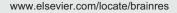


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## Difficulty-related changes in inter-regional neural synchrony are dissociated between target and non-target processing



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#### ABSTRACT

The major purpose of this study was to explore the changes in the local/global gammaband neural synchronies during target/non-target processing due to task difficulty under an auditory three-stimulus oddball paradigm. Multichannel event-related potentials (ERPs) were recorded from fifteen healthy participants during the oddball task. In addition to the conventional ERP analysis, we investigated the modulations in gamma-band activity (GBA) and inter-regional gamma-band phase synchrony (GBPS) for infrequent target and nontarget processing due to task difficulty. The most notable finding was that the difficultyrelated changes in inter-regional GBPS (33-35 Hz) at P300 epoch (350-600 ms) completely differed for target and non-target processing. As task difficulty increased, the GBPS significantly reduced for target processing but increased for non-target processing. This result contrasts with the local neural synchrony in gamma-bands, which was not affected by task difficulty. Another major finding was that the spatial patterns of functional connectivity were dissociated for target and non-target processing with regard to the difficult task. The spatial pattern for target processing was compatible with the top-down attention network, whereas that for the non-target corresponded to the bottom-up attention network. Overall, we found that the inter-regional gamma-band neural synchronies during target/non-target processing change significantly with task difficulty and that this change is dissociated between target and non-target processing. Our results indicate that large-scale neural synchrony is more relevant for the difference in information processing between target and non-target stimuli.

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#### 1. Introduction

The P300 event-related potential (ERP) component observed during the oddball task reflects multiple cognitive processes, including sensory perception, attention, working memory, memory updating, and decision making (Donchin and Coles, 1988; Picton, 1992). P300 has been used extensively to investigate important issues in basic and clinical cognitive neuroscience (Polich and Herbst, 2000; Polich, 2007). Using a traditional two-stimulus oddball paradigm, P300 is elicited when participants detect infrequent stimuli as a target when two stimuli with different frequencies are presented. In a three-stimulus oddball paradigm which includes another type of infrequent non-target stimulus in addition to the target, two distinctive subcomponents, P3a and P3b, have been identified (Courchesne et al., 1975; Polich, 2007). The non-target stimuli elicit an earlier and more anterior ERP component known as P3a. This result likely reflects involuntary attentional shifts to changes in the environment. P3a differs from the target P300 (also called P3b) in that the P3b is observed later at more posterior regions. P3b reflects the matching process between incoming information and voluntarily maintained memory content (Polich, 2007).

The amplitude and latency of P300 likely reflect the allocation of attentional resources (Kahneman, 1973) and the stimulus evaluation time (Kutas et al., 1977), respectively. The difficulty of target/standard discrimination significantly modulated these P300 features (Ford et al., 1976; Kok, 2001; Polich, 1986). This finding was attributed to greater attentional resource demands by increasing the task difficulty. Katayama and Polich (1998) showed the modulation of P300 amplitude and latency using task difficulty in the three-stimulus oddball task (Katayama and Polich, 1998). When auditory target/standard discrimination became more difficult, the target P300 (P3b) was significantly decreased and delayed, whereas the non-target P300 (P3a) was significantly increased. The same phenomena were also observed using a visual modality (Comerchero and Polich, 1999). Overall, these results confirm that task difficulty affects the cognitive processing involved in P300 generation, regardless of stimulus modality and the type of oddball paradigm.

Previous studies on the difficulty of the three-stimulus oddball task have focused on the amplitude and latency of the averaged P300 ERP component. The features of electroencephalogram (EEG) that reflect the local synchronization of a neuronal population and the global cooperation of cortical regions might provide valuable information that cannot be obtained via the analysis of averaged ERP waveforms. The spectral power in the gamma-band most likely reflects the association among the local neuronal assemblies that underlie specific information processing (Herrmann et al., 2004; Kaiser and Lutzenberger, 2005). Significantly increased gamma-band activity (GBA) at the P300 latency was found in two- and three-stimulus oddball tasks within EEG and magnetoencephalogram (MEG) studies (Akimoto et al., 2013; Gurtubay et al., 2001; Lee et al., 2007), and also in other goaldirected tasks (Bosman et al., 2010; Castelhano et al., 2013). Senkowski and Herrmann (2002) reported that GBA changed based on task difficulty during a visual discriminant task (Senkowski and Herrmann, 2002). Significant changes in GBA

based on task difficulty are also expected during the threestimulus oddball task.

Inter-regional phase synchronization likely underlies the functional integration of the widely distributed neural assemblies in task-relevant cortical regions (Rodriguez et al., 1999; Varela et al., 2001). Recent EEG and MEG studies reported large-scale neural synchronies during an oddball task (Akimoto et al., 2013; Fujimoto et al., 2013; Maurits et al., 2006). In particular, in two recent studies, we reported that large-scale neural synchronies in the gamma-band were significantly reduced and delayed for more difficult target processing using both auditory and visual oddball two-stimulus oddball tasks (Choi et al., 2010; Kim et al., 2008).

The purpose of the current study was to explore the changes in the local/global gamma-band neural synchronies during target/non-target processing due to task difficulty under an auditory three-stimulus oddball paradigm. We investigated the modulations in GBA and inter-regional gamma-band phase synchrony (GBPS) for infrequent target and non-target processing based on task difficulty; in addition, we performed a conventional ERP analysis. We investigated spatiotemporal patterns of the neural synchronies, focusing on the temporal period of P300 and compared these results with those of previous studies concerning the mechanisms of P300 amplitude/latency variation.

#### 2. Results

#### 2.1. Behavioral response

The response time for the difficult task (599.19 $\pm$ 37.86 ms) was significantly longer than that for the easy task (505.84 $\pm$ 46.72 ms; paired sample t-test, t(14) = -8.55, *p*<0.0001). The accuracy of the response for the difficult task (93.00 $\pm$ 6.83%) was significantly lower than that of the easy task (97.2 $\pm$ 3.38%; paired sample t-test, t(14)=3.28, *p*=0.005).

#### 2.2. Inter-regional gamma-band phase synchrony (GBPS)

Fig. 1A shows the time-frequency representations of the interregional phase-locking values (PLVs). These values were obtained by normalizing according to the PLVs of the baseline data (250 ms period prestimulus) for each electrode pair and then averaging all of the electrode pairs. Remarkable PLVs were found in low gamma-band (<35 Hz) at 300-800 ms for each task and stimuli. However, the difficulty-related changes of the PLVs were differentiated between the target and non-target stimuli. By increasing task difficulty, the PLVs decreased for target processing but increased for non-target processing. As Fig. 1B shows, the difference between difficulties was most evident at 350-600 ms, which is similar to the P300 period at 33-35 Hz. Statistical comparisons were performed by quantifying the averaged PLVs within the black boxes shown in Fig. 1A. The values of the normalized inter-regional PLVs are presented in Table 1. No significant main effect was observed. A significant interaction between difficulty and stimuli type was observed (F(1,14) = 16.77, p=0.001). A post-hoc test revealed that the target PLVs were significantly reduced for the difficulty task compared with the easy task (Easy:  $0.05 \pm 0.13$ ; Difficult:  $0.02 \pm 0.13$ ; t(14) = 3.28,

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