroencephalography acquisition and analysis
EEG was recorded with 128 Ag/Ag-Cl electrodes in an elastic net (Electrical Geodesics Inc., Eugene, Oregon, USA). Scalp voltages were recorded at a 500 Hz sampling rate and impedances were maintained under 100 kΩ. Data were high-pass filtered at 0.1 Hz to remove DC offset, re-referenced offline to average, and analyzed using the BESA software package (Megis Software 5.3, Grafelfing, Germany). All the channels were inspected visually for a poor signal. The signal from a small number of electrodes (≤ 10) showing poor quality was replaced with an interpolated signal from neighboring sites. The channels from the standard 10–20 montage were used for analysis. Because of the length of the trials, eye movement artifacts occurred in a majority of trials. Therefore, eye movement artifacts were corrected using the adaptive artifact correction algorithm [12]. Data were exported from BESA and further analyzed in MATLAB (MATLAB version 8.3.0.532; The Mathworks Inc., 2014, Natick, Massachusetts, USA) using custom scripts and EEGLAB functions [13].

For phase analysis, we first bandpass filtered the data to 0.5 and 30 Hz. EEG data were then epoched from

− 200 ms before to 1000 ms after each stimulus. Period − 200 to 0 ms was considered the baseline, and the average EEG amplitude in the period was subtracted from each trial. To calculate the phase angle and power for each trial, we used Morlet wavelet transform of single trials using the time frequency function of EEGLAB. Wavelet transformation was computed with 1 Hz steps and cycles starting from 0.5 to 0.5 and 15 to 30 Hz. The output of this function is a matrix of complex numbers. Thus, to calculate the phase angle of each trial, we used the angle function from MATLAB. To ensure that our results were not dependent on this particular wavelet transform, we also used Hilbert transform to calculate phases at the onset of the stimuli [14]. Both methods yielded consistent results.

Results
Behavioral results
In the word–nonword pair matching task, if the participant correctly matched the word with the nonword, it was labeled as 'hit' and 'nonhit' otherwise. As an example, consider Fig. 1a; if the participant chose the nonword 'hirmbth' in the testing phase, it is called a hit and all other choices nonhits. In this task, the participants matched correctly (64.7 ± 5.9 SEM) % of the words over all four blocks (chance level = 25%, Fig. 2).

P200 component
Event-related potentials (ERPs) provide a way to compare the differences in the average EEG amplitude between experimental conditions. We investigated the difference between one of the components of the grand average ERP (Fig. 3a). In particular, we investigated the P200 component, which has been reported to be modulated by different cognitive processes such as short-term memory [15] and selective attention [16]. Consistent with other studies [17,18], we observed a pronounced P200 component at the frontal sites around 150–200 ms after the stimulus onset (Fig. 3a). On the basis of paired two-tailed t-test results, there was no significant difference in the magnitude of the P200 component for hits (mean = 2.41 μV, SEM = 0.41 μV) and nonhits (mean = 2.62 μV, SEM = 0.35 μV) [$t_{(10)} = 0.43$, $P = 0.68$].

Fig. 3
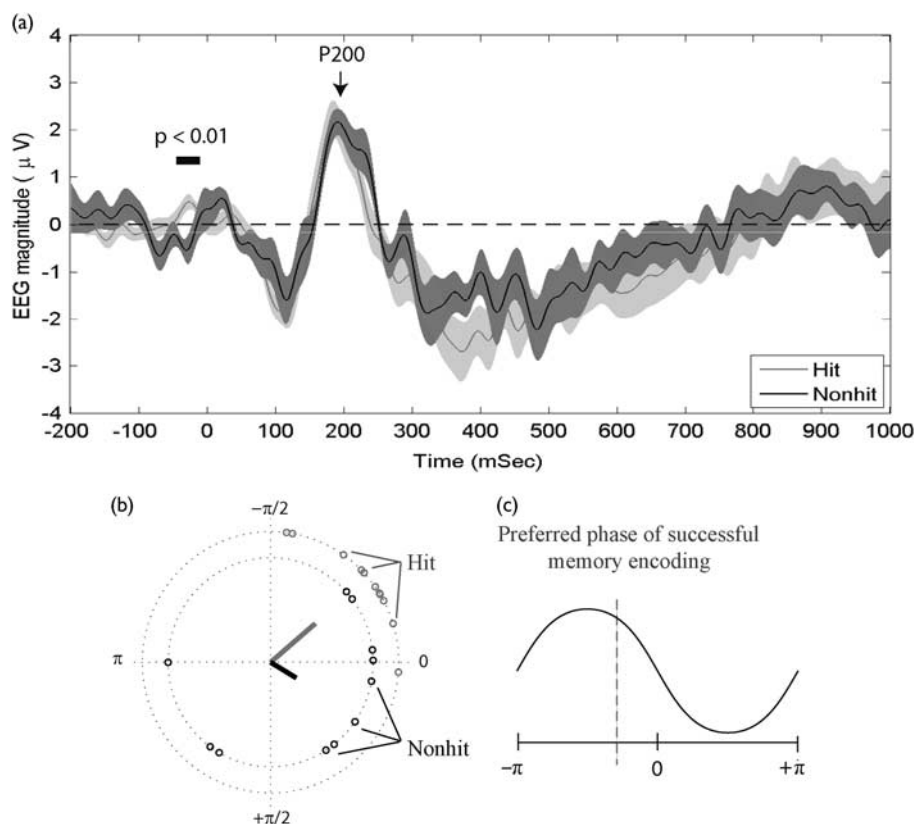
(a) Grand average event-related potential for channel F3 plotted as a function of time. Time = 0 corresponds to the onset of the stimuli. Shaded regions show the SEM at each time point. Horizontal bar denotes the interval −38 to −26 ms, where the amplitudes of the hit (light gray) and nonhit (dark gray) are significantly different before the onset of the stimuli. (b) Each small circle shows the average phase per participant for the hit trials (light gray) and nonhit trials (dark gray). For visualization, nonhit trials are depicted on a smaller radius. The light and dark gray bars show the direction and the magnitude of the average phase for all the participants for hits and nonhits, respectively. (c) One cycle of a sinusoidal wave illustrating the preferred phase of successful memory encoding.

This suggests that the amplitude of the P200 component, which is a typical EEG measure of cognitive processes, is not sensitive to performance in our memory encoding task.

Phase of the electroencephalography signal at the onset of the stimuli and memory performance

Next we investigated whether other features of the EEG signal correlate with performance in our memory task. In Fig. 3a, we show that the ERP magnitude of hits and nonhits is different at −38 to −26 ms before the onset of the stimulus ($P < 0.05$ for all points in that interval; two-tailed paired t-test). Considering previous work [19], we hypothesized that this prestimulus difference could be the result of a different EEG phase at stimulus onset, which could affect memory encoding. To obtain EEG phase information, we used wavelet decomposition (see 'Methods' section). For each participant, we calculated the average phase at the stimulus onset for hit and nonhit trials. We found that for the frequency band ~ 4–5 Hz at a frontal channel (F3), hit trials had a tendency to start at a descending phase (Fig. 3b and c), whereas nonhit trials did not show a specific phase preference.

To determine the significance of this effect across recording electrodes, we used the Rayleigh test to check whether the phase angles (across trials) are distributed uniformly for each condition. The test was performed on the phase angle of all the hit versus nonhit trials, and consisted of 569 hit and 311 nonhit trials for each channel. Figure 4 shows the P values for $f \sim 4$–5 Hz at the onset of the stimuli for 19 channels on the scalp. As seen from the figure, the angle phase of hit trials is significantly directional ($P < 0.01$) compared with the nonhit trials. This effect was most pronounced in the frontal regions on the scalp.

Discussion

This study investigated the effect of the phase of slow oscillations on memory recall using a word–nonword pair matching experiment. We found that the phase of the theta oscillations at the onset of the stimuli affects
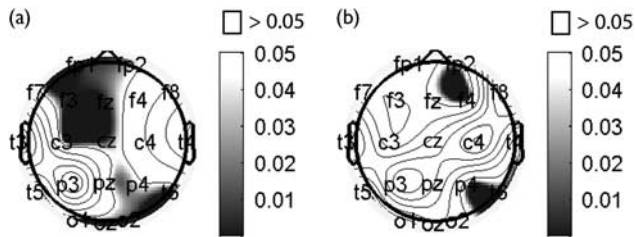
P values from the Rayleigh test for 19 channels on the scalp depicted using topographic maps for (a) hit and (b) nonhit trials at the onset of the stimuli calculated for $f \sim 4{-}5$ Hz. The angles for each condition were tested to check whether they were distributed uniformly using the Rayleigh test. The color bars indicate the *P*-value, and a lower *P*-value means higher directionality in the phase distribution.

memory recall. The phase of the hit and nonhit trials was calculated and compared using the Rayleigh test. It was observed that if the stimuli were delivered at a specific phase of theta oscillations, the participants were more likely to match the nonword with the correct word. This is the first study to show that for a memory task similar to many daily tasks, the phase of theta oscillation affects the success of later recollection.

Our results support the idea that theta oscillations play a crucial role in memory-related processing, as was postulated previously by studies carried out in monkeys [3] and humans [4]. Increases in theta power before the onset of the stimuli in the hippocampus and neocortex predict heightened memory performance in human participants with implanted electrodes [2]. Theta coupling has been shown between cortical area V4 and the prefrontal cortex in a monkey study on working memory maintenance [3]. In this study, we have shown that the phase of the theta oscillation in the occipital and frontal regions is a good indication of the performance of the participants.

Our results provide evidence that phase synchronization of theta oscillation is not prominent over the entire scalp. This effect is mostly observed in the frontal regions (Fig. 4). This is consistent with abundant evidence that the frontal areas are involved in memory consolidation [20–22]. Frontal regions are connected anatomically with the hippocampus, which plays a prominent role in memory formation and shows strong theta oscillations. These unilateral projections from the hippocampus to the prefrontal cortex are especially strong compared with other cortical regions (for a review, see Pandya and colleagues [23,24]). Thus, the relation observed between memory encoding and theta phase in frontal regions is consistent with what would be expected on the basis of the brain connectome.

Taken together, our findings suggest that the phase of the low-frequency oscillations, namely theta, plays a role in gating the information during the encoding phase. If the stimuli are presented at a specific phase of theta oscillations, the participants recall the word–nonword pairs later. We have shown that the phase of theta oscillation at the onset of the visual stimuli enhances the encoding of information during wakefulness. At the population level, information in cortical areas is considered to be processed not continuously, but in the form of discrete packets with a sequential structure [25]. We can speculate that if the stimuli are not delivered at the right phase of the occurring packets, it might be less optimal to integrate the information into the ongoing process. Hence, our observations are consistent with the proposition that the phase of low-frequency oscillations in frontal regions could be a fundamental component in the encoding of information.

Acknowledgements

Conflicts of interest

References
1   Moran RJ, Campo P, Maestu F, Reilly RB, Dolan RJ, Strange BA. Peak frequency in the theta and alpha bands correlates with human working memory capacity. *Front Hum Neurosci* 2010; **4**:200.
2   Sweeney-Reed CM, Zaehle T, Voges J, Schmitt FC, Buentjen L, Kopitzki K, *et al.* Pre-stimulus thalamic theta power predicts human memory formation. *Neuroimage* 2016; **138**:100–108.
3   Liebe S, Hoerzer GM, Logothetis NK, Rainer G. Theta coupling between V4 and prefrontal cortex predicts visual short-term memory performance. *Nat Neurosci* 2012; **15**:456–462.
4   Rutishauser U, Ross IB, Mamelak AN, Schuman EM. Human memory strength is predicted by theta-frequency phase-locking of single neurons. *Nature* 2010; **464**:903–907.
5   Kamiński J, Brzezicka A, Wróbel A. Short-term memory capacity (7 ± 2) predicted by theta to gamma cycle length ratio. *Neurobiol Learn Mem* 2011; **95**:19–23.
6   Mathewson KE, Gratton G, Fabiani M, Beck DM, Ro T. To see or not to see: prestimulus alpha phase predicts visual awareness. *J Neurosci* 2009; **29**:2725–2732.
7   Busch NA, Dubois J, VanRullen R. The phase of ongoing EEG oscillations predicts visual perception. *J Neurosci* 2009; **29**:7869–7876.
8   Strauß A, Henry MJ, Scharinger M, Obleser J. Alpha phase determines successful lexical decision in noise. *J Neurosci* 2015; **35**:3256–3262.
9   Mander BA, Rao V, Lu B, Saletin JM, Lindquist JR, Ancoli-Israel S, *et al.* Prefrontal atrophy, disrupted NREM slow waves and impaired hippocampal-dependent memory in aging. *Nat Neurosci* 2013; **16**:357–364.
10 Buchanan EM, Holmes JL, Teasley ML, Hutchison KA. English semantic word-pair norms and a searchable Web portal for experimental stimulus creation. *Behav Res Methods* 2013; **45**:746–757.
11 Rastle K, Harrington J, Coltheart M. 358,534 nonwords: The ARC nonword database. *Q J Exp Psychol A* 2002; **55**:1339–1362.
12 Ille N, Berg P, Scherg M. Artifact correction of the ongoing EEG using spatial filters based on artifact and brain signal topographies. *J Clin Neurophysiol* 2002; **19**:113–124.
13 Delorme A, Makeig S. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J Neurosci Methods* 2004; **134**:9–21.
14 Le van Quyen M, Foucher J, Lachaux J, Rodriguez E, Lutz A, Martinerie J, *et al.* Comparison of Hilbert transform and wavelet methods for the analysis of neuronal synchrony. *J Neurosci Methods* 2001; **111**:83–98.

15 Golob EJ, Starr A. Age-related qualitative differences in auditory cortical responses during short-term memory. *Clin Neurophysiol* 2000; **111**:2234–2244.

16 Hillyard SA, Hink RF, Schwent VL, Picton TW. Electrical signs of selective attention in the human brain. *Science* 1973; **182**:177–180.

17 Kenemans JL, Kok A, Smulders FT. Event-related potentials to conjunctions of spatial frequency and orientation as a function of stimulus parameters and response requirements. *Electroencephalogr Clin Neurophysiol* 1993; **88**:51–63.

18 Key APF, Dove GO, Maguire MJ. Linking brainwaves to the brain: an ERP primer. *Dev Neuropsychol* 2005; **27**:183–215.

19 Batterink LJ, Creery JD, Paller KA. Phase of spontaneous slow oscillations during sleep influences memory-related processing of auditory cues. *J Neurosci* 2016; **36**:1401–1409.

20 Peyrache A, Battaglia FP, Destexhe A. Inhibition recruitment in prefrontal cortex during sleep spindles and gating of hippocampal inputs. *Proc Natl Acad Sci USA* 2011; **108**:17207–17212.

21 Marshall L, Helgadóttir H, Mölle M, Born J. Boosting slow oscillations during sleep potentiates memory. *Nature* 2006; **444**:610–613.

22 Lynch MA. Long-term potentiation and memory. *Physiol Rev* 2004; **84**:87–136.

23 Pandya D, Petrides M, Cipolloni PB. *Cerebral cortex: architecture, connections, and the dual origin concept*. Oxford: Oxford University Press; 2015.

24 Petrides M, Pandya DN. The frontal cortex. In: Mai JK, Paxinos G, editors. *The Human Nervous System*. San Diego: Academic Press; 2011.

25 Luczak A, McNaughton BL, Harris KD. Packet-based communication in the cortex. *Nat Rev Neurosci* 2015; **16**:745–755.