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Event-related potentials in patients with adult attention-deficit/hyperactivity disorder versus schizophrenia

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ABSTRACT

Event-related potentials (ERPs) such as Nd, N2b, and P300 in an attentional task and an auditory oddball task were compared among 54 adult AD/HD patients, 43 schizophrenic patients (SZ), and 40 healthy age-matched volunteers (HC). It is known that Nd, N2b, and P300 reflect selective attention, voluntary attention, and cognitive context updating respectively. The peak amplitude of P300 was significantly lower in the adult AD/HD and SZ groups than in the HC group. The peak latencies of late Nd, N2b, and P300 were significantly longer in the SZ group than in the HC and adult AD/HD groups. Thus, attenuated amplitude and prolonged latency of various ERP components in the SZ group suggest the possibility of impairment of basic mechanisms underlying cognitive processing. Unlike the SZ group, the adult AD/HD group exhibited reduced amplitude of P300 but not prolonged latency. These findings suggest the existence of a different type of cognitive dysfunction in the adult AD/HD group, which might be closely related to attentional function.

1. Introduction

A number of studies have recently reported that patients with attention-deficit/hyperactivity disorder (AD/HD) failed to exhibit alleviation of symptoms such as inattentiveness and impulsiveness even when they grew into adulthood (McGough and Barkley, 2004; Barkley and Brown, 2008; Barkley, 2009). Several electrophysiological findings have been reported regarding the characteristics of event-related potentials (ERPs) in pediatric AD/HD patients (Strandburg et al., 1996; Jonkman et al., 1997a, 1997b, 2004). Jonkman et al. (1997b, 2004) reported that auditory P300, reflecting cognitive context updating (Donchin and Coles, 1988; Verleger, 1988), was significantly smaller in AD/HD children than in a control group, but also reported that subjects with AD/HD did not differ from normal individuals in N2b, a component of N2 related to voluntary attention (Simson et al., 1977; Fitzgerald and Picton, 1983). They hypothesized that in AD/HD children, there is a deficit in activation of the P300 process. Strandburg et al. (1996) reported that P300 amplitude during a visual continuous performance test was reduced in AD/HD children, and that its latency was longer than in a normal group. They found that AD/HD children had a diminished late frontal negative component, suggestive of reduced involvement in post-decisional processing. Groom et al. (2008) noted that it would be useful to compare schizophrenia and another neurodevelopmental disorder such as AD/HD. They reported that such a comparison would be supported by extensive evidence of early neurodevelopmental impairment in schizophrenia. They compared ERPs in adolescents with schizophrenia (SZ) with those in AD/HD patients, and reported that the SZ group exhibited reduced P300 amplitude during auditory oddball and visual go/no-go tasks, while the AD/HD group did not. However, both groups exhibited significantly decreased amplitude of N2 during the go/no-go task.

Recently, several studies have reported abnormality of ERPs in adult patients with AD/HD (Prox et al., 2007; Barry et al., 2009). Prox et al. (2007) reported that N2 amplitude was significantly increased in adults with AD/HD in a visual go/no-go task, compared with healthy subjects. P300 exhibited a tendency toward decreased activity in the AD/HD group. Barry et al. (2009) reported reduced N2 amplitudes to auditory targets, with no differences in target P300, in patients with AD/HD.

Dias et al. (2003) reported that AD/HD and SZ were associated with the impaired continuous performance task associated context, created by a cue stimulus, to guide response to a target. Olincy et al. (2000) insisted that AD/HD and SZ should be both conceptualized as disorders of attention. By examining the inhibition of the P50 auditory event-evoked potential, they found that adult with AD/HD did not show the inhibitory deficit as seen in patients with SZ, suggesting that the mechanism of attentional disturbance in the two illnesses might be fundamentally different. Thus, it must be important to investigate the difference of cognitive mechanism between SZ and AD/HD. It is, however, very difficult to simply compare findings for AD/HD with schizophrenia due to differences in age of onset. Oie et al. (2010) reported the neurocognitive decline in early-onset SZ compared with AD/HD. They argued that few studies comparing SZ and AD/HD have

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considered the possible effect of age of onset. Groom et al. (2008) compared ERPs in AD/HD group with schizophrenia group. Their data were not age-matched, because the participants in the SZ group were significantly older than those in the healthy controls (HC) and subjects with AD/HD. Since 2001, we have operated a clinic for psychiatric outpatients who are adults with developmental disorders in the Department of Neuropsychiatry of Fukushima Medical University. We have measured various types of ERPs as diagnostic tools in our patients, and compared the ERP data for adult AD/HD patients and schizophrenic patients with those for HC. The purpose of the present study was to examine cognitive function in adult AD/HD, in comparison with age-matched schizophrenia, by measuring ERPs including N2b, P300, and, in addition, Nd as an indicator of selective attention (Näätänen, 1982).

2. Methods

2.1. Participants

The subjects were 54 patients with adult AD/HD (31.9 ± 6.5 years, range: 20–42 years, male: 17) and 43 patients with SZ (29.6 ± 8.1 years, range: 18–48 years, male: 25) who satisfied the diagnostic criteria of DSM-IV, and 40 HC (31.1 ± 6.7 years, range: 20–44 years, male: 21). Forty-seven of the AD/HD patients were not taking medications for AD/HD. Two patients had been treated using methylphenidate, at dosages of 20 and 40 mg/day. Five patients were treated with anti-depressant drugs (i.e. fluvoxamine, milnacipran, clomipramine, sulpiride, and amoxapine), four with antianxiety agents (i.e. lorazepam, tandospirone, and loflazepate), and two with hypnotics (i.e. zolpidem and zopiclone). All SZ patients were taking antipsychotics. The mean dosage of neuroleptics was 815 ± 501 mg/day, in Chlorpromazine equivalents (Davis, 1976). None of the healthy volunteers had a history of alcohol addiction, drug addiction, psychiatric disease, or neurological disease. There were no significant differences in age among these groups (ANOVA: $F(2,134) = 1.364$, $p = 0.259$).

The investigation was carried out in accordance with the latest version of the Declaration of Helsinki. Prior to the study, consent was obtained in writing from each of the subjects after providing them with information about the design and contents of the study both verbally and in writing. The study was approved by the Ethics Committee of the School of Medicine of Fukushima Medical University, Japan.

2.2. ERP procedure

2.2.1. Auditory attentional task

Tones of 100 ms duration with 70 dBSL in intensity, 0.9 Hz intervals were presented binaurally via headphones. Stimulation was performed using a sound sequence of 1000 and 2000 Hz in frequency applied to the right ear and a sequence of 1000 and 500 Hz sounds applied to the left ear. The 1000 Hz sounds applied to the right or left ear served as the target stimulus, which was presented at a probability of 15% to both ears. Sessions were performed twice. Total number of stimulation (target sound) was counted in both sessions. There were 30 targets in each session. Two sessions were summed.

2.2.2. Auditory oddball task

Stimulation was performed using a sound sequence of 1000 and 2000 Hz in frequency, 70 dBSL in intensity, and 100 ms in duration with 0.5 Hz intervals. Either low- or high-frequency sound was designated the target stimulus, and was presented at a probability of 20%. Sessions were performed twice. There were 30 targets in each session. Two sessions were summed. Total counts were obtained during stimulation with the target sound irrespective of stimulus frequency (1000 Hz or 2000 Hz).

2.3. ERP analysis

Electroencephalography (EEG) was performed with the International standard 10–20 system (Fz, Cz, and Pz) using silver–silver chloride electrodes. Linked earlobe electrodes served as the reference. Brain waves were averaged, with the mean potential for the 100 ms period before start of the stimulation deemed 0. Electro-oculograms (EOGs) were simultaneously recorded. The vertical and horizontal EOGs were recorded from an electrode placed 1.5 cm above the outer canthus of the right eye. A ground electrode was attached to the middle of the forehead. All electrodes were maintained at an impedance of 10 kΩ or less. During the recording session the EEG was filtered (0.1–30 Hz). Trials with amplitudes > −90 and +90 μV were rejected when averaging.

The late Nd was identified from the data for the attentional task. Late Nd was identified as a negative deflection in the 150–400 ms period by subtracting the results for the non-target stimuli on the non-attentive ear side from those for the non-target stimuli on the attentive ear side.

The N2b and P300 were each identified from the data for the oddball task. N2b was identified as a negative deflection in the 130–300 ms period, obtained by subtracting the results for the non-target stimuli from those for the target stimuli. P300 was identified as the positive deflection during 250–500 ms.

The peak latency and peak amplitude for each component of the ERPs were statistically examined by one-way analysis of variance (ANOVA) on SPSS11.5 J Windows. Scheffe's test was employed for multiple comparisons.

3. Results

The number of stimulation was 64.9 ± 6.02 (mean ± S.D.), range: 59–89 for HC in the auditory attentional task. The number of total responses was 62.5 ± 7.1 (mean ± S.D.), range: 51–88 for HC in the auditory attentional task. The percentage of correct answer was 0.96 in HC. The number of stimulation was 65.9 ± 7.2 (mean ± S.D.), range: 60–96 for SZ in the auditory attentional task. The number of total responses was 58.1 ± 15.8 (mean ± S.D.), range: 32–114 for SZ in the auditory attentional task. The percentage of correct answer was 0.88 in SZ. The number of stimulation was 65 ± 5.5 (mean ± S.D.), range: 60–85 for AD/HD in the auditory attentional task. The number of total responses was 60.5 ± 7.9 (mean ± S.D.), range: 39–75 for AD/HD in the auditory attentional task. The percentage of correct answer was 0.93 in AD/HD.

The number of stimulation was 70 ± 10.3 (mean ± S.D.), range: 60–107 for HC in the auditory oddball task. The number of total responses was 69.4 ± 10.6 (mean ± S.D.), range: 52–102 for HC in the auditory oddball task. The percentage of correct answer was 0.99 in HC. The number of stimulation was 70 ± 13.4 (mean ± S.D.), range: 60–136 for SZ in the auditory oddball task. The number of total responses was 69.3 ± 13.3 (mean ± S.D.), range: 48–126 for SZ in the auditory oddball task. The percentage of correct answer in SZ was 0.98. The number of stimulation was 70.6 ± 10.5(mean ± S.D.), range: 60–96 for AD/HD in the auditory oddball task. The number of total responses was70.4 ± 10.7 (mean ± S.D.), range: 59–98 for AD/HD in the auditory oddball task. The percentage of correct answer was 0.99 in AD/HD.

The top of Fig. 1 showed different waveforms among late Nd groups. However, there were no significant differences in the amplitude of late Nd among the three groups, as shown in Table 1. The peak latency of late Nd in the SZ group was significantly longer than those in the HC group and the adult AD/HD group (ANOVA Fz: $F(2,129) = 7.246$, $p < 0.01$). Multiple comparison test (Scheffe's test) showed that the peak latencies in the SZ group differed from the AD/HD group and the HC group at Fz, Cz and Pz.

The peak amplitude of N2b in the SZ group amplitude was significantly lower than in the HC group at Cz, as shown at the middle of Fig. 1 and Table 1 (ANOVA Cz: $F(2,131) = 3.684$, $p < 0.05$). Multiple comparison test (Scheffe's test) showed that the peak amplitudes in the SZ group differed from the HC group at Cz. The peak latency of N2b in the SZ group was significantly longer than those in the HC group and the adult AD/HD group (ANOVA Fz: $F(2,131) = 14.063$, $p < 0.001$). Multiple comparison test (Scheffe's test) showed that the peak latencies in the AD/HD group differed from the SZ group at Fz, Cz and Pz, that the peak latencies in the SZ group differed from the HC group at Fz, Cz and Pz.

The peak amplitude of P300 was significantly lower in the adult AD/HD group and the SZ group than in the HC group (ANOVA Pz: $F(2,133) = 12.172$, $p < 0.005$), as shown in the bottom of Fig. 1. Multiple comparison test (Scheffe's test) showed that the peak amplitudes in the SZ group differed from the HC group at Fz, Cz, and Pz, that the peak amplitudes in the AD/HD group differed from the HC group at Fz, Cz, and Pz. The peak latency of P300 in the SZ group was significantly longer than those in the HC group and the adult AD/HD group (ANOVA Pz: $F(2,133) = 10.884$, $p < 0.005$). Multiple comparison test (Scheffe's test) showed that the peak latencies in the AD/HD group differed from the SZ group at Fz, Cz and Pz, and the peak latencies in the SZ group differed from the HC group at Fz, Cz and Pz.

4. Discussion

The present study measured ERPs in adults with AD/HD, compared to patients with SZ, and HC. The percentage of correct answer was