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Regional and inter-regional theta oscillation during episodic novelty processing

Gwan-Taek Lee [a,1], Chany Lee [a,1], Kyung Hwan Kim [b], Ki-Young Jung [c,*]

[a] Department of Neurology, Korea University College of Medicine, 73 Inchon-Ro, Anam-Dong, Seongbuk-Gu, Seoul 136-705, Republic of Korea
[b] Department of Biomedical Engineering, College of Health Science, Yonsei University, 234 Maeji-ri, Heungup-myun, Wonju, Gangwon-do, Republic of Korea
[c] Department of Neurology, Seoul National University College of Medicine, 101 Daehak-Ro, Jongno-Gu, Seoul 110-744, Republic of Korea

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ABSTRACT

Recent event-related potential (ERP) and functional magnetic resonance imaging (fMRI) studies suggest that novelty processing may be involved in processes that recognize the meaning of a novel sound, during which widespread cortical regions including the right prefrontal cortex are engaged. However, it remains unclear how those cortical regions are functionally integrated during novelty processing. Because theta oscillation has been assumed to have a crucial role in memory operations, we examined local and inter-regional neural synchrony of theta band activity during novelty processing. Fifteen right-handed healthy university students participated in this study. Subjects performed an auditory novelty oddball task that consisted of the random sequence of three types of stimuli such as a target (1000 Hz pure tone), novel (familiar environmental sounds such as dog bark, buzz, car crashing sound and so on), and standard sounds (950 Hz pure tone). Event-related spectra perturbation (ERSP) and the phase-locking value (PLV) were measured from human scalp EEG during task. Non-parametric statistical tests were applied to test for significant differences between stimulus novelty and stimulus targets in ERSP and PLV. The novelty P3 showed significant higher amplitude and shorter latency compared with target P3 in frontocentral regions. Overall, theta activity was significantly higher in the novel stimuli compared with the target stimuli. Specifically, the difference in theta power between novel and target stimuli was most significant in the right frontal region. This right frontal theta activity was accompanied by phase synchronization with the left temporal region. Our results imply that theta phase synchronization between right frontal and left temporal regions underlie the retrieval of memory traces for unexpected but familiar sounds from long term memory in addition to working memory retrieval or novelty encoding.

1. Introduction

Episodic novelty is provided by stimuli that are familiar in general but occur in a specific task situation for the first time. Studies of neural processes induced by novelty stimulus have revealed several cognitive stages for response to unexpected environmental change. In the early stage of processing, transient changes in the physical properties of the incoming stimulus are detected, and then attention is captured involuntarily (Friedman, Cycowicz, & Gaeta, 2001). Novelty processing may also be involved in automatic memory retrieval to recognize the meaning of an object (Mecklinger, Opitz, & Friederici, 1997; Opitz, Mecklinger, Friederici, & von Cramon, 1999).

The functional significance of episodic novelty processing is known to be related to memory encoding and retrieval, based on positron emission tomography (PET) and ERP combined fMRI studies (ERP-fMRI). It is suggested that novelty assessment is subserved by subcortical and temporal as well as parietal cortical regions and novelty encoding is subserved by the frontal lobes (Tulving, Markowitsch, Craik, Habib, & Houle, 1996; Tulving, Markowitsch, Kapur, Habib, & Houle, 1994). Opitz et al. suggested that the superior temporal gyrus is involved in novelty detection, whereas retrieving semantic concepts related to novel sounds additionally engages the right prefrontal cortex (Mecklinger et al., 1997; Opitz et al., 1999), which also showed that the effects of semantic retrieval are depending on the attention on incoming stimulus.

The neural mechanisms of novelty processing are reflected in the novelty P3 (Friedman et al., 2001). The novelty P3 has a

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* Corresponding author. Fax: +82 2 2072 7424.
E-mail address: jungky10@gmail.com (K.-Y. Jung).

[1] Gwan-Taek Lee and Chany Lee contributed equally as co-first authors to this study.

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frontocentral distribution, which may be due to engagement of the prefrontal cortex to control sensory-limbic integration (Knight, 1984). However, recent studies suggest that novelty processing involves not only the prefrontal cortex, but also a widespread neural network of cortical regions, including the anterior cingulate gyrus, insula, precentral gyrus, postcentral gyrus, inferior parietal lobule, superior temporal gyrus, cuneus, thalamus, and cerebellum (Strobel et al., 2008).

Although most ERP studies using novel stimuli have focused on the mean amplitude and latency of the novelty P3 evoked by the stimulus in a time-locked manner, investigating certain oscillatory characteristics of ERP components may provide additional information compared with that obtained in an averaged ERP analysis (Ko et al., 2012). The theta oscillation may be critical for temporal coding/decoding of active neuronal ensembles and the modification of synaptic weights (Buzsaki, 2002). Theta oscillation is consistently present during memory operations such as working memory (Jensen & Tesche, 2002; Sarnthein, Petsche, Rappelsberger, Shaw, & von Stein, 1998), encoding of new information (Klimesch, 1999), and memory retrieval (Bastiaansen, van der Linden, Ter Keurs, Dijkstra, & Hagoort, 2005; Guderian & Duzel, 2005; Klimesch et al., 2001). It is likely that distinct oscillatory changes in the theta band occur during novelty processing because memory functions are required for processing novel stimuli.

Demiralp et al. have reported that the novelty stimulus-evoked P3a component leads to considerable theta activity in distant brain regions (Demiralp, Ademoglu, Comerchero, & Polich, 2001). They interpreted this theta activity as a reaction to rare events that deviate from the stimulus context (Demiralp et al., 2001). However, it remains unclear whether this distant co-activation reflects functional communication of distributed brain regions because functional connectivity between stimulus-relevant cortical regions was not explored. Although local changes in spectral power reflect the synchrony of neuronal activities within a short range, exploring the inter-regional functional connectivity between brain regions presents additional valuable information for the integration of distributed neural activity and this is feasible by observing inter-regional phase synchronization. Phase-locking synchrony must instead reside in distant connections, either in cortico-cortical fibers or thalamocortical reciprocal pathways (Varela, Lachaux, Rodriguez, & Martinerie, 2001). Further, any mechanism for neural communication must involve interactions between participating local networks (Varela et al., 2001). Thus, both local spectral activity and inter-regional phase synchronization should be evaluated when examining the function of a neuronal network.

The aim of the present study was to identify regional and inter-regional spectral characteristics of EEG during episodic novelty processing in a three-stimulus oddball task. We conducted a single-trial analysis of theta oscillation using event-related spectral perturbation (ERSP) and the phase locking value (PLV) and evaluated specific responses elicited by novelty stimuli in comparison to those by target ones.

2. Methods

2.1. Subjects and stimulus presentation

Fifteen right-handed university students (13 males, mean age: 23.5 ± 1.6 years) with no history of neurological or psychiatric illness participated in this study. All participants provided written informed consent before the experiment. Subjects performed an auditory novelty oddball task that was based on the random sequence of three types of stimuli consisting of a target (1000 Hz pure tone, $p = 0.12$, $n = 48$), novel (familiar environmental sounds, such as dog bark, buzz, and car crashing sound, $p = 0.12$, $n = 48$), and standard (950 Hz pure tone, $p = 0.76$, $n = 304$) sounds. The stimuli duration was 300 ms, and inter-stimulus intervals were varied randomly within 1700–2300 ms. Subjects listened to stimuli delivered through earphones at 65 dB SPL and were instructed to respond only to target stimuli by pushing a button using the right index finger as quickly as possible. Each subject received three blocks of an auditory novelty oddball task containing a mixture of 400 tones. Commercial software (Presentation version 11.0; Neurobehavioral Systems, Inc., Albany, CA, USA) was used to present the stimuli.

2.2. EEG recording

EEG was recorded using a 64-channel digital EEG machine (Grass Neurodata Acquisition System, Grass Technologies, Quincy, MA, USA) with an EEG cap with 62 electrodes (Quick-Cap, Compumedics Neuroscan, Charlotte, NC, USA). The reference electrode was set to linked earlobes, impedance was kept below 10 kΩ, and the band-pass filter setting was set at 0.3–70 Hz with a sampling rate of 1600 Hz. Two electrooculography (EOG) channels (placed on the left and right outer canthi) were added to confirm eyeball movements and to remove EOG artifacts. Participants were seated in a comfortable chair and instructed to continuously focus their eyes on a fixation point on a computer screen.

2.3. Preprocessing and averaged ERP component analysis

EEG data was preprocessed using EEGLAB version 10.0b (Delorme & Makeig, 2004) operated under the MATLAB environment (version 7.1, The Mathworks, Natick, MA, USA). After down-sampling (200 Hz), EEG data were epoched between the −800-ms pre-stimulus and 1000-ms post-stimulus time points. Epochs containing waveforms that exceeded ±100 μV were removed by an automated process implemented in EEGLAB. Epochs with remaining artifacts were further eliminated by visual inspection. The mean numbers of epochs included in computations were 97.5 ± 33.1 for target, 91.3 ± 36.9 for novelty, and 887.1 ± 126.4 for standard stimuli. EEG data was re-referenced to the common average reference and bandpass filtered (0.5–30 Hz). For each epoch, a baseline correction was performed using data from 400 ms prior to the stimulus. Independent component analysis (ICA) was applied to correct stereotyped ocular and muscular artifacts. For each subject, the averaged ERP components for each electrode site were obtained. The time window (200–500 ms) was determined by visually inspecting individual waveforms at the midline electrodes (Fz, Cz, and Pz). A positive peak at the Fz electrode within this time window was defined as novelty P3 and, at the Pz electrode, was defined as target P3. Latency was defined for each individual as the point with a maximum positive peak within the time window from the stimulus onset. Amplitude was calculated by averaging ±20 ms intervals from latency.

2.4. Event-related spectral perturbation and phase locking value

Trial-by-trial time–frequency decomposition was applied in the frequency range of 3.9–7.8 Hz (0.4 Hz steps) using continuous wavelet transforms implementing Morlet wavelets of five-cycle lengths. ERSP was then computed as follows:

$$\mathrm{ERSP}(f,t) = \frac{1}{N}\sum_{n=1}^{N}|F_n(f,t)|^2,$$

where N is the total number of trials, F represents the complex numbers obtained by the wavelet transform, and f and t are discrete frequency and time instant values, respectively. ERSP values were normalized by the baseline average (400 ms preceding the stimulus