Difference in P300 response between hemi-field visual stimulation

（半側視野空間における視覚刺激に対する P300 反応の差異について）

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Abstract

I investigated differences in the cognitive/attention process following visual stimulation of the left and right hemi-visual fields. Visual P300 was recorded in thirty-one healthy right-handed subjects following target and non-target stimuli presented randomly in both visual fields. Counting and reaction time (RT) tasks using the left and right hands were performed. The P300 amplitude was significantly smaller in the RT session using the left hand. The amplitude was larger following target stimulation in the left hemi-visual field in the RT sessions using both the left and right hands. The P300 latency did not change in each stimulus condition and session, but the RT was longer for the target in the right hemi-visual field in the RT session using the left hand. I showed asymmetry of P300 response following each hemi-visual field in healthy subjects, and visual stimuli in the left hemi-visual field were dominantly processed.

Keywords: hemispatial neglect, ERP, reaction time, human, cognition

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1. Introduction

We do not normally recognize cognitive differences between visual hemi-fields. However, hemi-spatial neglect (HSN) is one of the major symptoms in patients with brain lesions, and lesions in the non-dominant hemisphere cause more frequent and severe symptoms of HSN (Schenkenberg et al., 1880; Ferro et al., 1987; Kleinman et al., 2007). Anatomical asymmetry of the brain regarding spatial attention has been reported based in the fact that lesions in the right hemisphere cause uncompensated left hemi-spatial neglect in right-handed people (Ciçek et al., 2007). However, other factors have been proposed (Malhotra et al., 2005; Karnath and Dieterich, 2006; Bartolomeo et al., 2007), and the pathophysiology remains unclear.

Since healthy people do not perceive visuo-spatial asymmetry, there have been only limited studies on whether there is asymmetry in cognitive responses following hemi-field stimulation. For specific information processed dominantly in one hemisphere, one side of the visual field has a relative advantage regarding the processing information. For example, lexical and mathematical stimuli in the right visual field were dominantly processed compared to those in the left visual field in right-handed subjects (Bruyer, 1986; Leventhal, 1988). The interpretation evidence was that the dominant side of the visual hemi-field was determined by the contents of the visual stimuli presented (McAuliffe and Knowlton, 2005; Zwaan and Yaxley, 2004). However, there has been no systematic study of the dominant side concerning visuo-spatial cognition itself in healthy subjects.

If there is hemispheric dominancy in visuo-spatial cognition, it is speculated that the visually evoked brain responses following unilateral stimulation cause different brain responses between stimulated sides. One of the technical problems to reveal different brain responses between stimulated sides is that any object presented or visual stimulation is processed differently in each hemisphere (McAuliffe and Knowlton, 2005; Zwaan and Yaxley, 2004). In addition, dipole location and direction were considerably different in the primary visual cortex in the studies of magnetoencephalography (Brecelj et al., 1998; Nakamura et al., 1997, 2000). Thus, it may not be surprising to identify asymmetry of visually evoked potentials following left and right unilateral stimulation. However, event-related potentials (ERPs), i.e., P300, recorded as a vertex potential during a discrimination task, were differently evoked depending on the difficulty of tasks (Polich , 2007), and not depending on the contents of stimulation.

Therefore, the hypothesis was that P300 following unilateral visual stimulation could be differently evoked depending on the dominancy of visuo-spatial recognition between hemi-field visual stimulation, which could be an evidence of visuo-spatial asymmetry of cognition in healthy subjects. In the present study, I recorded P300 following unilateral stimulation in healthy subjects, in which target and non-target stimuli were randomly presented in both hemi-fields visual stimulation (Suzuki and Hoshiyama, 2011). To my knowledge, no ERP study has investigated cognitive differences between hemi-visual fields in healthy subjects.

2. Methods

2.1. Subjects

Thirty-one healthy right-handed subjects participated in the study (15 males and 16 females, age: 28.2 ±5.1 years). They were post-graduate students of Nagoya University, and they had no specific training regarding visuo-spatial skills. No subject had a history of systemic disorders, neurological, psychological or ophthalmological diseases, e.g., diabetes, past head trauma, alcohol or psychotropic drug use, depression or visual disturbance. The natural or corrected visual acuity was 20/20 for the fractional visual acuity or better in each subject. All subjects were interviewed by a medical doctor prior to the study to check their mental/physical normality.

The handedness of the subjects was checked using the Edinburgh Handedness Inventory (Oldfield, 1971). The mean laterality quotient, which expresses handedness using a value between 100 (right handedness) and –100 (left handedness) was 99.2 ±3.6 (SD).

Written informed consent to participate in the study, which was first approved by the Ethical Committee of Fujita Health University (No. 08-019), was obtained from all participants prior to commencing the study.

2.2. Experimental design

One major objective of the present study was to investigate whether cognitive response revealed by an ERP, P300, was differently evoked by the right and left hemi-filed visual stimulation. Therefore, I measured the visual P300 evoked by a modified Oddball paradigm. On a 24-inch monitor screen 50 cm in front of the subjects, a fixation point (+, 1.0 x 1.0 cm) was presented as target (○, diameter: 1.0 cm) and non-target (●, diameter: 1.0 cm) symbols at a point 21.8 degrees lateral to the center of the screen in each visual field. The probability of viewing the target and non-target symbols was 25 and 75%, respectively. The symbols were randomly presented in each hemi-field. The presentation period was 1.0 sec, and the stimulus onset asynchrony (SOA) was random between 2.0 and 2.5 sec. Targets presented on the left and right sides were expressed as Lt-T and Rt-T, respectively.

The experiment comprised three sessions: left and right reaction time (RT) sessions and a counting session. The subject was seated on a chair and gazed at the fixation point. The subject held a button for pressing in the left and right hands for left and right RT sessions, respectively. The sessions were expressed as LPS and RPS for the left and right hand button-pressing sessions, respectively. The subjects were instructed to press the button as quickly as possible when they saw the target symbol. In the counting session (CS), the subject was instructed to count the number of target symbols presented without any movement, e.g., tapping finger. Each session was repeated twice; thus, six sessions were pseudo-randomly arranged in order for each subject. One session took 200-250 sec, including 25-30 target symbols in each visual field, and a short rest was provided between sessions.

2.3. ERP recording

ERP was recorded using a signal processor (MEB-2200, Nihon-Kohden, Japan). Electrodes were Ag-AgCl disc electrodes (diameter: 8.0 mm). The recording electrodes were placed at Fz, Cz, Pz, F3, F4, C3, C4, P3 and P4 using the International 10-20 system (Nuwer et al., 1999), and the reference was attached to the linked-earlobes. Impedance between electrodes was kept below 10 kOhm.

Electroencephalography (EEG) signals were collected for 1.0 sec after the onset of target and non-target stimuli, with a bandpass filter between 1 and 100 Hz. EEG signals were digitized at 1 kHz. Epochs with signals of more than 200 μV were rejected, and 50 artifact-free epochs were collected for both target and non-target stimuli in each visual field in each session. RT from the onset of stimulation was also recorded.

The baseline in each averaged waveform was determined based on the averaged value of 100 pre-trigger points (for 100 ms). The peak of P300 was determined as the maximal positive peak between 200 and 500 ms after stimulus onset, and P200 was determined as a component with a latency around 200 ms, which was a previous positive peak to P300. Therefore, I measured the amplitude and latency of the conventional P3b component (Polich, 2007). The amplitude of P200 and P300 was the negative values from the baseline to peak of the components.

2.4. Statistical analysis

I focused on P300 (P3b) components, and first I checked that the distribution of P300 was dominantly in C-P areas on the scalp (Fig. 1), subsequent analyses were carried out using values recorded from the central and parietal areas.

First, mean values of the P200 and P300 amplitude recorded at Cz and Pz areas in all sessions were compared by two-way (target side and electrodes) repeated measures ANOVA with Bonferroni-Dunn's correction for multiple comparisons in each session. For each parietal area, P3, P4 and Pz, the P300 amplitude was compared by two-way (target sides and sessions) repeated measures ANOVA followed by Bonferroni-Dunn's correction for multiple comparisons. Then, the P300 latency recorded from the Pz area and RT was compared among sessions, using two-way (sessions, target side) repeated measures ANOVA followed by Bonferroni-Dunn's correction for multiple comparisons. P values less than 0.05 were considered significant.

3. Results

P300 responses were successfully recorded in subjects (Fig. 1). First, I compared mean amplitude of P200 and P300 recorded from Cz and Pz in all sessions between the presented sides of the target. For P300, the main effect of target side was significant (F [1, 60] = 6.65, p = 0.012), but the effect of electrodes was not significant (F [1, 60] = 0.51, p = 0.48). Bonferroni-Dunn's correction showed significant larger P300 amplitude following the left side than the right side stimulation (p = 0.012). There was no effect of target side (F [1, 60] = 1.10, p = 0.29) and electrodes (F [1, 60] = 0.47, p = 0.49) on P200.

The main effect of target sides on the mean P300 amplitude recorded at Pz was significant (F [2, 90], p = 0.019), and the value was larger Lt-T than in the Rt-T condition in both RPS (p = 0. 033) and LPS (p = 0.023), but not in

CS condition (p = 0.071) (Fig. 2 and 3). The value was not significant between target sides in the P3 (RPS; p = 0. 054, LPS; p = 0.061) and P4 (RPS; p = 0. 046, LPS, p = 0.057) areas, although p-values were in a range of tendency of the difference in button-pressing sessions although p-values suggested tendency of the difference in button-pressing sessions in multiple comparisons.

There was no difference in the P300 latency at Pz between the sides of the target stimulus in any session (Fig. 4). Among the subjects (n = 31), 22 (71 %) showed larger P300 amplitudes when the target stimulus was presented on the left side in RPS, and 31 subjects also showed a similar difference in the P300 amplitude in LPS. The number of subjects who showed a larger P300 amplitude for Lt-T in the CS session was 15 (48.4 %).

The main effect of target side was significant (F [3, 30] = 2.27, p = 0.039), and RT was significantly longer for the Rt-T than Lt-T condition in LPS (p = 0.035, Fig. 5). There was no difference in RT between the conditions in other sessions.

4. Discussion

The main results of the present study can be summarized as follows. The P300 amplitude decreased in LPS. The P300 amplitude was larger following the target stimulus in the left hemi-visual field in RPS and LPS with motor performance, but a change in amplitude was not recognized in CS. An additional finding was that RT was longer when the target stimulus was presented on the right side in LPS. The present results indicated asymmetry in visuo-spatial cognition in healthy subjects, which was enhanced to be detectable with a motor task.

4.1. Difference in the P300 amplitude

The present results were interpreted in the light of the recent understanding of P300 and the pathophysiology of hemi-spatial neglect. When the primary task difficulty increased, the P300 amplitude decreased (Isreal , 1980; Wickens, et al., 1983). In other words, when the task required more attentional resources, the P300 amplitude became smaller (Kok, 2001). Therefore, a smaller amplitude in LPS than in RPS and CS indicated that pressing the button using the left hand was a relatively difficult task regarding the use of attentional resources. Similarly, in each session in RPS and LPS, the P300 amplitude was larger following Lt-T than Rt-T, which indicates that the task for Lt-T was easier than that for Rt-T. In the present study, the difficulty in discriminating between target and non-target signals was similar, but the spatial location of stimuli differed between Lt-T and Rt-T. Thus, the difference in the P300 amplitude between Lt-T and Rt-T was caused by a difference in spatial processing, or hemispheric differences in spatial processing.

4.2. Anatomical structure for P300

A recent study of anatomical differences between hemispheres regarding visuo-spatial cognition reported that the inferior parietal lobule in the right hemisphere was responsible for bilateral attention, while other areas showed a symmetric function for spatial attention (Ciçek et al., 2007), and Bartolomeo et al. (2007) reported that the inter-cortical connection for attention and spatial processing was dominant in the right hemisphere. When the brain activity responsible for spatial attention does not depend on the contents of visual information, but on the location in the visual filed, P300 could be different between stimuli in each visual field. Generators for P300 remain unclear, and I cannot simply conclude that the P300 difference between target locations in each hemisphere was related to the asymmetric neural structures for spatial attention. However, progress in the study of P300 generators has suggested that frontal, temporal, and also parietal activation were responsible for the P300 (P3b) generation (Polich, 2007; McCarthy and Donchin, 1981; Kirino et al., 2000; Macaluso et al., 2007). The dominancy of the right hemisphere for spatial attention might lead to relatively easier neural processing for the left compared to right hemi-visual field.

4.3. Reaction time and P300 latency

The difference in the P300 amplitude was observed only in the sessions with a motor task involving button pressing. Since the difference in the P300 amplitude was observed in both RPS and LPS, handedness was not the reason for the P300 amplitude difference. Based on the results of the P300 amplitude, as described above, target presentation in the right hemi-field during LPS was the most difficult task in the present study. I speculate that this might be the reason for the delayed RT for the target in the right hemi-field in LPS. On the other hand, there was no difference in the P300 latency between the target locations in LPS. Since RT is not always related to the P300 latency (McCarthy and Donchin, 1981), there might be no significant association between the P300 latency and RT in the present study.

4.4. Motor task and P300

The difference in the P300 amplitude could be explained by the task difficulty between hemi-visual field attention processing. I have to consider another factor, bimodal or inter-modal interaction, for the present results. A specific region of the brain, such as the posterior superior temporal sulcus, was activated by sensory input in any modality, and was responsible for signal transfer to the motor process (Macaluso et al., 2007). Another report (Kansaku et al., 2004) demonstrated that posterior superior temporal and premotor cortices in the right hemisphere were activated by multi-modal inputs in the absence of a motor task. Therefore, neural activity for multi-modality processes was considered to be dominant in the right hemisphere. Button-pressing task on visual target was a multi-modal task dominantly processed in the right hemisphere, and visual and motor processes could occur mainly in the right hemisphere at Lt-T in LPS, which might have resulted in the shorter RT at Lt-T in LPS. I do not conclude that the difference in the P300 amplitude corresponded to asymmetry in a specific brain activity, such as spatial attention and multi-modal activities, but that the asymmetry of visuo-spatial cognition could be shown by employing the ERP technique in healthy subjects.

4.5. Clinical consideration

In some patients with hemi-spatial neglect, the symptom became evident though motor/behavioral performance in patients who did not show significant symptoms on conducting visual tests at a desk (Heilman and Valenstein, 1979; Karnath and Niemeier, 2002; Coulthard et al., 2007). Subjects who showed a larger P300 amplitude for Lt-T in CS comprised 47.6%, while that in RPS and LPS both comprised 71.4%. These percentages were consistent with the range of a clinical report in which the appearance rate of hemi-spatial neglect in patients with right hemispheric lesions varied among tasks between 30-90% (Schenkenberg et al., 1980). In healthy subjects in the present study, there was no difference in latency between Rt-T and Lt-T in any session. I consider that the asymmetry in hemi-visual processing was compensated for to cancel out cognitive differences. Subjects might not perceive side dominancy of spatial cognition, although there might be functional asymmetry in the processes.

I considered that appropriate dual tasks might reveal the asymmetry of the spatial attention process.

In conclusion, using P300 recording, I showed functional asymmetry of the spatial attention process for each hemi-visual field in healthy subjects. Dual-task with motor performance revealed the dominant spatial attention process of the right hemisphere, and the results might relate to the clinical findings in patients with hemi-spatial neglect.

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Table 1: Mean amplitude (μV ± SD) and latency (ms ± SD) of P200 and P300 recorded at Pz.

		Pressing with the right hand (RPS)	Pressing with the left hand (LPS)	Counting (CS)
P200	Amplitude	4.3 ± 3.5	4.6 ± 3.7	5.2 ± 4.0
	Latency	208 ± 18.2	205 ± 15.2	202 ± 22.9
P300	Amplitude	14.3 ± 6.2	13.6 ± 5.4 *	14.6 ± 5.3
	Latency	402.4 ± 43.3	395.2 ± 44.3	386.6 ± 50.1

* $p < 0.05$, vs. RPS and CS

Figure 1

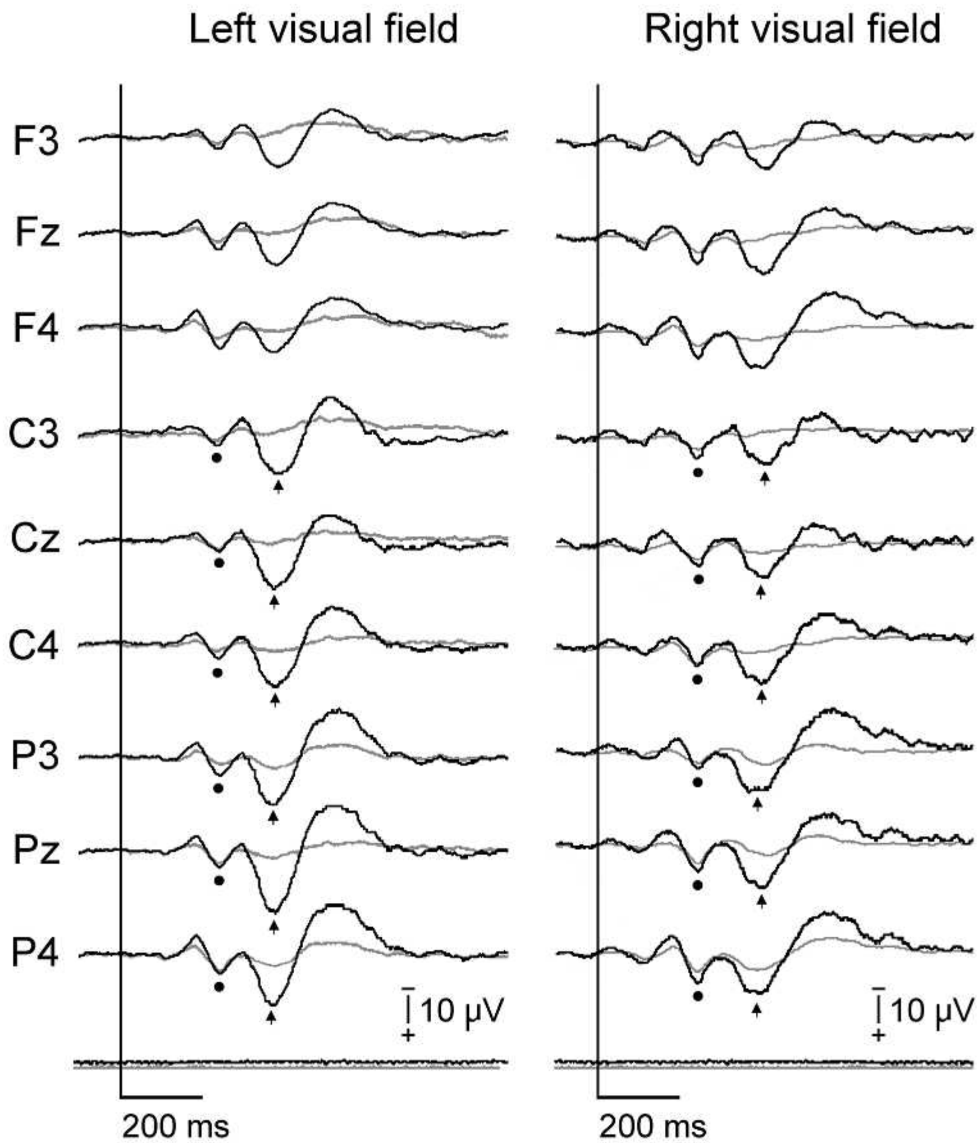

Figure 1: Grand average waveforms recorded in all subjects following target presentation in the left (left column) and right (right column) hemi-visual field in a button-pressing session using the left hand. P300 (P3b, arrow for C and P areas) and P200 (●) are indicated. Vertical solid lines indicate the trigger point for the EEG epoch. Gray lines indicated potentials following non-target presentation.

Figure 2

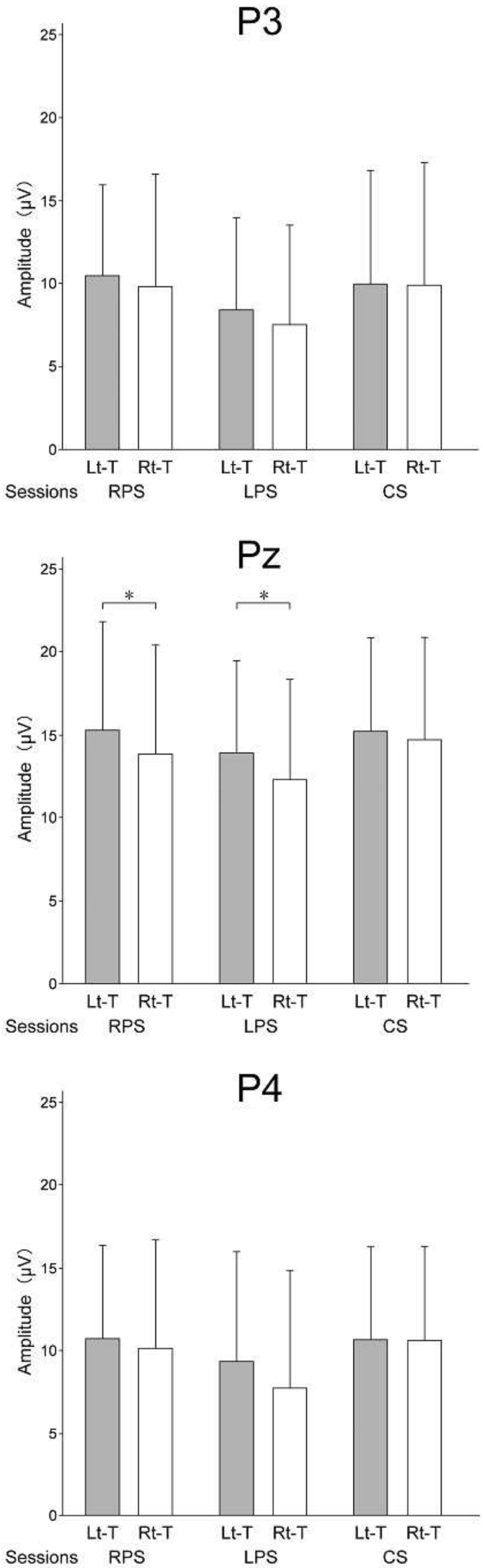

Figure 2: P300 amplitude at parietal areas, P3, Pz and P4, for targets in the left (Lt-T) and right (Rt-T) hemi-visual fields in each session. The amplitude was significantly smaller for Rt-T in the button-pressing sessions using the left (LPS) and right (PRS) hands at Pz area (*p<0.05). The values were not significant different between target sides, although tendency of the difference in button-pressing sessions was seen in P3 and P4 areas. However, there was no difference in amplitude in the counting session (CS). Each vertical bar indicates a standard deviation.

Figure 3

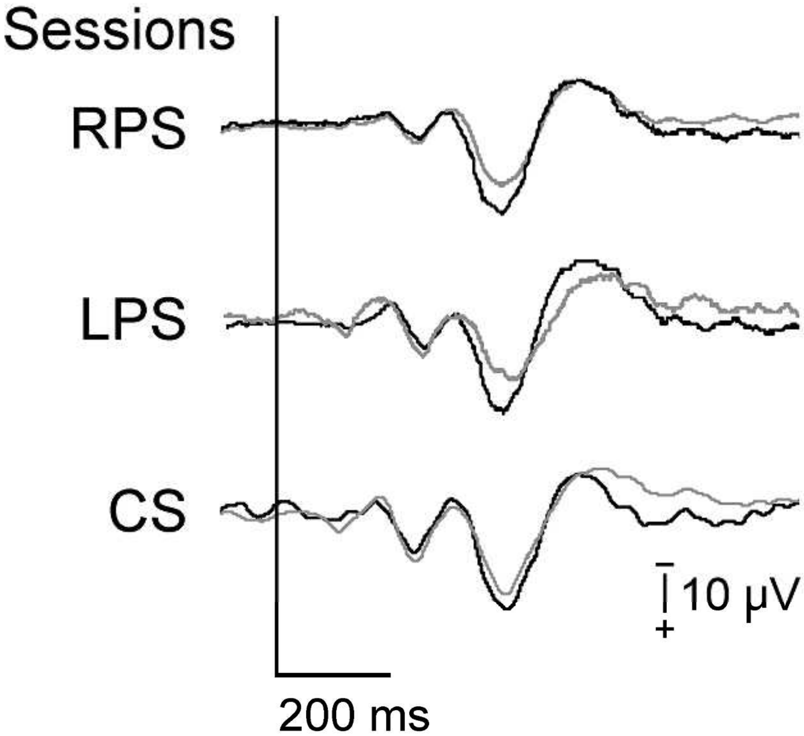

Figure 3: Grand average of waveforms of P300 recorded in all subjects following target presentation in the left (black lines) and right (gray lines) hemi-visual field in all sessions recorded at Pz area. The P300 amplitude was larger for the target in the left than in the right hemi-visual filed in both the right (RPS) and left (LPS) button-pressing sessions, while difference in P300 amplitude in counting session (CS) was small.

Figure 4

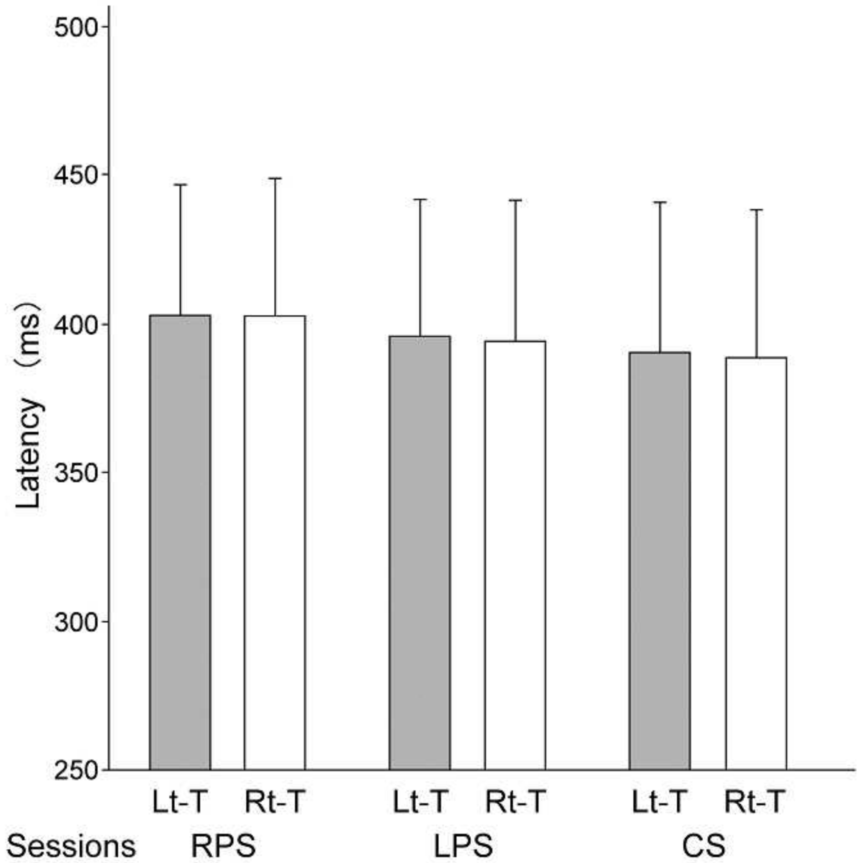

Figure 4: P300 latency at Pz for targets in the left (Lt-T) and right (Rt-T) hemi-visual fields in each session. The latency did not change between the locations of the target and sessions. Each vertical bar indicates a standard deviation.

Figure 5

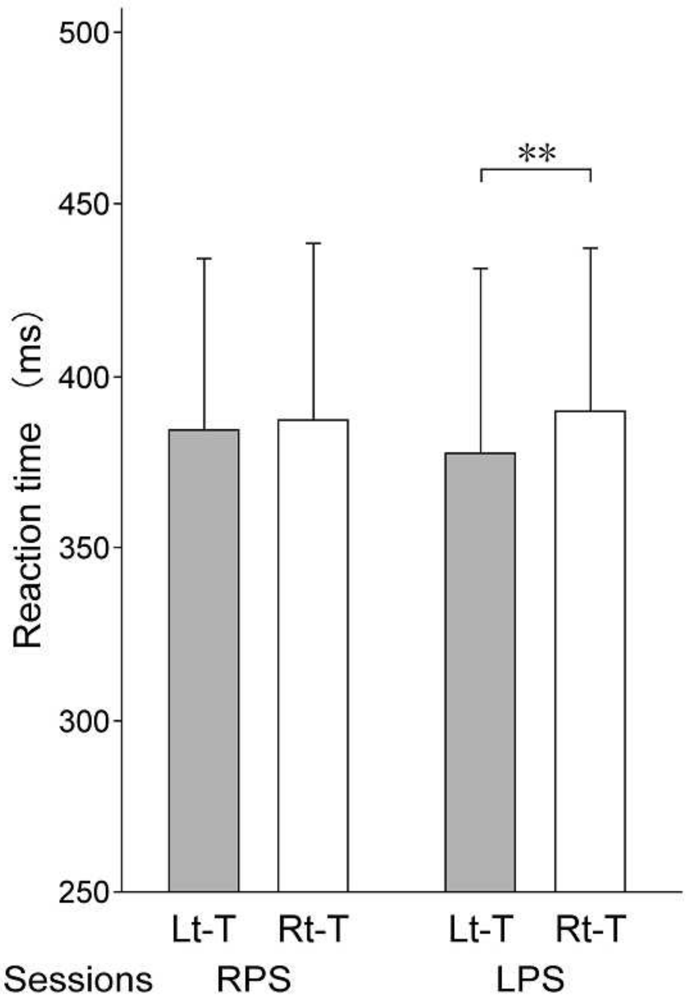

Figure 5: Reaction time (RT) for targets in the left (Lt-T) and right (Rt-T) hemi-visual fields in each button-pressing session. RT was longer for Rt-T than for Lt-T in the button-pressing session using the left hand ($p<0.01$). Each vertical bar indicates a standard deviation.