Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet



Changes in gamma- and theta-band phase synchronization patterns due to the difficulty of auditory oddball task

Jeong Woo Choi^{a,1}, Ki-Young Jung^{b,2}, Chi Hyun Kim^{a,3}, Kyung Hwan Kim^{a,*}

- a Department of Biomedical Engineering, College of Health Science, Yonsei University, 234 Maeji-ri, Heungup, Wonju, Kangwon-do, 220-710, South Korea
- b Department of Neurology, Korea University Medical Center Anam Hospital, Korea University College of Medicine, Seoul, South Korea

ARTICLE INFO

Article history: Received 3 September 2009 Received in revised form 15 October 2009 Accepted 27 October 2009

Keywords: Event-related potential (ERP) Auditory oddball task Task difficulty Gamma-band phase synchronization Theta-band phase synchronization (TBPS)

ABSTRACT

We analyze the pattern of inter-regional functional association between cortical activities during auditory oddball tasks, and the influence of task difficulty on it. Event-related electroencephalograms were recorded from 17 subjects during auditory oddball tasks with two task difficulty levels. The task difficulty was controlled by changing the difference between the frequencies of standard and target tones. The changes in behavioral response and P300 component due to the difficulty were consistent with previous findings, whereby successful control of difficulty was verified. Significant gamma- and theta-band phase synchronization (PS) was observed primarily between frontal and posterior electrodes along the midline, which is interpreted as functional connectivity among cortical regions devoted to the task execution. Apparent differences in PS were identified between two difficulties in both gamma- and theta-bands. On the whole, the number of electrode pairs showing significant PS was much smaller for higher task difficulty. The overall result is in agreement with our recent study which reported similar difference in PS due to the difficulty of 'visual' oddball task.

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The execution of oddball task involves multiple cognitive processes such as sensory perception, attention, working memory, and response generation. Analysis of event-related potential (ERP), especially P300, has been utilized in most cognitive and clinical neuroscience studies using oddball tasks [8,27]. It is recognized that task difficulty has significant effects on neuronal activity during oddball task execution. This is manifested by the changes in P300 amplitude and latency with respect to the difficulty [29], and attributed to the alteration in the demand for attentional resources [19], which is required to the update of contextual information in working memory [8].

Event-related spectral perturbation has been analyzed in various frequency bands, such as theta- and gamma-bands, to study the dynamics of the EEG spectra during cognitive tasks [22]. Emergences of theta rhythm have been repeatedly reported during a variety of cognitive tasks [4,5] Gamma-band activity (GBA) has received great interest since it is interpreted to reflect the coalition of neurons or neuronal assemblies underlying specific information processing [12]. Apparent gamma rhythms are associated with sensory perception [16], selective attention [10], and working memory [12]. Significant increase of GBA was observed during oddball tasks [11]. The task difficulty should modulate attentional demand [19] and its effect on the GBA is demonstrated in [35]. Difficulty-related changes in GBA have been recently reported for a visual oddball task as well [18].

The local changes of spectral power reflect the synchrony of neuronal activities in short range. Exploring the inter-regional functional connectivity between task-relevant cortical regions presents additional valuable information for the investigation of neuronal information processing mechanism and this is feasible by observing inter-regional phase synchronization (PS) [6,20,36]. We have recently shown that a distinct gamma-band phase synchronization (GBPS) occurs between anterior and posterior sites during visual oddball task and there is significant change in the spatiotemporal pattern of the GBPS according to task difficulty [18]. Long-range theta-band coherence was observed between prefrontal and posterior regions during memory retention [30] and oddball tasks [23].

In this regard, an integrative analysis of EEG based on interregional PS may enable more comprehensive understanding of neural information processing during oddball task and the influence of task difficulty on it, beyond conventional ERP analysis. The major purpose of this study is to elucidate whether the difficultyrelated changes in the long-range functional connectivity during auditory oddball task is comparable to those observed from visual oddball task in our recent study [18], and thus to determine

^{*} Corresponding author. Tel.: +82 33 760 2364; fax: +82 33 763 1953. E-mail addresses: cjw6427@hanmail.net (J.W. Choi), jungky@korea.ac.kr (K.-Y. Jung), chihyun@yonsei.ac.kr (C.H. Kim), khkim0604@yonsei.ac.kr (K.H. Kim).

¹ Tel.: +82 33 760 2932; fax: +82 33 763 1953.

² Tel.: +82 2 920 6649; fax: +82 2 925 2472.

³ Tel.: +82 33 760 2785; fax: +82 33 763 1953.

whether it is modality-independent feature of the difficulty of oddball tasks. We focus specifically on the gamma- and theta-band phase synchronization, based on their emergence in sensory perception, attention, and working memory, which are essential ingredients of the cortical information processing for oddball task.

Seventeen right-handed subjects (age: 23.9 ± 1.8 years, nine men) with no record of neurological or psychiatric illness participated in the experiment. Written informed consent was obtained from each subject before the experiment.

Standard and target stimuli were pure tones of 70 ms duration and 10 ms rising/falling times. Inter-stimulus interval was 2 s. Task difficulty was controlled by changing the perceptual distinctiveness between target and standard stimuli, i.e., by changing the difference between the frequencies of standard and target tones. For easy task, the frequencies of the standard and target tones were 1000 and 2000 Hz, respectively. For difficult task, the frequencies of standard and target tones were 1900 and 2000 Hz, respectively. To induce concentration on the experiment, a yellow fixation mark '+' with black background was presented for 100 ms before the stimuli on the center of a 17-inch LCD monitor. The ratio between the standard and target stimuli was 4:1. The order of presenting the easy and difficult tasks was also randomized. All the tones were presented using a pair of headphones (Sennheiser HD25SP1).

The subjects were requested to respond only to the target stimuli by pressing a mouse button as quickly as possible. The overall experiment for each subject was divided into four blocks (two for each task difficulty level), and the order of blocks was counterbalanced. In each block, 270 stimuli were presented for 9 min. The subjects rested for more than 5 min between blocks.

61-Channel EEG signals (10–10 system; American Electroencephalographic Society, 1991), along with a vertical electrooculogram (EOG, from a site below the right eye), were recorded at a sampling rate of 500 samples/s using an EEG recording system (Brain Products GmbH, Munich, Germany). An electrode cap with 61 sintered Ag/AgCl electrodes was used (EASYCAP, FMS, Munich, Germany). Impedances of all the electrodes were reduced below $10\,\mathrm{k}\Omega$. The reference electrode was formed by linked mastoid electrodes, and the ground electrode was placed between Fpz and Fz. A bandpass filter (0.03–100 Hz) and a notch filter (60 Hz) were applied to reduce background noise. Before the stimulus presentation, background baseline EEG was recorded for $\sim\!5\,\mathrm{min}$ with eyes open and staring at blank black screen.

Stereotyped artifacts (ocular and muscular artifacts) were corrected using independent component analysis, as described in [15]. Baseline correction was performed by subtracting the mean level during the 100 ms interval before stimulus onset. We removed those single-trial waveforms from further analysis for which visual inspection showed severe contamination from non-stereotyped artifacts such as drift or high-frequency muscular artifacts. Additionally, EEG segments were excluded from further analysis if the absolute value of EOG exceeded $\pm\,100\,\mu\text{V}$.

The inter-regional phase synchronization was calculated and compared to two null distributions of phase-locking value which were obtained from randomly shuffled surrogate data [20] and prestimulus baselines. For each electrode pair, the distribution of phase-locking value (PLV) for the randomly shuffled surrogate data was obtained and utilized as null distribution to determine whether the PLV increase was statistically significant. In addition, the distribution of PLVs of the EEG in prestimulus baseline was obtained and utilized as the null distribution to determine whether the PLV increase was significant with respect to the prestimulus baseline condition. The prestimulus baselines were set to -200-0 ms and -400-0 ms for gamma- and theta-band, respectively. The frequency ranges of gamma- and theta-bands were defined as 30-50 and 4-8 Hz, respectively.

Since the phase synchronization between adjacent channels was meaningless due to volume conduction, 17 electrodes were selected sparsely (Fp1, Fpz, Fp2, F3, Fz, F4, C3, Cz, C4, T7, T8, P3, Pz, P4, O1, Oz, and O2), hence 136 electrode pairs were observed in total. The EEG signals were first transformed into narrowband signals in the gamma- and theta-bands by bandpass filtering (30–50 Hz for gamma, and 4–8 Hz for theta-band, respectively), using a linear phase finite impulse response FIR filter. Instantaneous phase for each time point was calculated from the narrowband signal and its Hilbert transform [6,20]. And then, to quantify the degree of phase synchronization, the PLV between two electrodes was calculated by averaging the phase difference over overall trials [20].

Next, we determined whether the PLV of a specific electrode pair indicated significant phase synchronization. For this purpose, we devised a double-threshold strategy based on two criteria as mentioned above [18]. The first step involved checking whether the PLV change under consideration was meaningful with respect to the PLVs of surrogate data, following the permutation method of Lachaux et al. [20]. Surrogate data were obtained from 200 random shufflings of trials for each electrode pair. From the distribution of PLVs of the surrogate data for same electrode pairs, we were able to determine the level of significance, as explained in [7,20]. We set the significance level at 1%; that is, we decided that the PLV was significantly increased if it was higher than the first percentile of the distribution of PLVs for surrogate data.

Second, we determined whether the PLV increased significantly during task execution compared to the PLV for prestimulus baseline. After obtaining the distribution of baseline PLVs during the prestimulus period (200 samples) by averaging across trials, we could set the level of significance as the first step. This figure was again set to 1% of the distribution of PLVs for the baseline. In other words, we determined whether the PLV significantly increased such that it became higher than the first percentile of the PLV values obtained from the EEG during the prestimulus period. When both criteria were met, it was decided that the PLV indicated significant PS.

Significant differences in response times were observed between two task difficulties. The response time for the easy task $(372.65 \pm 132.55 \text{ ms})$ was significantly shorter than that of the difficult task $(442.51 \pm 111.47 \text{ ms})$ (t-test, t(16) = 4.94, p < 0.0001). Also, the accuracy of response for the easy task $(99.94 \pm 0.24\%)$ was significantly higher than that of the difficult task $(98.4 \pm 2.65\%)$ (t(16) = 2.21, p = 0.044).

Fig. 1(a) shows the spatial pattern of gamma-band phase synchronization (GBPS), and its temporal evolution. The upper and lower panels correspond to the easy and difficult tasks, respectively. The solid lines in Fig. 1(a) denote significant increases in the GBPS, determined on the basis of the criteria described above The significant GBPS was observed primarily between frontal and posterior electrodes along the midline. For the easy task, significant GBPS was observed as early as \sim 50 ms and lasted thereafter. The most noteworthy GBPS were observed at \sim 300–400 ms. The degree of GBPS increase was much weaker for the difficult task over entire epoch of task execution, and significant increases of GBPS were monitored from much less pairs of electrodes for the more difficult task. The numbers of the significant GBPS denoted by solid lines in Fig. 1(a) are presented in the boxes below each pattern.

Fig. 1(b) shows the spatiotemporal pattern of theta-band phase synchronization (TBPS). Similarly to the case of GBPS, significant increases in TBPS were observed between posterior and frontocentral regions along the midline. The significant TBPS increases were also observed between frontal and temporal, and temporal and posterior channels. Differently from GBPS, the significant TBPS increases were also observed between frontal and temporal, and temporal and posterior channels, and considerable amount of

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