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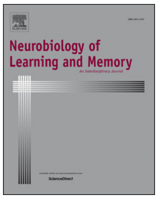

Theta oscillations promote temporal sequence learning

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ABSTRACT

Many theoretical models suggest that neural oscillations play a role in learning or retrieval of temporal sequences, but the extent to which oscillations support sequence representation remains unclear. To address this question, we used scalp electroencephalography (EEG) to examine oscillatory activity over learning of different object sequences. Participants made semantic decisions on each object as they were presented in a continuous stream. For three "Consistent" sequences, the order of the objects was always fixed. Activity during Consistent sequences was compared to "Random" sequences that consisted of the same objects presented in a different order on each repetition. Over the course of learning, participants made faster semantic decisions to objects in Consistent, as compared to objects in Random sequences. Thus, participants were able to use sequence knowledge to predict upcoming items in Consistent sequences. EEG analyses revealed decreased oscillatory power in the theta (4–7 Hz) band at frontal sites following decisions about objects in Consistent sequences, as compared with objects in Random sequences. The theta power difference between Consistent and Random only emerged in the second half of the task, as participants were more effectively able to predict items in Consistent sequences. Moreover, we found increases in parieto-occipital alpha (10–13 Hz) and beta (14–28 Hz) power during the pre-response period for objects in Consistent sequences, relative to objects in Random sequences. Linear mixed effects modeling revealed that single trial theta oscillations were related to reaction time for future objects in a sequence, whereas beta and alpha oscillations were only predictive of reaction time on the current trial. These results indicate that theta and alpha/beta activity preferentially relate to future and current events, respectively. More generally our findings highlight the importance of band-specific neural oscillations in the learning of temporal order information.

1. Introduction

Episodic memories can be conceptualized as temporally-organized sequences of events (Allen & Fortin, 2013). Computational models suggest that neural oscillations—rhythmic fluctuations in the excitability of large neuronal populations—might play a role in the coding of temporal sequences (Lisman & Idiart, 1995; Lisman & Jensen, 2013). In humans, oscillatory power in the theta band (4–7 Hz) is readily observable in scalp electroencephalography (EEG), magnetoencephalography (MEG), and intracranial recordings. Available evidence indicates that theta oscillations may be generated by a network that includes the hippocampus, medial prefrontal cortex, and medial/lateral parietal cortex (see Hsieh & Ranganath, 2014, for review). Critically, neuroimaging studies have implicated these regions in encoding (e.g. Ekstrom & Bookheimer, 2007; Jenkins & Ranganath, 2010; Tubridy & Davachi, 2011) and representation (Hsieh and Ranganath, 2015; Hsieh, Gruber, Jenkins, & Ranganath, 2014; Kalm, Davis, & Norris, 2013) of event sequences.

Scalp EEG studies have provided evidence that theta power is critical for successful episodic encoding and retrieval (Fuentemilla, Barnes, Düzel, & Levine, 2014; Long, Burke, & Kahana, 2014; Rozengurt, Barnea, Uchida, & Levy, 2016; Sederberg, Kahana, Howard, Donner, & Madsen, 2003). Available evidence also suggests that theta activity might contribute to sequence processing (e.g., Heusser, Poeppel, Ezzyat, & Davachi, 2016; Hsieh et al., 2011; Roberts et al., 2013). For instance, EEG studies of working memory (Hsieh et al., 2011; Roberts et al., 2013) have shown that theta power is higher during active maintenance of temporal order information than during maintenance of detailed object information. These findings indicate that theta power could reflect online maintenance of temporal order relationships. Some evidence, however, suggests an alternate possibility—that theta activity could reflect prediction errors. Indeed,

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numerous studies have found that theta power is increased following erroneous responses, and the evidence indicates that these increases reflect feedback or error-driven learning (Cavanagh & Frank, 2014; Cavanagh et al., 2012; Cavanagh, Frank, Klein, & Allen, 2009, 2010; Cohen, 2011; Cohen, Elger, & Ranganath, 2007). Recordings from non-human primates (Brincat & Miller, 2015) have also provided support for the importance of theta oscillations in error-driven learning, showing increased oscillatory synchrony in the theta band between hippocampus and prefrontal cortex following errors that decrease as a function of learning. Thus, it is possible that theta oscillations would be most prominent as participants are learning sequence information (i.e., when prediction error is high), and that it should decline as one learns to use sequence knowledge to predict upcoming events (see Clarke et al., 2017).

To examine the extent to which theta oscillations support sequence learning or representation, we used scalp electroencephalography (EEG) to record oscillatory activity as participants performed a sequence-learning task. EEG was recorded as participants made simple semantic judgments on a stream of consecutively presented objects, consisting of sequences of objects that were presented in the same order on each repetition (“Consistent”) and sequences of objects that appeared in a different order on each repetition (“Random”). Because objects in Consistent and Random sequences were equally familiar, comparison of the two conditions allowed us to investigate learning of temporal relationships that enabled prediction of upcoming objects in Consistent sequences. To investigate the role of oscillatory activity during learning of structured order information, we directly contrasted activity between Consistent and Random sequences over the course of learning. We characterized the timing and functional characteristics of activity in the theta, alpha, and beta bands, thereby allowing us to identify whether any learning-related effects were band-specific.

2. Materials and Methods

2.1. Participants

Twenty healthy (6 males) undergraduate students from the University of California at Davis were included in this study. All participants had normal or corrected-to-normal vision. The Institutional Review Board at the University of California at Davis approved the study. Written informed consent was obtained from each subject before the experiment.

2.2. Task procedures

Task procedures were modified from Hsieh et al. (2014). The current study consisted of two parts: a sequence learning session and a sequence retrieval session. EEG data were only acquired during the sequence learning session. Therefore, EEG analyses and results reported in this paper focus on the sequence-learning portion of the experiment. The learning session consisted of four study-test blocks. During the study phase of each block, participants were presented with a stream of objects, each presented for 1000 ms, and separated by a 1500 ms fixation cross. The stream consisted of repetitions of six different five-object sequences. The Fixed sequence consisted of five distinct objects, presented in the same order on each repetition. Objects in the Fixed sequence did not overlap with objects in other sequences (see Fig. 2A). Two overlapping sequences (“X1” and “X2”) also consisted of five objects presented in the same order on each repetition, but unlike the Fixed sequence, X1 and X2 sequences shared common objects in positions 2 and 3 (see Fig. 2A). Two Random sequences that each consisted of five distinct objects, presented in a different pseudorandom order on each repetition. As a result, participants could not learn a consistent temporal relationship between objects in the Random sequences. Lastly, a “Novel” sequence was presented, consisting of trial-unique objects that were only presented once in the entire experiment. In other words, a completely new set of five objects was presented on every repetition of the Novel sequence. Novel sequences were not included in the analyses reported here, as this manuscript is focused on changes in EEG oscillations over the course of sequence learning, rather than item learning.

Each object sequence was presented six times during the study phase of each study-test block, with the constraints that: (1) there were no back-to-back repetitions of the same sequence type, and (2) all object sequences must have been presented before subsequent repetitions. To keep participants actively engaged and obtain behavioral measures of sequence learning, participants were required to make a semantic decision to each presented object in the continuous object stream, based on a semantic question (e.g. “Is the presented object living?”) provided at the beginning of the study phase of each study-test block. A different semantic question was used in different study-test blocks. Because the sequences were presented contiguously, there were no obvious divisions between different object sequences. However, participants were instructed to look out for, and learn, the sequence relationships.

During the test phase of each block, participants were asked to recall each object sequence (except for the Novel sequences). On each self-paced test trial, five objects from a sequence were simultaneously presented in a random order from left to right on the screen. Participants were asked to reconstruct the temporal order in which these objects appeared during the study phase. Participants were additionally instructed that, if there was no consistent temporal order (which was true for objects in the Random sequences), then they were to put the items in any order. After each test trial, the correct order of the objects was presented on the screen. For the Random sequences, the objects were shown in a random order during the feedback period. Each sequence type was tested two times in each test block, with the constraint that: (1) there were no back-to-back tests of a particular sequence type, and (2) each sequence was tested once before any sequence was retested.

2.3. Behavioral analyses

Our primary hypotheses were centered on sequence learning, and we therefore focused on contrasting EEG and behavioral data between the Consistent sequences (collapsed across Fixed, X1, and X2 sequences) and the Random sequences. Study blocks were also divided into early (Blocks 1 and 2) and late (Blocks 3 and 4) blocks. ANOVAs were conducted using the AFEX package in R (Singmann et al., 2017). The Greenhouse Geisser Correction (Greenhouse & Geisser, 1959) was applied to account for violations of sphericity where appropriate.

2.4. EEG data acquisition

EEG was recorded from 128 silver/silver chloride electrodes mounted in an elastic cap using an ActiveTwo EEG recording system (Biosemi, https://www.biosemi.com/). The positioning of the 128 electrodes was in accordance with an extended version of the international 10/20 system (Klem, Luders, Jasper, & Elger, 1958; Oostenveld & Praamstra, 2001). Additional electrodes were placed on the mastoids, outside the outer canthi of both eyes, and above and below the left eye. Data were collected at a sampling rate of 2048 Hz.

2.5. EEG Analysis

All data analyses were performed offline using the EEGLab Toolbox (Delorme and Makeig, 2004) and Fieldtrip Toolbox (Oostenveld, Fries, Maris, & Schoffelen, 2011). The continuous EEG data were first high-pass filtered at 0.5 Hz and then down sampled to 512 Hz. Channels with excessive noise due to channel failure were identified and their data were interpolated using spherical interpolation (Perrin, Pernier, Bertrand, & Echallier, 1989). Continuous EEG data were then segmented to single trials time-locked to response onsets (−600 ms to