

Figure 4.

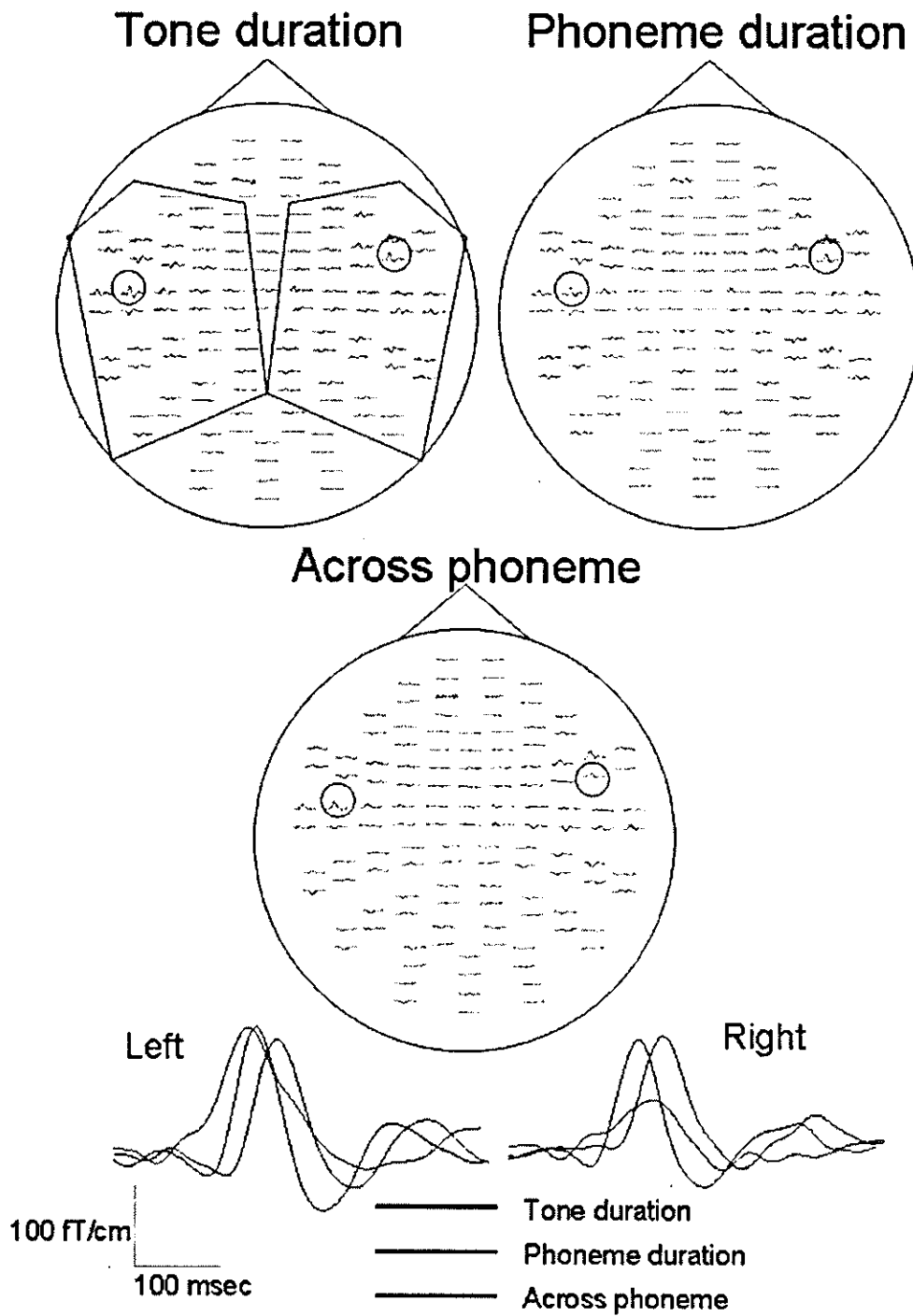
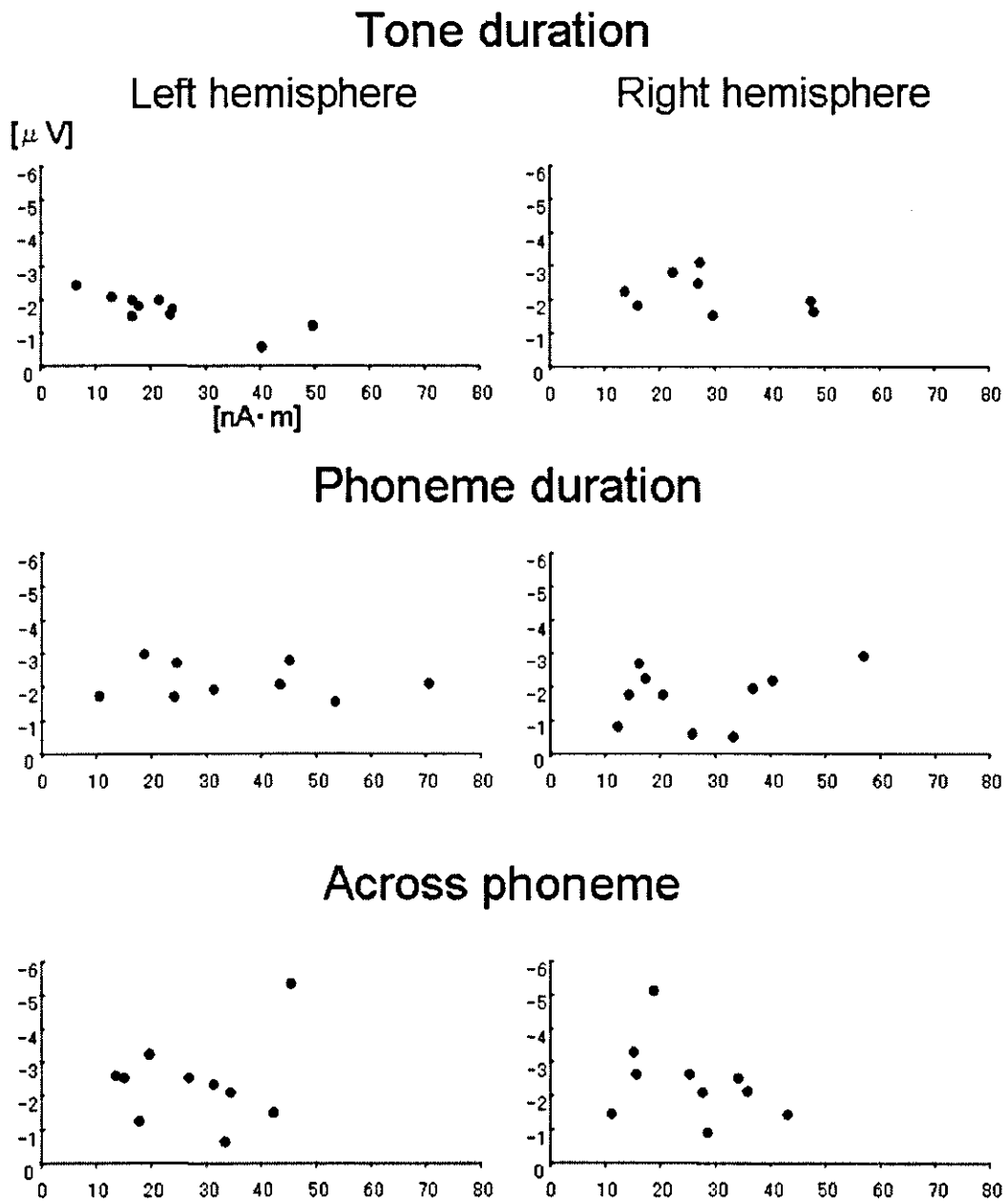


Figure 5.





Brain electric activity for active inhibition of auditory irrelevant information

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Abstract

We applied high resolution event-related potentials (ERPs) to assess brain activities associated with inhibition of irrelevant information processing during auditory selective attention. Ten healthy subjects performed an auditory selective attention task. ERPs in response to standard stimuli delivered to the unattended ear (irrelevant stimuli) and those delivered to the attended ear (relevant stimuli) were evaluated using temporally sequential scalp current density (SCD) mappings. For the irrelevant stimuli, current sources were located in the mid-frontal regions at 140–220 ms post-stimuli, and these SCD values were significantly larger than those for the relevant stimuli. These results suggest that auditory selective attention process involves not only focusing attention on relevant information, but also inhibitory processing of irrelevant information mediated by the frontal cortex.

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Keywords: Auditory; Event-related potentials (ERPs); Frontal lobe; Inhibition; Selective attention

Auditory selective attention [7,25] is a crucial brain function for appropriate human behavior. This process is thought to consist of two different aspects. One aspect is focusing attention on relevant information and the other is inhibitory processing of irrelevant information [2,15,17]. This dichotomy is compatible with that proposed for the visual selective attention process [19]. Brain activities for these two processes can be simultaneously and separately examined by measuring event-related potentials (ERPs) during an auditory selective attention task. In this task, subjects are instructed to focus attention on, and respond to, deviant tones among a sequence of tones delivered to one ear (relevant stimuli), and

to actively keep attention away from both deviant and standard tones delivered to the other ear (irrelevant stimuli). The facilitation of auditory selective attention to relevant information can be assessed by ERPs elicited by relevant standard stimuli (processing negativity, PN), or those obtained by subtracting ERPs elicited by irrelevant standard stimuli from those elicited by relevant standard stimuli (negative difference wave, Nd) [18,25]. On the other hand, the inhibition of irrelevant information processing could be assessed by ERPs elicited by irrelevant standard stimuli.

The Nd/PN has been shown to consist of two temporally and spatially dissociable subcomponents [18]: the early Nd, associated with a matching process between deviant stimuli and the neural trace encoding the physical features of standard stimuli, is located in the bilateral temporal regions; the late Nd, associated with the selective rehearsal and the maintenance of the attentional trace, is generated from the mid-

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frontal regions. Corroborating findings, although not addressing the temporal sequence, have been obtained by positron emission tomography [1] and functional magnetic resonance imaging studies [11] showing activation of several portions of the frontal and temporal cortex during auditory selective attention.

On the other hand, few studies have been devoted to determining the characteristics of inhibitory processing of irrelevant stimuli during auditory selective attention. Alho et al. [2] observed positive deflections in ERPs elicited by irrelevant tones, and they considered that the positivity might reflect active inhibition of the processing of an irrelevant stimulus after it is found incompatible with the attentional trace, or reflect temporary relaxation after the stimulus is found irrelevant. Michie et al. [17] also found positive deflections elicited by irrelevant stimuli during the active auditory attention task in comparison with auditory ERPs recorded during the visual control task. Furthermore, there are a number of studies that demonstrate positive deflections of ERPs to be associated with the inhibitory processing [8,9,12]. These findings suggest the presence of a positive ERP component associated with inhibition of irrelevant information processing during auditory selective attention; however, these previous studies, due to the use of montages with fewer electrodes, have not elucidated spatiotemporal characteristics of these components. The low temporal resolution of hemodynamic measures, at least to date, has not been able to disentangle these activities from those associated with relevant information processing [1,11].

Accordingly, the present study assessed spatiotemporal characteristics of brain activities associated with processing of irrelevant stimuli during auditory selective attention. We used high-spatial-resolution ERPs for two reasons: (1) high temporal resolution of ERPs, unlike hemodynamic measures, would allow a simultaneous recording and evaluation of relevant and irrelevant information processing during auditory selective attention; (2) the scalp current density (SCD) computation based on a high-density montage would reveal spatial characteristics of these processes. Our use of high-resolution EEG montage enabled a more correct computation of scalp current density distribution than that from low-resolution EEG montage relying on the interpolation of the real data. We predicted that spatiotemporal characteristics of the inhibitory process of irrelevant information are dissociable from those of the facilitatory process of relevant information, with the latter having been found to activate bilateral temporal regions at approximately 160–220 ms and mid-frontal regions at around 320 ms subsequent to the presentation of stimuli [13].

This experiment and the results of the Nd component have been described in Kasai et al. [13]. The present study describes the post hoc analysis of that study; here we focus on ERPs elicited by standard stimuli delivered to the irrelevant ear. Ten healthy subjects (six females and four males; mean age = 21.9 [S.D. = 1.6]; one left-handed subject as determined using the Edinburgh Inventory [20]) participated. All of the

subjects were recruited from college students or graduates. The mean years of education was 14.7 (S.D. = 1.3). This study was approved by the Ethical Committee of the Faculty of Medicine, University of Tokyo. After a complete explanation of the study to the subjects, their written informed consent was obtained.

The subjects performed an auditory selective attention task, during which tones of 70 dB SPL (rise/fall time: 10 ms) were presented dichotically via headphones. The entire task included 8 blocks of tones. Through half of the blocks, the left ear stimuli were set at 1 kHz and the right ear stimuli at 2 kHz; through the other half of the blocks, the frequencies were reversed. The order of 1 and 2 kHz blocks were counterbalanced across subjects. Each block consisted of 200 standard stimuli (probability: 80%; duration: 100 ms) and 50 deviant stimuli (20%; duration: 50 ms), presented to each ear in random order. The interstimulus interval (ISI) was 600 ms. The subjects were required to focus on one ear and silently count the deviant stimuli while ignoring all the stimuli delivered to the other ear. Ear designation was counterbalanced across the blocks.

While performing the task, the subjects sat comfortably in a dimly lit, sound-proof, electrically shielded room. EEGs were recorded via a 128-electrode cap (Neurosoft, Inc.), including channels according to the international 10–20 system. The vertex was used as the reference for all the electrodes. Two electrodes were placed at the outer canthus and above the left eye to monitor eye movements. The sampling rate was 500 Hz, and the analog filter band-pass was 0.1–100 Hz. The analysis period was 512 ms, including a 64-ms prestimulus baseline. The baseline was corrected separately for each channel according to the mean amplitude of the EEG over the 64 ms preceding stimulus onset. Averaging and artifact rejection were conducted offline. The EEG epochs that contained peak-to-peak amplitudes exceeding 50 μ V at any site and EOG waves exceeding 150 μ V in amplitude were automatically excluded from the averaging. The average waveforms were obtained separately for deviant and standard stimuli for each ear, and digitally filtered with a cutoff frequency of 30 Hz. The number of accepted responses for the standard stimuli was more than 320.

The SCD computation strengthens near electric fields and filters far electric fields; thus, it is suitable for differentiating multiple generators of activities near the cortical surface. Moreover, the SCD is reference-independent; thus it is not affected by the substantial potentials elicited in the reference electrode. The topographic SCD mapping methodologies employed in the present study have been described in detail elsewhere [13,14]. Briefly, peripheral electrodes beyond the 10–20 system areas were excluded, and for the remaining 104 channels the scalp potential was reconstructed by spherical spline interpolation [22,23]. The scalp current density distributions were then obtained by computing the spatial derivatives of the spherical spline functions used in the potential map interpolation [$J = -\sigma((d^2V/dx^2) + (d^2V/dy^2))$] [21,24].

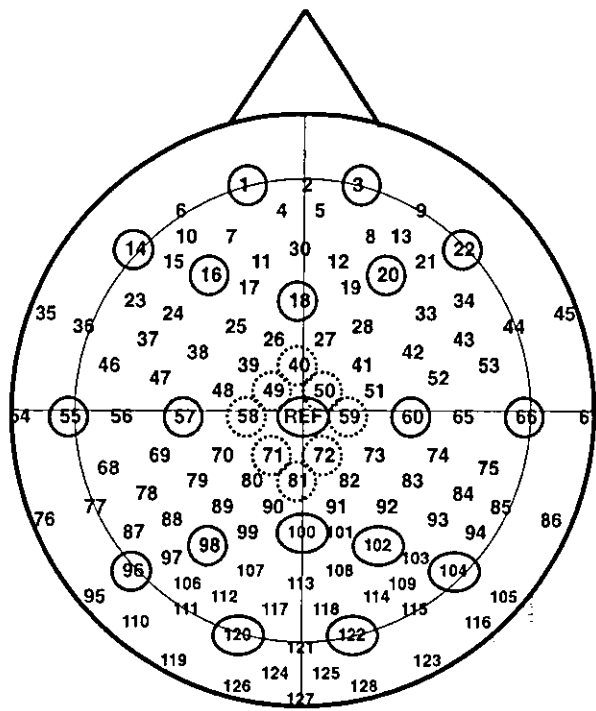


Fig. 1. Electrode position map for the 128-channel EEG recording system. Position numbers encircled by thick line indicate the international 10–20 system positions. Eight channels selected for statistical analysis on scalp current density values are indicated by dashed circles.

Counting performance (error rate) was assessed by calculating the average rate of deviation of the actual counts from the current number of targets for each ear stimulated.

We tested whether SCD values for irrelevant standard stimuli were significantly more positive than those for standard relevant stimuli. The SCD values were averaged across eight electrodes around Cz where the positive current densities in response to irrelevant standard stimuli were maximal (Fig. 1), and across the time window of 130–150 ms, 150–170 ms, 170–190 ms, 190–210 ms, and 210–230 ms. We performed a repeated measures analysis of variance (ANOVA) adopting ear stimulated, relevance (relevant, irrelevant), and latency (five time windows) as within-subject factors.

Spearman's ρ was calculated for the correlation between the SCD values and the counting performance for each ear stimulated and latency.

A preliminary inspection of the data revealed no outliers, or distribution effects due to the participation of the left-handed subject; thus this subject was not excluded in the further analyses. Moreover, since the amplitudes and topographic distribution of ERPs in 1 and 2 kHz blocks were not significantly different, these responses were collapsed during the averaging. For both ears stimulated, waveforms at Oz (where the most prominent ERP deflection could be seen because of the Cz reference) indicated a positive deflection at around 100 ms and a negative deflection at around 140–220 ms for both relevant and irrelevant stimuli (Fig. 2). Considering that Cz was the reference electrode, the former

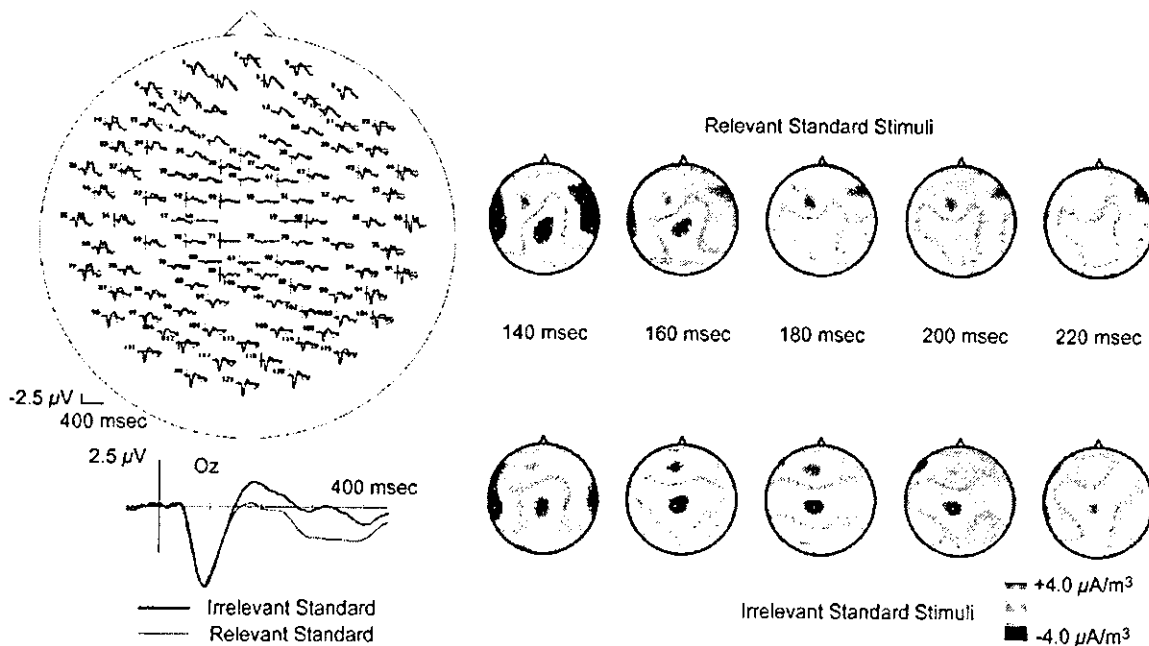


Fig. 2. (Left) Grand-averaged waveforms (Cz reference) for relevant and irrelevant standard stimuli under the selective attention condition. Negativity is denoted by upward deflection. (Right) Scalp current density mappings. Since there was no significant effect of ear stimulated, only the right-ear condition was illustrated.

deflection was considered to be the N100 component. The deflection at around 140–220 ms was considered to be a positive ERP component, corresponding to the current sources (positive SCD values) over central regions. At around 180–220 ms in particular, the current sources for irrelevant stimuli appeared to have larger positive values than those for relevant stimuli.

The repeated measures ANOVA did not show a significant main effect of ear ($F[1,9]=1.53$, $p=0.248$, $\epsilon=1.0$) or interactions with ear (ear-by-relevance: $F[1,9]=1.45$, $p=0.26$, $\epsilon=1.0$; ear-by-latency: $F[4,36]=0.986$, $p=0.38$, $\epsilon=0.42$; ear-by-relevance-by-latency: $F[4,36]=1.91$, $p=0.19$, $\epsilon=0.34$). Therefore, amplitudes were averaged across ear stimulated for further analyses. There was a trend toward significant main effect of relevance ($F[1,9]=4.98$, $p=0.053$, $\epsilon=1.0$) and a significant relevance-by-latency interaction ($F[4,36]=6.34$, $p=0.013$, $\epsilon=0.42$), allowing a separate analysis for each latency. The follow-up analysis indicated that SCD values for irrelevant stimuli had a significantly larger positivity than those for relevant stimuli at 170–190 ms (trend-level), 190–210 ms, and 210–230 ms time windows (Table 1).

The mean counting performance (error rate) was 5.6% (range: 0.0–14.0, S.D. = 4.3) when the right ear received relevant stimuli, and 5.0% (range: 0.0–10.0, S.D. = 3.3) when the left ear received relevant stimuli. The current sources were not significantly correlated with the counting performance for either ear stimulated at any latency (left: $n=10$, $\rho=-0.122$ to 0.170, $p=0.64$ –0.85; right: $n=10$, $\rho=-0.41$ to 0.21, $p=0.24$ –0.59).

To our knowledge, this is the first high-resolution EEG study that evaluated spatiotemporal characteristics of brain electric activity associated with active inhibition of irrelevant information during auditory selective attention. The main finding of the present study is that SCD mappings for irrelevant stimuli revealed temporally sequential current sources in the mid-frontal regions at around 140–220 ms subsequent to the onset of tones. These current sources had significantly larger positive values than those for relevant standard stimuli at around 180–220 ms. Thus, as predicted, the high-resolution SCD analyses allowed us to identify dissociable brain activities for facilitatory processing of relevant information and inhibitory processing of irrelevant information during auditory selective attention.

These activities are unlikely to be the consequence of mental counting and/or “No-Go” trials, since this was most evidently seen in the irrelevant standard ERPs. These positive values also had a different SCD distribution from the “P200” and “P300a”, since these components have generators at least in part from the bilateral auditory cortex [3,10]. We speculate that this temporal P200 activity may be suppressed for irrelevant standard stimuli under the auditory selective attention condition.

In this study, we did not find a significant association between SCD values of the positive component and the performance level. This may be partly because the task was not so

Table 1
Scalp current density values for relevant and irrelevant standard stimuli

	Latency				
	T1 (130–150 ms)	T2 (150–170 ms)	T3 (170–190 ms)	T4 (190–210 ms)	T5 (210–230 ms)
	Mean ($\mu\text{A}/\text{m}^2$) (range)	Mean ($\mu\text{A}/\text{m}^2$) (range)	Mean ($\mu\text{A}/\text{m}^2$) (range)	Mean ($\mu\text{A}/\text{m}^2$) (range)	Mean ($\mu\text{A}/\text{m}^2$) (range)
Left ear					
Relevant	2.75 (0.95–5.17)	2.74 (0.90–5.03)	1.92 (0.09–4.90)	1.60 (0.59–4.01)	1.64 (0.96–3.73)
Irrelevant	2.96 (–0.09–6.87)	2.86 (–0.01–6.54)	2.37 (–0.90–5.54)	2.41 (0.17–4.72)	2.42 (–0.69–5.66)
Right ear					
Relevant	2.42 (0.10–6.48)	2.30 (0.55–6.54)	1.34 (–0.60–4.08)	0.93 (–0.70–3.22)	0.93 (–1.27–4.37)
Irrelevant	2.64 (1.20–5.65)	2.93 (0.88–6.06)	2.61 (–1.16–6.23)	2.49 (–0.93–5.14)	2.40 (0.68–5.46)
Average ^a					
Relevant	2.58 (1.18–5.82)	2.52 (0.82–5.79)	1.63 (–0.14–4.49)	1.27 (–0.35–3.61)	1.28 (–0.84–4.05)
Irrelevant	2.80 (0.67–6.26)	2.90 (0.85–6.26)	2.49 (–1.03–5.88)	2.45 (0.02–4.91)	2.41 (–0.01–5.56)
Paired <i>t</i> -test	–1.04	–1.13	–2.03	–2.71	–2.78
<i>p</i> -value	0.33	0.29	0.073	0.024	0.022
S.D.					
T1 (130–150 ms)	1.18	1.47	1.58	1.56	1.56
T2 (150–170 ms)	1.77	1.97	1.94	1.48	1.48
T3 (170–190 ms)	1.65	1.86	1.62	1.40	1.40
T4 (190–210 ms)	1.47	1.85	2.12	1.81	1.81
T5 (210–230 ms)	1.33	1.58	1.52	1.38	1.38
Average ^a	1.55	1.82	1.97	1.57	1.57

^a Averaged SCD between left and right ear stimulated was calculated for post hoc analysis (paired *t*-test) since there was no significant effect of ear stimulated.

difficult for subjects to perform, resulting in a restricted range of distribution of the performance data. Thus, further studies will be necessary to clarify the psychological significance of the positive deflections and the mechanisms of how the inhibition of irrelevant information processing contributes to the facilitation of auditory selective attention.

Although speculative, there may be several candidate regions for the anatomical source of the positive deflections observed in the current study. One possibility may be the anterior cingulate cortex, which has been shown to play an important role in the control of response to incongruent stimuli [16]. Although the anterior cingulate cortex is located somewhat deep in the frontal lobe, previous studies have detected anterior cingulate activities from scalp current density calculations [4,6]. Another possibility, although not exclusive, may be the supplementary motor and/or premotor cortex, which have been implicated in voluntary cognitive control even in the absence of actual movement [5]. These possibilities should be regarded as tentative, however, due to the limitation of the spatial resolution of data from the scalp EEG recording. This issue may be clarified in future studies using intracranial recordings.

The present high-resolution ERP study revealed that the frontal cortex is activated for the inhibitory processing of irrelevant information during auditory selective attention in humans. These findings may revisit the importance of simultaneous and separate evaluation of facilitation of relevant information processing and inhibition of irrelevant information processing during auditory selective attention.

Acknowledgements

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Spatial attention in individuals with pervasive developmental disorders using the gap overlap task

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Abstract

The present study examined spatial attention in individuals with pervasive developmental disorders (PDD) using the gap overlap task and analyzed the express saccade, which is defined by its extremely short reaction time, as a measure of the state of attention. Participants were required to move their eyes to the target stimulus appearing on the left or right side of a fixation point. In this task, participants had to disengage their attention from the central fixation point and shift it to the peripheral target stimulus. In the gap condition, the fixation point disappeared 200 ms before the target stimulus was presented, and in the overlap condition, the fixation point remained while the target stimulus was presented. Saccade latencies were not different between the groups. However, the express saccade was more frequent in the PDD group than in the normal group in the overlap condition. We conclude that individuals with PDD have deficiencies in attentional engagement. Moreover, our study suggests that analysis of the express saccade will be useful in further examinations of attentional processes in PDD.

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Keywords: Autism; Attention process; Saccadic eye movement

1. Introduction

Despite a tremendous increase in research, the causes of autism are still unclear. Autism is diagnosed on the basis of behavioral and developmental features such as impairments in reciprocal social interaction, communication, and imagination, and the presence of repetitive and ritualistic behavior (American Psychiatric Association, 1994). Some

researchers have proposed that attentional abnormalities, particularly in spatial attention, underlie such features of autism as inflexibility, repetitive behavior and overselectivity (Lovaas et al., 1971; Casey et al., 1993; Wainwright-Sharp and Bryson, 1993; Wainwright and Bryson, 1996; Townsend et al., 1996, 1999, 2001).

According to Allport (1989), spatial attention is a function of spatially directed attention and spatial selectivity. Regarding spatial attention, Posner and Cohen (1984) outlined a model in which the critical components of spatial attention are defined

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as disengagement, shift, and engagement of attentional sources. The findings from patients with acquired brain damage suggest that these components are correlated with specific brain areas (i.e. disengagement is correlated with the parietal cortex, shift is correlated with the superior colliculus, and engagement is correlated with the thalamus) (Posner et al., 1982; Posner and Cohen, 1984; Posner and Petersen, 1990).

Some studies on spatial attention in individuals with pervasive developmental disorders (PDD) have indicated problems in attentional disengagement and shift (Casey et al., 1993; Wainwright-Sharp and Bryson, 1993; Wainwright and Bryson, 1996; Townsend et al., 1996, 1999, 2001), and in attentional engagement (Kemner et al., 1998; van der Geest et al., 2001).

The present study follows the same line as a study by van der Geest et al. (2001), which examined attentional engagement and disengagement in children with autism using a gap overlap task. In the gap overlap task, when a temporal gap is introduced between the disappearance of a central fixation point and the appearance of a new target stimulus, the saccade reaction times are reduced compared to when no gap is introduced (gap effect; Saslow, 1967). This difference in saccade reaction times has been explained by the difference in attentional disengagement (Fischer and Weber, 1993). In the gap condition, in which an initial fixation point disappears before a target appears, attention on the fixation point is disengaged automatically. However, in the overlap condition, in which the fixation point remains after the target appears, attention on the fixation point is disengaged due to the appearance of the peripheral target stimulus. Therefore, the saccade reaction times in the overlap condition are longer than in the gap condition.

Fischer and Ramsperger (1984) examined the express saccade, which is defined by its extremely short reaction time (70 ms in the monkey, 100 ms in man). Fischer and Weber (1993) reported that engaged visual attention tends to inhibit the express saccade, and disengagement of attention leads to the express saccade; thus, the express saccade is a useful measure of the state of attention. Regarding the neurophysiological mechanism

for producing express saccades, Sparks et al. (2000) described the express saccade as being triggered by a motor burst of collicular neurons. Furthermore, Munoz and Wurtz (1992) showed that when fixation cells in the rostral pole of the superior colliculus are inhibited artificially after microinjection of muscimol, an express saccade occurred. These fixation cells discharge tonically when the eyes are fixated and pause during saccades, and have been implicated in the control of active visual fixation and suppression of saccadic eye movements (Dorris and Munoz, 1995).

Developmental studies of attentional disengagement (Atkinson et al., 1988; Hood and Atkinson, 1993; Matsuzawa and Shimojo, 1997) have suggested that the inability of young infants to disengage their attention from a stimulus on which they are fixated is responsible for their difficulty in orientation. Different developmental time courses were shown for the gap and overlap disengagement, with early maturation of the gap disengagement ability and later maturation of the overlap disengagement ability.

Van der Geest et al. (2001) concluded that children with autism have a weak attentional engagement on a visual stimulus because of a reduced gap effect (i.e. the difference in saccade reaction times between the overlap condition and the gap condition). Moreover, as the overall saccadic reaction times did not become slower, they also concluded that there were no specific problems in attentional disengagement. However, van der Geest et al. did not analyze the express saccade as a measure of the state of attention. Furthermore, it is possible that anticipatory responses might be included in the data of van der Geest et al.

Thus, in this study, we investigated spatial attention in individuals with PDD using the gap overlap task. To clarify whether a problem of spatial attention exists in engagement only, or in both engagement and disengagement in individuals with PDD when using the gap overlap task, we analyzed the occurrence of express saccades as a measure of the state of attention. To clarify the meaning of express saccades, we used a procedure that excludes anticipatory reactions (i.e. varying the duration of the fixation point, and randomizing gap trials and overlap trials).

Table 1
Age and IQ scores for groups

Group	<i>n</i>	Age (Range)	Measure	IQ (\pm S.D.)
PDD	5	30.3 (20.1–40.5)	WAIS-R	78.4 \pm 8.41
	2	30.9 (28.4–33.4)	Tanaka–Binet Test	44.5 \pm 4.95
Normal	9	24.9 (19.0–34.7)	WAIS-R	100.4 \pm 9.89

Note: IQ for the normal group is estimated IQ based on four subtests of the WAIS-R.

2. Methods

2.1. Participants

The participants of this study were seven adults with autistic disorders ($n=4$, male: 3, female: 1) or Asperger syndrome ($n=3$, male: 3) and nine normal adults (male: 8, female: 1). The mean ages were 30.5 (PDD) and 24.9 (normal). Characteristics of each group with respect to age, sex, and IQ are shown in Table 1. IQs were evaluated with the Wechsler Adult Intelligence Scale-Revised (WAIS-R), Japanese version, for five of the PDD participants and normal adults, and the Tanaka–Binet Test for two of the PDD participants. Estimated IQs were based on four subtests of the WAIS-R. Diagnosis of PDD was determined according to DSM-IV criteria (American Psychiatric Association, 1994). All participants had uncorrected or corrected visual acuity greater than 0.8 and no subjects wore contact lenses. All participants were right-handed [determined using the Edinburgh Inventory (Oldfield, 1971): laterality index >0.8]. Informed consent was obtained from all participants and their parents before the experiment.

2.2. Stimuli and apparatus

The stimuli were presented on a 17-inch CRT display with a black background that was positioned 1 m in front of the subject's eyes. The fixation stimulus was a 0.5° white cross. The peripheral target stimulus was a $0.3 \times 0.3^\circ$ white solid square appearing 4° to the right or left of the fixation point.

Eye movements were recorded using electro-oculography (EOG). The horizontal EOG was recorded at the outer canthi of the eyes. EOGs were recorded and analyzed using a SCAN system

with SynAmps (NeuroScan, Inc.). EOGs were digitized at 500 Hz. While subjects performed the task, their head movement was recorded using a digital video camera so that we could later eliminate artifacts caused by these movements.

2.3. Procedure

Participants initiated each trial by pressing a button, and after 1 s, a fixation point was presented in the center of the CRT monitor. A target stimulus was then presented to the right or left side of the central fixation point. To minimize the possibility that participants anticipate the timing of target onset, the fixation point was presented at intervals varying between 1500 and 2500 ms. Subjects were required to execute a saccadic eye movement as soon as the target appeared. In the gap condition, the fixation point disappeared 200 ms before the target stimulus was presented, and in the overlap condition, the fixation point remained while the target stimulus was presented. Two hundred and forty trials composed of 60 trials each in four conditions (gap vs. overlap \times right vs. left) were performed in four blocks of 60 trials each, with stimuli presented randomly to prevent subjects from predicting the upcoming stimulus. Only three blocks (total 180 trials) were conducted with two normal adults, and three with PDD subjects due to lack of time.

2.4. Data analysis

A saccade was defined as the first moment at which the velocity of the eye exceeded $22^\circ/s$. The trials included in the analysis (correct trials) were only those in which the eyes did not move before the target onset, the saccade occurred in the correct direction, and SRTs were between 80 and 600 ms.

The express saccade was defined as occurring between 80 and 130 ms after the target presentation (Fischer and Weber, 1993).

3. Results

A three-way analysis of variance (ANOVA) was performed on the percentages of correct trials. The PDD group had significantly fewer correct trials than the normal group [$F(1,14)=4.59$, $p<0.05$] in the gap condition ($57.6\pm 17.8\%$, $73.4\pm 15.2\%$, respectively) and the overlap condition ($58.1\pm 14.5\%$, $71.5\pm 13.8\%$, respectively). With the Spearman Rank Correlation, SRT, gap effect and express saccade rate were correlated with neither IQ (SRT: $r=0.07$, $p=0.736$; gap effect: $r=0.29$, $p=0.163$; express saccade: $r=-0.11$, $p=0.378$) nor chronological age (SRT: $r=-0.03$, $p=0.845$; gap effect: $r=-0.27$, $p=0.120$; express saccade: $r=0.049$, $p=0.715$). Express saccade rate correlated with percentages of correct trials ($r=-0.32$, $p<0.01$).

3.1. SRT

The mean SRTs for each group and condition are shown in Fig. 1. First, a three-way analysis of variance (ANOVA) was performed on the SRT. The main effect of the fixation condition was significant [$F(1,14)=124.64$, $p<0.0001$, power=0.1988]. Group and direction had no significant effects [$F(1,14)=0.901$, $p=0.3672$, N.S., power=0.1988; $F(1,14)=0.16$, $p=0.729$, N.S., power=0.416, respectively). The interaction group \times fixation condition was significant [$F(1,14)=4.973$, $p<0.05$, power=0.4033]. Thus, in order to test the difference groups within each condition and the difference in conditions within each group, we performed *t*-tests (two-tailed). SRTs between the PDD group and the normal group showed no difference in either the gap (177 ± 23 ms, 179 ± 32 ms, respectively, $t(14)=0.542$, $p=0.596$, N.S.) or the overlap conditions (220 ± 37 ms, 239 ± 36 ms, respectively, $t(14)=1.186$, $p=0.255$, N.S.). SRTs in the gap condition were significantly shorter than in the overlap condition in the normal group [$t(8)=11.038$, $p<$

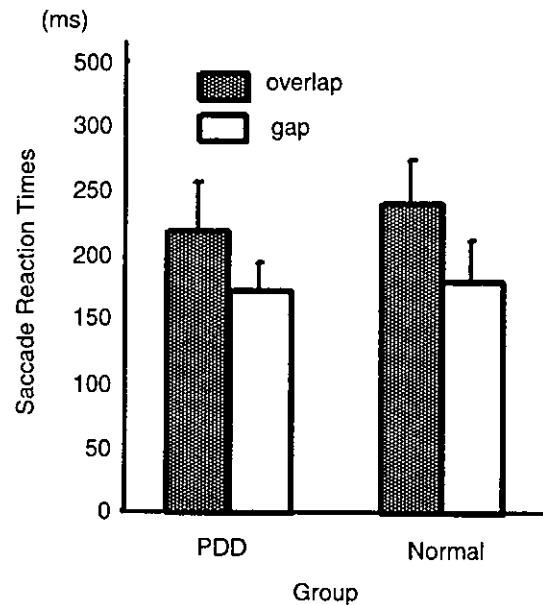


Fig. 1. Mean saccade reaction times (\pm S.D.) for the PDD ($n=7$) and normal ($n=9$) groups in the gap and the overlap conditions. SRTs in the gap condition were significantly shorter than those in the overlap condition for both the PDD and normal groups.

0.0001] and in the PDD group [$t(6)=6.483$, $p<0.001$].

Next, a two-way analysis of variance (ANOVA) was performed on the gap effect. No significance was found in the main effects of group and direction [$F(1,14)=2.239$, $p=0.156$, N.S., power=0.1957; $F(1,14)=2.58$, $p=0.131$, N.S., power=0.416, respectively) or in the interaction ($F(1,14)=0.375$, $p=0.549$, N.S., power=0.416).

3.2. Express saccade

The mean express saccade rates for each group and condition are shown in Fig. 2. We performed Mann–Whitney's *U* test for the inter-group comparison and Wilcoxon Signed-Ranks Test for the intra-group comparison after angular transformation of the ratios. In the overlap condition, the express saccade occurred more frequently in the PDD group than in the normal group (median: 18.2%, range: 10.2–31.4%; median: 8.2%, range: 7.0–26.9%, respectively, $z=-1.96$, $p<0.05$),

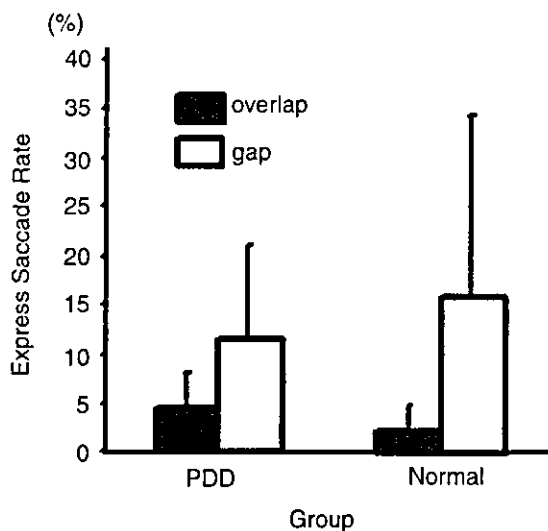


Fig. 2. Mean express saccade rate (\pm S.D.) for the PDD ($n=8$) and normal ($n=9$) groups in the gap and the overlap conditions. In the normal control group, the express saccade occurred significantly more frequently in the gap condition than in the overlap condition. However, in the PDD group, no difference between the gap and overlap conditions was shown.

while in the gap condition, the mean express saccade rate showed no difference between the PDD group and the normal group (median: 28.1%, range: 15.0–53.2%; median: 21.7%, range: 6.9–84.3%, respectively, $z=-0.16$, $P=0.873$). In the normal group, express saccades occurred more frequently in the gap condition than in the overlap condition ($z=-2.31$, $p<0.05$). However, in the PDD group, the mean express saccade rate showed no difference between the gap condition and the overlap condition ($z=-1.86$, $P=0.063$).

4. Discussion

We examined spatial attention in individuals with PDD using the gap overlap task. The results of the present study confirm the findings of van der Geest et al. (2001) that the attentional engagement processes in individuals with autism were different from those in normal individuals. In our study, the analysis of express saccades enabled us to examine the spatial attention in individuals with PDD in detail.

First, in this study, as described in many previous studies (see, for example, Fischer and Weber, 1993), SRT in the gap condition was shorter than in the overlap condition. The disappearance of the fixation point prior to the appearance of a target stimulus reduced the latency of saccades to the target stimulus. Our results were consistent with the data of van der Geest et al. (2001), as saccade reaction times did not show significant group differences. Similarly, Minshew et al. (1999) found no significant difference between individuals with autism and normal adults in saccade latency and accuracy using a visually guided saccade task, which had no competing responses or demands and was not dependent on voluntary/endogenous regulation of attentional processes.

The gap effect was observed in both the PDD group and the normal group, but unlike in the study of van der Geest et al. (2001), no significant group differences were observed in the gap effect. However, since in SRT the interaction fixation \times group was significant both in our results and in those of van der Geest et al., it is possible that the results for the gap effect in our study might have been due to the small size of the sample, as the powers described were small values. In the results of van der Geest et al., the children with autism showed a reduced gap effect compared with the control children; therefore, they concluded that the children with autism had a weaker engagement to visual stimuli.

The PDD group differed from the normal group in the mean express saccade rate. Our results showed that in the overlap condition the express saccade in the PDD group occurred more frequently than in the normal group, whereas in the gap condition the express saccade in the PDD group was not different from that in the normal group. The express saccade usually occurs in the gap condition and not in the overlap condition, because in the gap condition attentional disengagement is triggered by the disappearance of the fixation point, whereas in the overlap condition attention remains engaged on the fixation point. In the normal group, as expected, the express saccade was rarely observed in the overlap condition, and frequently observed in the gap condition, whereas in the PDD group no difference in the express

saccade rate was observed between the gap and overlap conditions.

However, it can be argued that participants could anticipate the timing of the target presentation. In this experiment, we used variable duration of the fixation point and random presentation of each condition in a block so that the timing of the disappearance of the fixation point and the type of the next trial (gap or overlap, and left or right direction) could not be anticipated. Furthermore, saccades that occurred too rapidly were excluded. Thus, it can be said that these results regarding the express saccade were not caused by anticipation. Based on the relationship between the express saccade and the state of attention as described by Fischer and Weber (1993), the result of the overlap condition suggests that participants in the PDD group engage their attention on a central stimulus ambiguously. Likewise, Burack (1994) suggested that individuals with autism are unable to constantly focus on the target stimulus presented in the center of the screen when the area of the visual field is not narrowed, and particularly when distracters are presented. We could attribute these results to deficiencies in attentional engagement.

As shown in Section 3, the express saccade rate correlated with percentages of correct trials, and there were more rejected trials in the PDD group than in the normal group because of the eye movement before the target onset. These results were consistent with a prior study (Kemner et al., 1998) in which the children with autism made more saccades during the presentation of frequent stimuli in an oddball task. As suggested by Kemner et al., this may possibly be related to abnormalities in subcortical mechanisms involved in saccade eye movement. Neural mechanisms underlying the initiation and suppression of saccadic eye movements were studied by recording the activity of certain neurons in the superior colliculus, fixation cells, in the monkey (Dorris and Munoz, 1995; Munoz and Wurtz, 1992, 1993a,b). Furthermore, Dias and Bruce (1994) and Muri et al. (1999) reported that the prefrontal cortex could prime the superior colliculus. As for the cortical mechanism, event-related potential (ERP) studies also have shown a frontal negativity preceding the saccade during the gap condition (Everling et al., 1996; Gomez et al.,

1996; Spantekow et al., 1999), and a parietal activity prior to the saccade execution in the overlap condition (Csibra et al., 1997). Thus, it is possible that individuals with PDD will have abnormalities not only in subcortical but also in cortical mechanisms.

Prior studies using the Posner task showed that individuals with autism were slow to detect targets preceded by an invalid cue (Casey et al., 1993; Wainwright-Sharp and Bryson, 1993; Townsend et al., 1996, 1999, 2001). In these studies it was concluded that individuals with autism have a deficiency in attentional disengagement. In our study, we could find neither longer SRTs nor larger gap effects in the PDD group. Thus, the present data do not show evidence for abnormalities in attentional disengagement in individuals with PDD and seem to contradict these earlier studies. However, in consideration of Posner's model, it is not logical to discuss attentional disengagement under the premise that the PDD group cannot engage attention sufficiently. Thus, to conclude that individuals with autism have a deficiency in attentional engagement and not in attentional disengagement in the gap overlap task, we need to examine attentional disengagement in further experiments using the gap overlap task under a condition in which the PDD group can engage attention sufficiently. We are interested in the brain activity related to attentional disengagement and engagement processes. This study shows only behavioral features, but in future studies we will report ERP data acquired during the gap task.

Finally, using the gap overlap task, the present study provides evidence to support the hypothesis that individuals with autism have deficits in attentional engagement. In future studies, we will add more samples and examine express saccades of individuals with Asperger syndrome separately from individuals with high-functioning autism, and thus move towards a better understanding of the cognitive dysfunction in individuals with PDD.

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Effects of corollary discharge on event-related potentials during selective attention task in healthy men and women

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Abstract

Corollary discharge is a brain electrical activity associated with self-monitoring, which distinguishes self from others in thoughts or behaviors. Corollary discharge can be non-invasively assessed using event-related potential (ERP) recordings in humans. Previous studies have revealed that the amplitude of the N100 component elicited during an “odd-ball” task is reduced while a healthy subject is vocalizing, which may index the effect of corollary discharge on auditory ERPs. In this study, we attempted to assess the effect of vocalization on ERP components including N100, mismatch negativity (MMN), negative difference wave (Nd), and P300 during a selective attention task in 22 healthy adults. We also evaluated the possible contribution of gender to these effects. N100 amplitudes elicited by unattended standard stimuli were reduced under the vocalization condition compared with those under the baseline condition. However, there were no significant effects of vocalization on MMN, Nd or P300. Moreover, there was no significant effect of gender to the corollary discharge. These results suggest that the effect of corollary discharge on auditory ERPs is limited to the perceptual stage of information processing in healthy men and women. © 2003 Published by Elsevier Ireland Ltd and The Japan Neuroscience Society.

Keywords: Event-related potential; N100; Selective attention task; Corollary discharge; Vocalization; Gender

1. Introduction

In voluntary movements, there is an adjustment mechanism: (1) expected results of intended movement (efference copy) are feed-forwarded from motor to sensory structures in advance (Paus et al., 1996a); (2) the actual results are checked; and (3) his/her movement is controlled. The electric activity related to this for the feed-forward system is called, the corollary discharge. Self-produced vocalization also has inhibitory influence on the auditory cortex due to the corollary discharge, and thus, one can distinguish self-generated sensory-perceptual events from externally generated ones. In this way, the corollary discharge is associated with self-monitoring, which distinguishes self from others in

thoughts or behaviors. Moreover, some researchers have hypothesized that certain positive symptoms of schizophrenia, such as auditory hallucination and delusion, may be a consequence of impaired self-monitoring attributable to the abnormality of corollary discharge (Feinberg, 1978; Frith, 1995; Feinberg and Guazzelli, 1999).

The corollary discharge can be non-invasively assessed in humans using event-related potentials (ERPs) or magnetoencephalography (MEG) (Numminen et al., 1999; Numminen and Curio, 1999; Curio et al., 2000; Ford et al., 2001a,b,c). For example, Ford et al. (2001a) recorded the auditory N100 component in response to repetitive tones during talking in patients with schizophrenia and normal adults. The investigators noted a reduced N100 amplitude under the talking condition compared with the baseline condition in healthy subjects, whereas they did not observe such reduction in patients with schizophrenia. The authors suggested that these findings could be interpreted as

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an abnormality of the corollary discharge during auditory perception in schizophrenic patients.

To our knowledge, however, no studies have assessed the effect of corollary discharge on ERP components besides N100, such as mismatch negativity (MMN; an index of automatic attention), negative difference wave (Nd; selective attention), and P300 (context updating) in healthy subjects. The selective attention task can estimate these components in an identical state of focused attention, and thus, was utilized in this study. Moreover, a possible effect of gender on corollary discharge is also an important issue, considering its potential usefulness as an assay of self-monitoring ability in clinical population. For example, in patients with schizophrenia, gender difference has been suggested for certain cognitive domains (Reite et al., 1997; Turetsky et al., 1998). Consequently, we attempted to assess the effect of vocalization on ERP components including N100, MMN, Nd and P300 elicited during a selective attention task in healthy men and women.

2. Materials and methods

2.1. Subjects

Twenty-two healthy adults (11 males and 11 females) participated in the study. All the subjects were right-handed (determined using the Edinburgh Inventory, Oldfield, 1971); we used a laterality index >0.8 as the cutoff for right-handedness). The mean ages of the male and female subjects were 27.8 (S.D. = 3.03) and 26.8 (S.D. = 2.89) years, respectively, and were not significantly different (Student's *t*-test: $t[20] = -0.79$, $P = 0.44$). The ethical committee of the University of Tokyo approved this study. After a complete explanation of the study to the subjects, written informed consent was obtained.

2.2. Procedure

ERPs were recorded during an auditory selective attention task. Each tone burst had a short (25 ms) or long (100 ms) duration, delivered to the left or right ear randomly (left short, 35%; left long, 15%; right short, 35%; right long, 15%). The subjects were required to press a button as quickly as possible in response to the target stimuli, which were the long tone bursts delivered to one attended ear. The pitch of the tones differed between the attended (2 kHz) and unattended ears (1 kHz). The rise/fall time of each stimulus was 5 ms, and the stimulus intensity was set at 75 dB sound pressure level. The interstimulus interval was fixed at 750 ms. The total number of averaged responses was at least 40 for rare stimuli. After the subjects performed the tasks for both left and right attended conditions (baseline condition), they performed the same tasks while they were uttering /a/ sound continuously (vocalization condition). The order of ear designation through the sequential blocks was counterbalanced

across all the subjects. The performance level was assessed based on the response time (RT) and hit rate for each task condition. The ear designation was collapsed since statistical analyses revealed neither significant effect of ear designation nor interaction between ear designation and task condition.

2.3. ERP recordings

Electroencephalograms (EEGs) were recorded via 16 electrodes placed according to the International 10–20 Electrode System at Fp1, Fp2, F3, Fz, F4, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6 and Oz. The linked earlobes were used as the reference for all of the electrodes. Horizontal and vertical eye movements were monitored with electro-oculogram (EOG) electrodes placed at the outer canthus and below the left eye. The sampling rate was 400 Hz, and the analog filter band pass was 0.15–120 Hz. The analysis period was 600 ms, including a 40 ms prestimulus baseline. EEG epochs that contained peak-to-peak amplitudes $>100 \mu\text{V}$ at any site and EOG waves $>75 \mu\text{V}$ in amplitude were excluded from the averaging. Average waveforms were separately obtained for each type of stimulus and ear of stimulation, and for each condition.

2.4. ERP measurements

The N100 amplitude was defined as the average amplitude across 50–150 ms after stimulus onset in the ERPs in response to standard stimuli delivered to the unattended ear. The P300 amplitude was defined as the average amplitude across 250–500 ms after stimulus onset in the ERPs in response to deviant stimuli delivered to the attended ear (i.e., target stimuli). The Nd waveform was calculated by subtracting ERPs in response to standard (frequent) stimuli delivered to the unattended ear from those delivered to the attended ear. The Nd amplitude was defined as the average amplitude within a 150 ms window starting at 150 ms after stimulus onset. The MMN waveform was calculated by subtracting ERPs in response to standard stimuli from those in response to deviant (rare) stimuli delivered to the unattended ear. The MMN amplitude was defined as the average amplitude within a 100 ms window starting at 150 ms after stimulus onset. N100, Nd and MMN amplitudes were measured at Fz, T3, Cz, and T4; and P300 amplitude was measured at Fz, T3, Cz, T4 and Pz for each subject and condition. Since we did not have any hypothesis for difference in effect of corollary discharge between ERPs for stimulation of left and right ears, they were collapsed for not finding any spuriously significant effect by multiple statistical comparisons.

2.5. Statistical analyses

For behavioral data, the repeated measures ANOVA was performed separately for RT and hit rate, adopting gender (male, female) as the between-subject factor, and task condition (baseline, vocalization) as the within-subject factor.

Main effects or interactions were considered significant if the P level was less than 0.05.

For ERP data, the repeated measures ANOVA was performed for each component adopting gender as the between-subject factor, and task condition and electrode sites as within-subject factors. Since there were four separate ANOVAs (N100, MMN, Nd and P300) and we did not make any specific assumptions regarding which component was associated with significant effects, main effects or interactions were considered significant if the P level was less than 0.0125 (Bonferroni correction) to avoid type I errors. The Greenhouse–Geisser correction was applied whenever necessary.

3. Results

Since there was no violation for sphericity assumption for the main effect of condition (vocalization versus baseline) for RTs or any ERP component (Mauchly's $W = 1.0$), we did not perform the adjustment of the degrees of freedom using Greenhouse–Geisser correction.

3.1. Behavioral performance

Mean RTs (baseline/vocalization) were 399 ms [S.D. = 34]/400 ms [36] for males and 419 ms [57]/436 ms [35] for females. Mean hit rates (baseline/vocalization) were 92.0% [S.D. = 12.0]/89.6% [13.0] for males and 94.2% [6.6]/92.1% [11.0] for females. As for RT, the repeated measures ANOVA revealed no significant main effect of task condition ($F[1, 20] = 2.56$, $P = 0.13$) or gender ($F[1, 20] = 2.83$, $P = 0.11$) or gender-by-condition interaction ($F[1, 20] = 1.81$, $P = 0.19$). Similarly, there was no significant main effect of task condition ($F[1, 20] = 2.01$, $P = 0.17$), gender ($F[1, 20] = 0.35$, $P = 0.56$) or gender-by-condition interaction ($F[1, 20] = 0.02$, $P = 0.90$) for the hit rate (as shown in Table 1).

3.2. N100 component

The repeated measures ANOVA revealed no main effect of gender ($F[1, 20] = 0.60$, $P = 0.45$), gender-by-condition interaction ($F[1, 20] = 4.28$, $P = 0.052$), or gender-condition-electrode interaction ($F[3, 60] = 0.077$, $P = 0.95$).

Table 1

Mean amplitude of each ERP component for each condition, calculated as the mean voltage within the following time windows: N100, 50–150 ms; MMN, 150–250 ms; Nd, 150–300 ms; and P300, 250–500 ms

	Average ($n = 22$)				Male ($n = 11$)				Female ($n = 11$)			
	Baseline		Vocalization		Baseline		Vocalization		Baseline		Vocalization	
	Mean amplitude (μV)	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
N100 (Fz)	-2.25	1.14	-1.27	1.08	-2.28	0.97	-1.02	-0.74	-2.23	1.31	-1.52	1.31
MMN (Cz)	-0.88	2.02	-0.20	1.63	-0.83	2.10	-0.34	1.66	-0.93	1.98	-0.07	1.64
Nd (Cz)	-1.17	1.93	-0.26	1.24	-1.03	0.96	0.41	1.20	1.30	2.58	0.10	1.29
P300 (Pz)	3.62	1.97	2.85	2.04	3.54	2.04	2.61	1.84	3.69	1.95	3.09	2.24

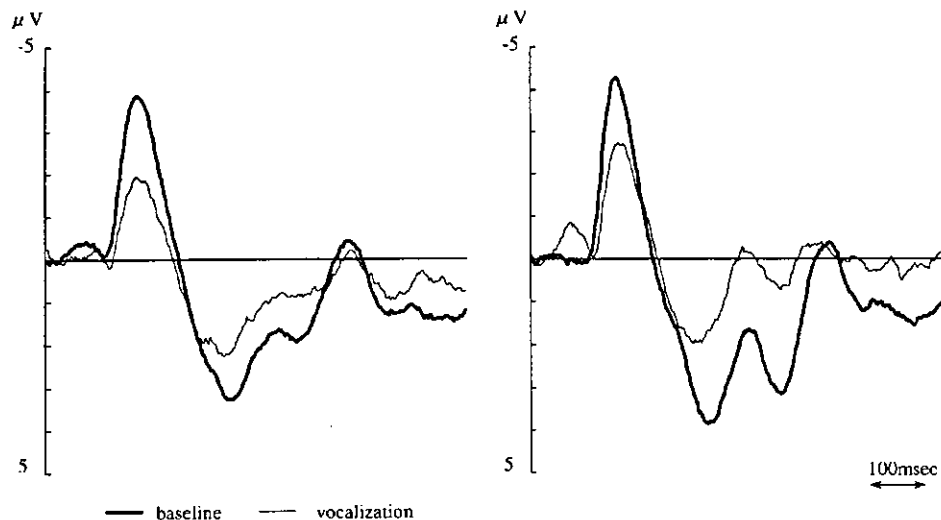


Fig. 1. Grand average waveforms of ERPs for non-attended standard stimuli at Fz. Male subjects (left); female subjects (right). Negativity is denoted by the upward deflection.

There was a significant main effect of condition ($F[1, 20] = 24.5, P < 0.001$) and a significant condition-by-electrode interaction ($F[3, 60] = 9.85, P < 0.001$). The secondary analysis using a paired t -test for each electrode site (gender was collapsed since there was no effect of gender) revealed significant differences between baseline and vocalization conditions at Fz ($t[21] = 6.35, P < 0.001$), Cz ($t[21] = 3.64, P = 0.002$) and T4 ($t[21] = 3.79, P = 0.001$); but not at T3 ($t[21] = 2.17, P = 0.042$), where the significance level was set at $P < 0.0125$ (0.05/4 electrodes; Bonferroni correction, as shown in Fig. 1).

3.3. MMN component

The repeated measures ANOVA revealed no main effect of gender ($F[1, 20] = 0.43, P = 0.52$), gender-by-condition interaction ($F[1, 20] = 0.75, P = 0.40$), or gender-by-condition-by-electrode interaction ($F[3, 60] = 0.10, P = 0.91$). There was also no significant main effect of condition ($F[1, 20] = 2.25, P = 0.15$) or condition-by-electrode interaction ($F[3, 60] = 2.18, P = 0.12$, as shown in Fig. 2 [top]).

3.4. Nd component

The repeated measures ANOVA revealed no main effect of gender ($F[1, 20] = 0.16, P = 0.69$), gender-by-condition interaction ($F[1, 20] = 1.43, P = 0.25$), or gender-by-condition-by-electrode interaction ($F[3, 60] = 0.075, P = 0.89$). There was also no significant main effect of condition ($F[1, 20] = 6.72, P = 0.017$) or condition-by-electrode interaction ($F[3, 60] = 3.89, P = 0.039$), as shown in Fig. 2 [middle].

3.5. P300 component

The repeated measures ANOVA revealed no main effect of gender ($F[1, 20] = 0.37, P = 0.55$), gender-by-condition interaction ($F[1, 20] = 0.61, P = 0.44$), or gender-by-condition-by-electrode interaction ($F[4, 80] = 1.36, P = 0.26$). There was also no significant main effect of condition ($F[1, 20] = 4.27, P = 0.052$) or condition-by-electrode interaction ($F[4, 80] = 0.94, P = 0.43$), as shown in Fig. 2 [bottom].

4. Discussion

The present study demonstrated attenuation of the auditory N100 amplitude during vocalization using a selective attention task. The selective attention task has an advantage in assessing the N100 component independent of the attention effect, that is, by measuring N100 in response to the standard stimuli delivered to the unattended ear, thus confirming the findings from previous studies (Ford et al., 2001a,b). Our results showing the lack of effect of vocaliza-

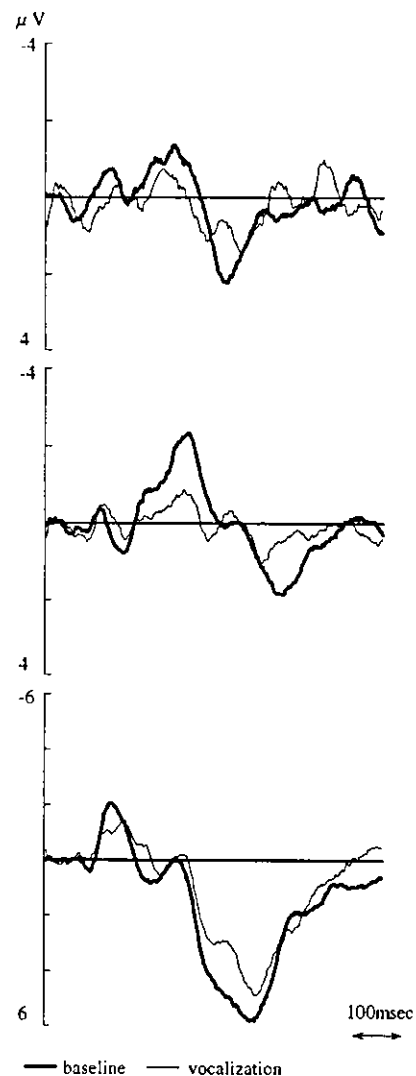


Fig. 2. Grand average ERPs representing MMN at Cz. The MMN waveform was calculated by subtracting ERPs in response to standard stimuli from those in response to deviant (rare) stimuli delivered to the unattended ear (top). Grand average ERPs representing Nd at Cz. The Nd waveform was calculated by subtracting ERPs in response to standard (frequent) stimuli delivered to the unattended ear from those delivered to the attended ear (middle). Grand average ERPs for the attended target stimuli (AT) at Pz. Negativity is denoted by the upward deflection (bottom).

tion on MMN, Nd, or P300 add more information to previous findings regarding the effects of corollary discharge on auditory ERPs. Moreover, there was no significant effect of gender on the corollary discharge.

The concept of corollary discharge, or efference copy, is well known as the system for adjusting movements, which was proposed by Sperry and von Holst originally for the visual perception (see Evars, 1971). Namely, when the eyeball is turned passively, the visual field may move across the retina. If we move our eyes voluntarily, however, the optical image is perceived as being stationary. The difference is explained by the existence of corollary

discharge, that is, it plays the role of an adjuster using feed-forwarded neuronal movement commands, so that we are able to maintain the stability of our visual field. On the other hand, corollary discharge is also represented in the auditory perception. Previous studies suggest that there is a region in the auditory cortex that reacts to others' voices, but not to the self-uttered voice, which further indicates that some neuronal populations are inhibited by the corollary discharge in the auditory system (Muller-Preuss and Ploog, 1981; Paus et al., 1996b). Our present finding and those of other workers of auditory N100 attenuation during self-uttering thus provide further evidence for presence of corollary discharge in the auditory system in humans.

Our findings of N100 attenuation under the vocalization condition are in line with previous findings. Curio et al. (2000) compared magnetic counterpart of N100 (N100m) during speaking with that during playback of recorded speech using MEG in healthy subjects, and they observed that N100m in response to vowels were dampened and delayed during speaking. They suggested that the N100m amplitude may be reduced by corollary discharge. Ford et al. (2001a) measured ERPs elicited by auditory and visual stimulations during talking in normal subjects and schizophrenic patients. The amplitude of auditory N100 was reduced during talking compared with that for the baseline task in normal subjects, while this difference was not evident in schizophrenic patients. On the other hand, when recorded self-utterances were presented, the amplitude of auditory N100 during the listening task was reduced compared with that during the baseline task in both groups. The authors suggested that a smaller magnitude of amplitude reduction in patients with schizophrenia during talking results from dysfunction of corollary discharge in schizophrenia.

We used a selective attention task in this study, examining the effects of corollary discharge on the N100 component and other ERP components representing distinct stages of auditory information processing. Although there was a reduction of N100 amplitude during vocalization compared with the baseline condition, amplitudes of MMN, Nd or P300 were not altered significantly by task manipulation. A possible interpretation may be that the effect of corollary discharge on auditory ERPs is limited to the perceptual stage of information processing in healthy men and women. However, we note here that the main effect of condition on Nd was a trend level ($P = 0.017$; significant level = 0.0125, trend level = 0.025), although we originally intended to avoid interpreting the trend-level results as potentially significant. One reason for this observation may be that self-utterances attenuated the subject's ability to selectively attend to stimuli, with the mechanism at least partially independent of corollary discharge.

The lack of significant effects of gender may have useful information for any attempt to apply this index as an assay of self-monitoring ability in clinical populations. The evaluation of gender effects of ERPs are important since this

is pertinent to the selection of participants in experimental groups to avoid, for example, obscuring real effects by combining male and female subjects. Since we did not observe significant gender effects, the implication is that this factor is not of great relevance to the effects of corollary discharge on auditory ERPs. However, we cannot fully rule out the possibility that a lack of significant main effect of gender may have been driven by relatively small sample size. We should certainly await replications of our data to draw a definitive conclusion.

The methodological issue in our study needs to be commented upon. First, to evaluate different kinds of attention-related ERP components simultaneously, we adopted a selective attention task and a linked ear-lobe reference. However, an ear-lobe reference is not optimal for recording ERPs that primarily originate in the superior temporal gyrus, such as MMN. We should consider the optimal recording conditions such as the use of nose reference, and examine the specific effect of corollary discharge on MMN. Second, it was difficult to rule out the possibility that the signal to noise (S/N) ratio of perceived tones may have been reduced under the vocalization condition, which resulted in an attenuation of N100 amplitude. However, a decrease in the S/N ratio should lead to reduced discriminability of auditory stimuli, which should have some influences on not only N100 but also on other components. Since a significant effect was confined to N100, we cannot attribute our findings solely to reduced S/N ratio during self-utterance. To clarify these issues, in future investigations we should adopt a control condition in which subjects hear recorded self-utterances.

In summary, we noted the effects of corollary discharge on auditory N100 amplitude during a selective attention task in healthy subjects. There were no significant effects on MMN, Nd, or P300. Moreover, there was no significant effect of gender on the corollary discharge. These results suggest that the effect of corollary discharge on auditory ERPs is limited to the perceptual stage of information processing in healthy men and women.

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