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Task dependent prefrontal dysfunction in persons with Asperger's disorder investigated with multi-channel near-infrared spectroscopy

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ABSTRACT

Dysfunction of the prefrontal cortex has been previously reported in individuals with Asperger's disorder. In the present study, we used multi-channel near-infrared spectroscopy (NIRS) to detect changes in the oxygenated hemoglobin concentration ([oxy-Hb]) during two verbal fluency tasks. The subjects were 20 individuals with Asperger's disorder and 18 age- and IQ-matched healthy controls. The relative [oxy-Hb] in the prefrontal cortex was measured during the category and letter fluency tasks. The mean total [oxy-Hb] during the category fluency task did not differ significantly between the groups; however, during the letter fluency task, the mean [oxy-Hb] in persons with Asperger's disorder was significantly lower than that in controls. These results suggested task-relevant or task-specific prefrontal dysfunction in persons with Asperger's disorder.

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1. Introduction

According to the criteria of the DSM-IV (American Psychiatric Association, 1994) and ICD-10 (World Health Organization, 1993), Asperger's disorder (AS) is a subtype of pervasive developmental disorders (PDDs). This disorder is defined as a syndrome in which the individuals meet the criteria for autism but have no history of delay in cognitive or language development. Recent studies indicated that the prevalence of PDD is higher than previously estimated. Fombonne (2003) estimated that the prevalence of PDD ranges from 30 to 60/10,000, while Kogan et al. (2009) indicated that the prevalence is as high as 110/10,000.

Persons with Asperger's disorder sometimes show repetitive maladaptive behaviors, stereotyped motor mannerisms, and rigid adherence to routines (Gaus, 2007). Clinical traits reported in studies of individuals with Asperger's disorder include superior systemizing (Wakabayashi et al., 2007), as well as problems organizing themselves in their environment (Happé, Booth, Charlton, & Hughes, 2006), understanding other people's feelings (Kaland, Smith, & Mortensen, 2007), and sympathizing with others (Baron-Cohen & Wheelwright, 2004). Kanai et al. (in press) reported high scores on the Schizotypal Personality Questionnaire (SPQ) and on the 'Neuroticism' and 'Psychoticism' scores of the Eysenck Personality Questionnaire (EPQ) in persons with Asperger's disorder. These clinical characteristics suggest the existence of neuropsychological dysfunction in persons with Asperger's disorder.

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Some neuropsychological studies have shown impairment of executive function, including planning, flexibility and working memory in persons with PDD including Asperger's disorder (Corbett, Constantine, & Hendren, 2009; Happé et al., 2006; Ozonoff, Pennington, & Rogers, 1991). In functional magnetic resonance imaging (fMRI) studies, individuals with PDD including Asperger's disorder have abnormalities of hemodynamic responses in the prefrontal cortex associated with spatial working memory (Luna, Minshew, Garver, Lazar, & Thulborn, 2002; Ring, Baron-Cohen, Wheelwright, Williams, & Brammer, 1999), motor inhibition (Schmitz, Rubia, Daly, Smith, & Williams, 2006), and visuomotor control (Müller, Kleinhans, Kemmotsu, Pierce, & Courchesne, 2003). In addition, PET study showed reduced dorsomedial prefrontal activation in adults with PDD (Happé, Ehlers, Fletcher, Frith, & Johansson, 1996). However, other reports have found no prefrontal impairment in persons with Asperger's disorder. In a study by Silk, Rinehart, Bradshaw, Tonge, and Egan (2006) in which a visual-spatial task similar to a Stroop-type task was employed, persons with Asperger's disorder performed similarly to age- and IQ-matched control subjects, even at higher levels of cognitive complexity.

Multi-channel near-infrared spectroscopy (NIRS), a recently developed functional neuroimaging technology, enables the non-invasive detection of spatiotemporal characteristics of brain function near the brain surface (Boas, Dale, & Franceschini, 2004; Strangman, Boas, & Sutton, 2002). NIRS has enabled bedside measurement of the concentrations of oxygenated ([oxy-Hb]) and deoxygenated hemoglobin ([deoxy-Hb]) in capillary blood vessels. In contrast to other neuroimaging methodologies such as fMRI, PET, electroencephalography (EEG), and magnetoencephalography, NIRS can be performed in a restraint-free environment that is especially suitable for psychiatric patients. Indeed, NIRS has been used to assess brain function in several psychiatric disorders (Kameyama, Fukuda, & Yamagishi, 2006; Matsuo et al., 2003; Suto, Fukuda, Ito, Uehara, & Mikuni, 2004).

Kuwabara, Kasai, Takizawa, Kawakubo, and Yamasue (2006) reported that prefrontal activation, assessed by 24-channel NIRS, during the letter fluency task was reduced in adults with PDD as compared with healthy adults. Using the same task, Kawakubo et al. (2009) reported similar results, although no significant difference was found between children with PDD and healthy children. However, these reports used only one activation task. In the present study, we used two types of verbal fluency tasks to investigate [oxy-Hb] changes in persons with Asperger's disorder.

2. Methods

2.1. Subjects

Subjects with Asperger's disorder and normal controls provided written informed consent prior to completing the testing in this study, which was approved by the ethics committee of the Faculty of Medicine of Showa University.

The clinical group comprised 20 outpatients at Showa University Hospital (mean age [\pm SD], 27.2 [8.5] years; 14 males and 6 females). Inclusion criteria were age of 18–60 years, no current use of psychotropic medications, and formal diagnosis of Asperger's disorder based on DSM-IV criteria (American Psychiatric Association, 1994). Subjects with a history of electroconvulsive therapy, alcohol or other drug abuse or dependence, or any neurologic illness affecting the central nervous system were excluded.

The interview sheet for persons with Asperger's disorder comprised five main questionnaires: (1) major complaint; (2) history of visit to medical and educational organizations/consultation services; (3) problems in fetal and newborn period; (4) developmental delays; and (5) education and occupation of the subject and their parents. Subjects with Asperger's disorder were also required to bring records from elementary school to high school as well as a maternal and child health handbook. The maternal and child health handbook includes records of pregnancy, childbirth, and the neonatal and infant periods, and are provided by local government offices in Japan.

A team of five experienced psychiatrists and two clinical psychologists performed the assessment. The assessment consisted of two detailed interviews of the patients about development and behavior from their infancy to adolescence. The subjects were also asked to bring suitable acquaintances who knew them in early childhood. At the end of the clinical interview, the subjects were diagnosed by the psychiatrist according to DSM-IV criteria, based on consensus between the psychiatrist and the clinical psychologist. Approximately 3 h were necessary for the diagnosis.

The normal control group comprised 18 adults who were recruited by e-mail, posters, and via acquaintances at Showa University Hospital (mean age [\pm SD], 31.1 [4.7] year; 12 males and 6 females). All the control subjects volunteered to participate in the study after receiving an adequate explanation about the study.

The subjects were asked to complete the Autism-Spectrum Quotient (AQ) test developed by Baron-Cohen, Wheelwright, Skinner, Martin, and Clubley (2001). The AQ is a 50-item self-administered measurement tool for adults with normal intelligence to assess for the presence of autistic traits. Each item is scored as 0 or 1 and the highest score is 50. A higher score indicates more autistic traits. Baron-Cohen et al. (2001) showed that a cut-off of 32 discriminates between Asperger's disorder/high-functioning autism and normal controls. The Japanese version of the AQ is standardized (Wakabayashi, Baron-Cohen, & Wheelwright, 2006) and is reported to have good internal consistency, test-retest reliability, and discriminant validity (Kurita, Koyama, & Osada, 2005; Wakabayashi et al., 2006).

All subjects were interviewed by the clinical psychologist based on an assessment using the Japanese version of the Mini-International Neuropsychiatric Interview (MINI; Otsubo & Kamijima, 2000). Subjects with any psychiatric disorders were excluded. The Japanese version of MINI is a short structured diagnostic interview for the DSM-IV and ICD-10, which has satisfactory reliability and validity (Otsubo et al., 2005). Intellectual ability was assessed using the Japanese version of the

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