ies of PPI using several approaches, such as positron emission tomography and anatomical/functional magnetic resonance imaging (MRI), provided important evidence to understand the neurophysiological mechanisms of PPI.

The Kumari *et al.*[85] research group has published numerous important studies that addressed the biological nature of PPI. In an MRI volumetric voxel-based morphometry study, healthy subjects showed significant positive correlations between PPI and grey matter volume in the hippocampus extending to parahippocampal gyrus, basal ganglia, including parts of putamen, globus pallidus, and nucleus accumbens, superior temporal gyrus, thalamus, and inferior frontal gyrus. Patients with schizophrenia[86] showed significantly positive correlations between PPI and grey matter volume in the dorsolateral prefrontal, middle frontal and the orbital/medial prefrontal cortices. Functional MRI (fMRI) studies[87,88] showed that the PPI of healthy subjects was associated with increased activation in the striatum extending to hippocampus and thalamus, inferior frontal and inferior parietal regions, and that all activated regions had significantly greater response in healthy subjects than schizophrenic patients.[88] Patients treated with risperidone or olanzapine, but not with typical antipsychotics, showed significant activation in the PPI-relevant regions.[87]

Other research groups have found similar results. In an fMRI study of Campbell *et al.*,[89] PPI was found associated with activation in pons, thalamus, caudate nuclei, left angular gyrus and bilaterally in anterior cingulate. Also by fMRI, Hazlett *et al.*[90] showed that, using attend/ignore PPI paradigm, lower left caudate activation during the attended PPI condition was associated with more deficient sensorimotor gating among schizotypal personality disorder, schizophrenia, and healthy controls. In a PET[91] study, normal controls showed a positive association between PPI and metabolic activity rates of glucose in prefrontal (Brodmann's areas 8, 9, and 10 bilaterally) and lower in visual cortex, while patients only showed this association for area 10 in the left hemisphere.

These findings demonstrate the involvement of the striatum, hippocampus, thalamus, and frontal and parietal cortical regions in PPI. Dysfunctions in any of these regions may underlie observations of reduced PPI in psychiatric diseases, including schizophrenia, which might be improved by atypical antipsychotic medication.

## GENETIC BASIS OF PPI

The use of PPI as an endophenotype in schizophrenia has been recently becoming consensual.[44,46,92] As PPI can be easily measured, it has the advantage to collect large sample sizes necessary for genetic approaches that conduct multi-site studies.[12] Several research groups have been investigating the relationship between PPI and the genome.

Roussos *et al.* and Giakoumaki *et al.*[93-96] have reported associations of PPI with several genotypes in healthy males. Examination of the Catechol O-methyltransferase (*COMT*) Val158Met polymorphism,[93] the main catabolic pathway of released dopamine (DA) in the prefrontal cortex (PFC), showed that Val (low PFC DA) /Val individuals had the lowest PPI, Met (high PFC DA)/Met the highest, and Val/Met were intermediate. In addition, the non-stimulant *COMT* inhibitor tolcapone increased PPI significantly in the Val/Val group and tended to have the opposite effect in the Met/Met group.[94] In a study examining the influence of the Dopamine D3 receptor Ser9Gly polymorphism on human PPI,[95] Gly/Gly individuals had the lowest PPI and Ser/Ser individuals had the highest PPI, while Ser/Gly individuals were intermediate. Investigation of the relationship between PPI and haplotypes comprising three Proline dehydrogenase (oxidase 1) single nucleotide polymorphisms (SNPs; 1945T/C, 1766A/G, 1852G/A) located in the 3' region of the gene,[96] CGA carriers, which are preferentially transmitted in schizophrenia patients,[97,98] exhibited attenuated PPI compared with the noncarriers. Furthermore, Roussos *et al.* examined the relevance for PPI of SNPs in promising schizophrenia risk genes, such as the D-amino acid oxidase (*DAO*) gene (rs4623951, rs2111902, rs3918346, rs3741775, and rs3825251)[99] and the Neuregulin 1 (*NRG1*) gene (rs6994992, SNP8NRG221132, SNP8NRG241930, rs3924999, rs2439272 and rs10503929),[100] and reported that reduced PPI was associated to the rs4623951_T-rs3741775_G and rs4623951_T-rs2111902_T diplotypes of *DAO* gene,[99] and to the SNP8NRG241930 G allele and particularly the rs6994992 T allele and rs2439272 C allele *NRG1* gene.[100]

The laboratory of Quednow *et al.*[101-103] has reported associations of PPI with several genotypes in both healthy subjects and patients with schizophrenia. An association of PPI with the serotonin-2A receptor (*5-HT$_{2A}$R*) A1438G/T102C (rs6311/rs6313), *COMT* Val158Met (rs4680) and *NRG1* Arg38Gln (rs3924999) were investigated in healthy Caucasian subjects,[101] and increased PPI levels were found in homozygous for the *5-HT$_{2A}$R* T102C-T/A-1438 G-A allele. Increased PPI levels were also found in male subjects with the *COMT* Met158Met-genotype, but no significant association of PPI with the *NRG1* Arg38Gln genotype was detected. Investigation of the impact of three *5-HT$_{2A}$R* polymorphisms (A-1438G, T102C, H452Y) on PPI in Caucasian schizophrenia patients[102] showed that patients carrying the T102C TT and the A-1438G AA allele present significantly higher PPI levels compared with all other variants. In contrast, the H452Y polymorphism did not affect PPI. Quednow *et al.*[103] also investigated the impact of the *COMT* Val158Met polymorphisms on PPI in Caucasian schizophrenic inpatients, and reported that patients carrying the Met/Met allele showed elevated PPI levels compared to other two genotypes. PPI was also influenced by two common nicotinic acetylcholine receptor (nAChR) $\alpha$ 3 subunit (*CHRNA3*) polymorphism (rs1051730/rs1317286) in healthy subjects and in patients with schizophrenia.[104] Recently,[105] the impact of the transcription factor 4 (TCF4) gene (rs9960767), a susceptibility gene for schizophrenia, on PPI was investigated in healthy subjects and in a schizophrenia spectrum group (including schizophrenia patients and individuals at high risk for schizophrenia), and in both samples PPI was strongly decreased in carriers of the schizophrenia risk allele C of the TCF4 gene.

Hong *et al.*[106] examined the effects of the *NRG1* Arg38Gln polymorphism on PPI in patients with schizophrenia and in normal controls. They reported that PPI was lowest in the subjects who were homozygous for the minor allele A/A carriers, intermediate in A/G carriers and highest in homozygous major alleles G/G carriers in both patient and control groups. Greenbaum *et al.*[107] reported an association of the reelin SNP rs7341475 with PPI. In addition, Hokyo *et al.*[108] reported that, in both healthy subjects and patients with schizophrenia, human N-methyl-D-aspartate (NMDA) receptor 2B subunit gene (*GRIN2B*) polymorphism rs1019385 (T200G) did not show any significant influence on PPI, although it was significantly related to habituation of startle response. Finally, Hashimoto *et al.*[109] reported that PPI deficits in schizophrenia were associated with PPI schizophrenia risk genotypes of three SNPs (rs11820062, rs2306365, rs7119750) in the v-rel avian reticuloendotheliosis viral oncogene homolog A gene, which encodes the major component of the Nuclear factor kappa B (NF-$\kappa$B) complex.

All together, these data strongly support PPI as a polygenetic trait that involves several neurotransmitter pathways and the use of PPI as a valid schizophrenia endophenotype. However, as noted previously, PPI can be affected by several factors, such as gender, smoking status and antipsychotic medication, and future studies with large sample sizes that consider these effects are deemed required. Investigation of mechanism how these factors effect on PPI across genotypes will contribute to a better understanding of the fundamental neural mechanisms underlying sensorimotor gating and will certainly be most valuable in devising future approaches that aim to investigate the complex pathogenesis of psychiatric diseases.

## EARLY PSYCHOSIS AND PPI

Research on early psychosis (ER) has been growing and PPI might also play an important role in this field.

In a 2-year follow-up study,[110] comparing ultra-high risk (UHR) adolescents with matched control group, UHR individuals showed reduced PPI at both baseline and 2 years compared with controls. Clinical improvement in UHR individuals was associated with an increase in PPI parameters. In another study,[111] PPI of acoustic startle response was assessed in subjects with prodromal symptoms of schizophrenia, first-episode schizophrenia patients and healthy control subjects. Prodromal subjects and unmedicated patients with first-episode schizophrenia showed significant PPI deficits, whereas schizophrenia patients treated with risperidone had almost normal PPI. These studies, together with the evidence that antipsychotic-naive schizophrenia patients[65,68,77-80] present PPI impairment, suggest that PPI disruption might be already present before the onset of psychosis and that PPI may represent a vulnerability marker for psychosis.

Intriguing results were found in a study[112] investigating PPI in EP, at risk (AR) for psychosis and comparison subjects at baseline and 6 months later. PPI was stable with repeated assessment and EP subjects had reduced PPI. The unexpected findings regard the fact that medication-naive EP subjects, as well as AR subjects who later developed psychosis, had greater PPI compared to EP subjects with antipsychotic medication, and to AR subjects who did not develop psychosis, respectively, introducing the possibility of early compensatory changes that diverge from findings in chronic patients. Therefore, longitudinal studies following up the pathological change of startle modulation in a long period prior to the onset of the disease are required to determine the use of PPI for early detection of psychosis.

## PPI IN CHILDREN AND DEVELOPMENTAL DISORDERS

Startle modulation is not consistent through children to adults. The neurophysiological mechanisms of PPI are considered to undergo development during early childhood and do not mature until about 8 years of age in both male and female subjects.[113,114]

Several studies have revealed PPI impairment in children with psychiatric disease, such as the 22q11 deletion syndrome,[115] Tourette's syndrome[116] and primary nocturnal enuresis.[117] On the other hand, children with autism,[118,119] attention deficit hyperactivity disorder (ADHD),[120,121] PTSD,[122] did not show PPI deficits (in traditional PPI experimental paradigm).

It should be noted that discrepancy in PPI between children and adults can be found in some psychiatric diseases. For instance, although children with autism did not[118,119] show PPI deficits, adults with ASD, such as autism[123] or Asperger's syndrome,[124] presented PPI impairments. Adults with PTSD also exhibited PPI deficits,[125,126] while children[122] or adolescent[127] with PTSD did not. The neurophysiological development related to PPI of startle response might not be relevant for some psychiatric diseases, such as ADHD, which did not exhibit PPI impairment in both children[120,121] and adults,[128,129] but might affect the discrepancy in PPI impairment between children and adults in other diseases, such as ASD or PTSD. Although PPI did not differ significantly between children with autism and normal age-matched controls, PPI of some controls were not evaluated, since they were rejected from the study for reasons such as drowsiness or small response.[119] Patients with autism are known to have hyperacusia, and they might present a lower threshold of startle and elicit startle by weak stimuli which might not elicit startle in normal controls. It is important to determine an experimental paradigm which can assess sensorimotor gating in both children with ASD and typical development. Although PPI impairment is not apparent in children with autism, there might be deficits in the mechanism of startle response in children with ASD which would develop to PPI impairment when they become adults, and comprehensive investigation of startle response, including threshold to elicit startle, startle magnitude, as well as PPI, might contribute to uncover the impairment of the neural circuitry in autism. There are several attempts to develop experimental paradigm of PPI,[114,130-135] including attentional modulation of PPI,[114,132-135] and application of these paradigms might inform neurobiological basis underpinning PPI deficits in both children and adults with ASD.

## CONCLUSION

PPI is a well-established neurophysiological index for translational research in psychiatric diseases. Recent studies from a variety of research areas all over the world have provided us important evidence to understand the neural mechanisms of sensorimotor gating, assessed by PPI. These findings will be most valuable in devising future studies that aim at investigating and understanding the complex pathogenesis of psychiatric diseases.

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Research in Developmental Disabilities

# Evaluation of the Japanese version of the Developmental Coordination Disorder Questionnaire as a screening tool for clumsiness of Japanese children

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ABSTRACT

Developmental Coordination Disorder (DCD) is characterized by clumsiness and coordination difficulties. DCD interferes with academic performance and participation in physical activities and psychosocial functions, such as self-esteem, cognition, or emotion, from childhood through adolescence to adulthood. DCD is a common pediatric condition and its prevalence is estimated to be 6% worldwide. Although English questionnaires are available, there is no questionnaire to identify DCD in Japan, and therefore, no information on its prevalence is available. Recently, we developed the Japanese version of the Developmental Coordination Disorder Questionnaire (DCDQ-J). The purpose of this study was to describe the applicability of the DCDQ-J for use with a community-based population of children in Japan and to investigate the relationships between coordination and attention-deficit hyperactivity disorder (ADHD) tendencies or intelligence. The DCDQ-J was completed by 6330 parents or guardians of children and adolescents. We employed the ADHD-rating scale and determined the intelligence quotient (IQ) of the children. Two-way analysis of variance showed that the scores linearly increased as the children's grades advanced in 2 subscales, namely, control during movement and fine motor. In contrast, non-linear changes were found in the scores of the general coordination subscale. The total scores of the DCDQ-J and ADHD-RS were significantly correlated, but no relationship between DCDQ-J scores and IQ was found. The DCDQ-J is expected to be a useful screening tool to identify and assess motor coordination difficulties of children in Japan and enable cross-cultural comparisons.



## 1. Introduction

Daily living and school activities of children require various motor skills. Such motor skills depend on coordination of a wide range of movements of body parts, such as appropriate speed and strength, precise timing of movements, and control of posture and balance. The sum of the above-mentioned functions is called "coordination" and is one of the important brain functions that develops along with children's growth (Zwicker, Missiuna, & Boyd, 2009).

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Insufficient coordination function is likely to induce delayed motor development, clumsiness, limited manual dexterity, and difficulty in posture. In addition, children with insufficient coordination tend to show retarded development of activities of daily living, including eating, toileting, dressing, and tool using, as well as school activities, including writing, drawing, playing musical instruments, gymnastics, and outdoor play. In fact, many clinical reports show that difficulty in coordination correlates with slow learning of basic daily living, studying, and various other activities (Missiuna, Moll, Law, King, & King, 2006; Polatajko & Cantin, 2005; Tseng, Howe, Chuang, & Hsieh, 2007).

However, the cause of such coordination problems is likely to be mistakenly considered as the lack of discipline by parents or poor motivation of children. If inappropriate measures against such problems are continuously taken, a feeling of self-denial and/or emotional difficulties may occur in children, which may result in self-distrust, exacerbate a repugnance to exercise and school activities, and may worsen the problems (Missiuna et al., 2006; Piek, Baynam, & Barrett, 2006; Polatajko & Cantin, 2005; Skinner & Piek, 2001; Tseng et al., 2007). Parents/guardians (Missiuna, Moll, King, King, & Law, 2007; Stephenson & Chesson, 2008) and teachers (Rivard, Missiuna, Hanna, & Wishart, 2007; Sugden & Chambers, 2003) may often lose patience with their developmental delay or feel disgusted with themselves, which may result in a bad relationship with the child (Cairney, Veldhuizen, & Szatmari, 2010). In addition, some studies have pointed out that coordination is deeply related to children's development of cognition and socialization because coordination increases children's ability to explore and manipulate their environment and encourages them to participate in social activities (Cairney et al., 2010; Missiuna et al., 2006; Piek et al., 2006).

The 4th edition of the diagnostic and statistical manual of mental disorders (DSM-IV) (American Psychiatric Association; Diagnostic and statistical manual of mental disorders: DSM-IV-TR, 2000) defines developmental coordination disorder (DCD) as "a marked impairment in the development of motor coordination, which interferes with daily living and studying." The incidence rate of DCD is 6%, and it is a relatively common pediatric condition (American Psychiatric Association; Diagnostic and statistical manual of mental disorders: DSM-IV-TR, 2000); however, there is no scale to facilitate the screening of DCD in Japan, which makes it difficult to evaluate the children's actual motor performance. The Developmental Coordination Disorder Questionnaire (DCDQ) is a parent rating scale for screening pediatric DCD (Wilson, Kaplan, Crawford, Campbell, & Dewey, 2000; Wilson et al., 2009). Recently, we developed a Japanese version of the DCDQ (DCDQ-J) (Nakai et al., 2009) for the Japanese children and conducted a preliminary investigation on both the reliability of our questionnaire and the psychometric properties.

This relatively large-scale school-based study aimed to study the applicability of the DCDQ-J as a screening tool for DCD in Japanese children. Furthermore, in order to evaluate the validity of the DCDQ-J, we investigated the relationships between coordination and ADHD tendencies or intelligence. DCD interferes with coordination in children whose intellectual level is within the normal range (American Psychiatric Association; Diagnostic and statistical manual of mental disorders: DSM-IV-TR, 2000); thus, the scores of the DCDQ-J should not be significantly related to intelligence. On the other hand, the scores of the DCDQ-J may be positively associated with ADHD tendencies, since DCD is frequently associated with ADHD (Fox & Lent, 1996; Kopp, Beckung, & Gillberg, 2010; Lingam et al., 2010).

## 2. Methods

### 2.1. Participants

Parents/guardians of all students in public nursery schools, elementary schools, and junior high schools in the participating city were invited to take part in this study. Nursery school students (middle class: 4- to 5-year-old students; senior class: 5- to 6-year-old students) and all elementary and junior high school students were included in this study. The questionnaire was sent to the parents/guardians via the teachers. The responses from the 6330 respondents were analyzed. Table 1 shows the details of the children, as reported by the respondents. The majority (94%) of the respondents were mothers. Approximately 5% of the respondents were fathers, and the rest were grandparents. Data from parents and guardians of children in special classrooms was excluded from the study. The number of data inputs varied at analysis because missing data was excluded.

### 2.2. Development of the DCDQ-J

DCDQ 2007 is a parent questionnaire consisting of 15 items and was designed to screen for coordination disorders in children aged 5–15 years (Wilson et al., 2000, 2009). There are 3 subscales, namely, "control during movement (6 subitems)", "fine motor (4 subitems)", and "general coordination (5 subitems)". The descriptions of each item are scored as follows by a 5-point scale based on the comparison between the child and other (children): "Not at all like your child (1 point)", "A bit like your child (2 points)", "Moderately like your child (3 points)", "Quite a bit like your child (4 points)", and "Extremely like your child (5 points)", with higher scores indicating better coordination. Recently, the DCDQ-J was developed and adapted to the Japanese culture (Nakai et al., 2009) in accordance with the International Guidelines (Beaton, Bombardier, Guillemin, & Feraz, 2000).

We employed the Japanese version of the ADHD-rating scale (Japanese version ADHD-RS) developed by DuPaul, Power, Anastopoulos, & Reid (1998), DuPaul, Power, Anastopoulos, & Reid (2008). Based on the ADHD criteria of DSM-IV (American Psychiatric Association; Diagnostic and statistical manual of mental disorders: DSM-IV-TR, 2000), this scale consists of 2

**Table 1**
Details of grade and sex of participants of this survey.

| | Male | Female | Total |
|---|---|---|---|
| Nursery school | | | |
| Middle (4–5) | 174 | 167 | 341 |
| Senior (5–6) | 154 | 176 | 330 |
| Elementary school | | | |
| 1 (6–7) | 422 | 350 | 772 |
| 2 (7–8) | 343 | 374 | 717 |
| 3 (8–9) | 378 | 363 | 741 |
| 4 (9–10) | 314 | 319 | 633 |
| 5 (10–11) | 328 | 352 | 680 |
| 6 (11–12) | 310 | 292 | 602 |
| Lower-secondary school | | | |
| 7 (12–13) | 292 | 268 | 560 |
| 8 (13–14) | 229 | 255 | 484 |
| 9 (14–15) | 219 | 251 | 470 |
| Total | 3163 | 3167 | 6330 |

subscales to measure the 2 major characteristics of ADHD, namely, Inattentive (9 items) and Hyperactive-Impulsive (9 items). Both the school and home forms of the ADHD-RS have been confirmed to have sufficient reliability and validity (DuPaul, Power, Anastopoulos, & Reid, 1998; DuPaul, Power, McGoey, Ikeda, & Anastopoulos, 1998; DuPaul et al., 2008). As in prior surveys, parents or rearers rated each item on a 4-point Likert scale ranging from "Not at all or rarely (0)" to "Sometimes (1)," "Often (2)," or "Very often (3)." Therefore, the higher a child's score, the more the ADHD tendency.

Our survey employed the DCDQ-J and ADHD-RS and asked the parents or guardians to respond to all of the items for their children.

We measured the intelligence of elementary school children and lower-secondary schoolchildren by using the New Kyoken Support to Intelligence Tests for Each School Grade (Tatsuno, Ishida, & Hattori, 2002). This is a collective intelligence test conducted at the beginning of a school year to assess each child's intelligence quotient (IQ).

### 2.3. Procedure

This study was approved by the ethics committee of the Hamamatsu University School of Medicine. To request the cooperation of the target city, we provided the education committee of that city with an explanation of the purpose and method of our study, as well as an outline of our plan to protect the privacy of participants. We obtained consent from all the preschools and elementary and junior high schools in the participating city and performed the survey using the described questionnaires. We informed the parents and guardians before starting the study that participation was optional and that they would be notified of the results after the compilation of statistics.

### 2.4. Statistical analysis

SPSS version 16 (IBM Corporation, NY, USA) was used for statistical analysis.

## 3. Results

### 3.1. Scaling method of the DCDQ-J, confirmatory factor analysis, and reliability of DCDQ-J

A confirmatory-factor analysis of the DCDQ-J was performed by assuming the 3 factors reported by Wilson et al. (Schoemaker et al., 2006; Wilson et al., 2000, 2009). All factor loading values were ≥0.5, while indicators of good fit were slightly low, such as comparative fit index (CFI) = 0.86 and mean square error of approximation (RMSEA) = 0.13. Therefore, 4 error covariances were added according to the modification indices. As a result, the CFI increased to 0.94 and RMSEA decreased to 0.09, which were acceptable results. The α factors were calculated by subscale yielded values for control during movement, fine motor, and general coordination as 0.91, 0.91, and 0.81, respectively, which indicated that the subscales had high levels of internal consistencies. Accordingly, the study employed 3-factor analysis, and total scores per item were defined as subscale scores. The correlation coefficient between the subscales ranged from 0.59 to 0.73. The total scores of all items were defined as all scores of the DCDQ ($\alpha = 0.93$).

### 3.2. Gender difference and school grade difference in the DCDQ-J

Two-way analysis of variance (ANOVA) with factors of age and school grade was performed to evaluate the subscale scores of the DCDQ-J (Table 2). The main effects of gender ($F(1, 6218) = 78.88$, $p < 0.001$) and school grade ($F(10, 6218) = 36.70$, $p < 0.001$) were significant, while the interaction effect ($F(10, 6218) = 0.54$) was not significant in the control





**Table 2**
Descriptive statistics of the Japanese version of Developmental Coordination Disorder Questionnaire.

| Grade (age) | Control during movement | | | | Fine motor | | | | General coordination | | | | DCDQ total | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | | Female | | Male | | Female | | Male | | Female | | Male | | Female | |
| | *M* | *SD* | *M* | *SD* | *M* | *SD* | *M* | *SD* | *M* | *SD* | *M* | *SD* | *M* | *SD* | *M* | *SD* |
| Middle (4–5) | 19.46 | 5.40 | 19.04 | 5.35 | 12.44 | 4.17 | 14.78 | 4.02 | 16.09 | 4.76 | 17.19 | 4.79 | 47.99 | 12.84 | 50.97 | 12.69 |
| Senior (5–6) | 21.31 | 5.46 | 19.99 | 5.26 | 13.63 | 4.20 | 15.59 | 3.76 | 17.23 | 4.27 | 17.73 | 4.59 | 52.51 | 12.11 | 53.38 | 12.50 |
| 1 (6–7) | 21.22 | 5.48 | 20.38 | 5.32 | 14.53 | 3.72 | 16.12 | 3.63 | 16.75 | 4.57 | 17.99 | 4.59 | 52.55 | 12.24 | 54.56 | 12.03 |
| 2 (7–8) | 21.51 | 5.22 | 20.45 | 5.12 | 13.82 | 3.63 | 15.70 | 3.39 | 16.27 | 4.39 | 17.66 | 4.34 | 51.73 | 11.58 | 53.81 | 11.31 |
| 3 (8–9) | 22.29 | 5.38 | 20.76 | 5.01 | 14.17 | 3.56 | 15.60 | 3.50 | 16.98 | 4.26 | 17.53 | 4.16 | 53.44 | 11.71 | 53.94 | 11.00 |
| 4 (9–10) | 22.94 | 5.43 | 21.27 | 5.38 | 14.91 | 3.51 | 16.02 | 3.44 | 17.76 | 4.33 | 17.77 | 4.20 | 55.79 | 11.67 | 55.18 | 11.51 |
| 5 (10–11) | 23.29 | 5.21 | 21.86 | 5.64 | 14.98 | 3.74 | 16.58 | 3.47 | 17.83 | 4.46 | 18.41 | 4.44 | 56.10 | 11.96 | 56.99 | 12.00 |
| 6 (11–12) | 23.39 | 5.77 | 22.09 | 5.21 | 14.88 | 4.00 | 16.71 | 3.35 | 17.72 | 4.75 | 18.30 | 4.15 | 55.99 | 13.29 | 57.12 | 11.34 |
| 7 (12–13) | 23.64 | 5.26 | 22.39 | 5.41 | 14.88 | 3.93 | 16.45 | 3.53 | 17.78 | 4.50 | 18.35 | 4.40 | 56.39 | 12.33 | 57.16 | 12.01 |
| 8 (13–14) | 24.62 | 5.10 | 23.03 | 5.52 | 15.97 | 3.77 | 17.05 | 3.26 | 19.07 | 4.46 | 18.62 | 4.55 | 59.72 | 12.19 | 58.59 | 12.08 |
| 9 (14–15) | 25.11 | 4.92 | 23.73 | 5.55 | 16.00 | 3.70 | 17.39 | 3.44 | 19.04 | 4.61 | 18.96 | 4.64 | 60.36 | 12.00 | 60.04 | 12.22 |
| Sex | | 78.88*** | | | | 284.13*** | | | | 21.44*** | | | | 6.86** | | |
| Grade | | 36.70*** | | | | 25.35*** | | | | 13.33*** | | | | 29.67*** | | |
| Sex × grade | | 0.54 | | | | 1.20 | | | | 2.26* | | | | 1.30 | | |

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

during movement subclass. In addition, the main effect of gender was higher in boys than in girls, and the main effect of school grade tended to increase as the grade level increased. The main effects of gender ($F(1, 6251) = 284.13$, $p < 0.001$) and school grade ($F(10, 6251) = 25.35$, $p < 0.001$) were significant in the fine motor subclass, while the interaction effect ($F(10, 6251) = 1.20$) was not significant. The main effect of gender was higher in girls than in boys, and the main effect of school grade tended to increase as the grade level increased. The main effects of gender ($F(1, 6231) = 21.44$, $p < 0.001$) and school grade ($F(10, 6231) = 13.33$, $p < 0.001$) and the interaction effect ($F(10, 6231) = 2.26$, $p < 0.001$) were significant in the general coordination subclass. The simple main effect by school grade was significant in the middle class students of the nursery school ($F(1, 6231) = 5.07$, $p < 0.001$), the elementary Year 1 schoolchildren ($F(1, 6231) = 14.60$, $p < 0.001$), and the Year 2 children ($F(1, 6231) = 17.14$, $p < 0.001$), and was higher in girls than in boys. The simple main effect of school grade was significant in both genders, boys ($F(10, 6231) = 11.86$, $p < 0.001$) and girls ($F(10, 6231) = 3.50$, $p < 0.001$), but the difference in school grade tended to be greater in boys than in girls. When the total scores of the DCDQ-J were analyzed using two-way ANOVA, the main effect of gender ($F(1, 6150) = 6.86$, $p < 0.01$) and that of school grade ($F(10, 6150) = 29.67$, $p < 0.001$) were significant, while the interaction effect ($F(10, 6150) = 1.30$) was not significant. The main effect of gender was greater in girls than in boys, and the main effect of school grade tended to increase as the grade level increased.

A main effect of school grade was observed at the subscale level and the total scores of the DCDQ-J; thus, the tendency of their developmental changes was evaluated using multiple regression analysis. The 1st to the 10th items were prepared by assigning a value of 1–11 to the middle class students of the nursery school through to Year 9 students. The influence of gender against each subscale and the total score were controlled at Step 1, and the items regarding their school grade from the 1st to the 10th were input by using a forward selection method at Step 2. The first item was significant in the control during movement subclass ($\beta = 0.23$, $p < 0.001$), and it tended to increase as the grade level increased. In the fine motor subclass, the first item was significant ($\beta = 0.17$, $p < 0.001$), and it tended to increase as the grade level increased. In the overall coordination subclass, an interaction of gender and school grade was observed, so that multiple regression analysis by gender was performed. The 2nd item was significant in boys ($\beta = 0.17$, $p < 0.001$), and in girls ($\beta = 0.09$, $p < 0.001$), and it increased as the grade level increased. In the total scores of DCDQ-J, the first item was significant ($\beta = 0.21$, $p < 0.001$), and it tended to increase as the grade level increased. Fig. 1 shows the plot of scores by school grade and the approximation curve.

### 3.3. Subgroups of coordination

Using the standard scores of the 3 subscales of the DCDQ-J, *k*-means clustering was performed to study the subgroups of coordination by changing the number of clusters from 2 to 4. In consideration of the interpretive potentiality, a 4-cluster analysis was used. Fig. 2 shows the subscale scores of the DCDQ-J by cluster. All of the subscale scores of Cluster 1 ($n = 1414$, 22.87%) were lower than the mean value; especially, the subscale score of the fine motor subclass was low. Therefore, Cluster 1 was defined as a "poor fine motor group." Cluster 2 ($n = 2307$, 37.31%) was characterized as having high subscale scores, and it was defined as an "excellent coordination group." The subscale score of fine motor alone in Cluster 3 ($n = 1377$, 22.27%) was greater than the mean value, and other 2 subscale scores were lower than the mean value, and it was defined as an "excellent fine motor group." All of the subscale scores of Cluster 4 ($n = 1086$, 17.56%) were far lower than the mean values, and it was defined as a "poor coordination group."

The frequency of cluster occurrence was studied when school grade and gender were different. The bias between the cluster and school grade was significant ($\chi^2(30) = 294.66$, $p < 0.001$). As the grade level increased, the number of participants

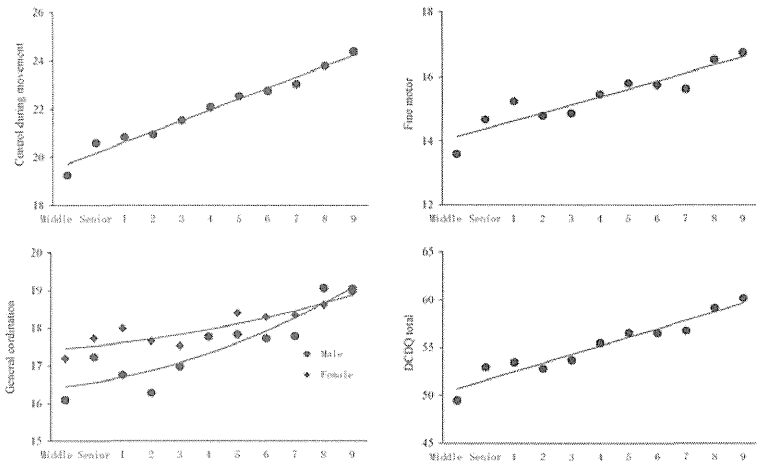


Fig. 1. The score of Japanese version of Developmental Coordination Disorder Questionnaire by grade.

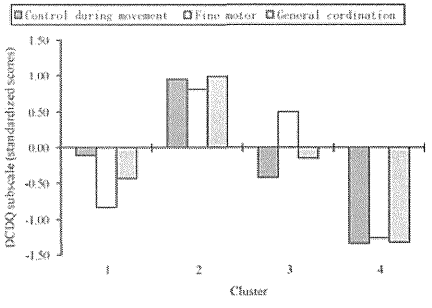


Fig. 2. The score of Japanese version of the Developmental Coordination Disorder Questionnaire subscales by cluster (standardized scores).

in the excellent coordination group increased, while those in the poor coordination group decreased (Fig. 3). The frequency of cluster occurrence of the other 2 groups was approximately 20% regardless of their school grade. In addition, there was a significant bias between the cluster and gender ($\chi^2(3) = 275.13$, $p < 0.001$), which indicated that the poor fine motor group had more boys than girls, while the excellent fine motor group had more girls (Fig. 4).

### 3.4. Relationship of the DCDQ-J with intelligence and ADHD-RS

In the Japanese version ADHD-RS, each subscale was averaged, and the resulting data was defined as inattentive ($\alpha = 0.90$) and hyperactive/impulsive ($\alpha = 0.86$); further, the total score of all items indicated ADHD tendencies ($\alpha = 0.93$). The correlation between the subscales was 0.75. The correlation coefficient between the DCDQ-J, the IQ, and the Japanese version ADHD-RS was calculated (Table 3). The 3 subscale scores and the total scores of the DCDQ-J were slightly positively associated with intelligence. Furthermore, a negative correlation of −0.2 to −0.5 was observed between the 3 subscale scores and the total scores of the DCDQ-J and the Japanese version ADHD-RS.





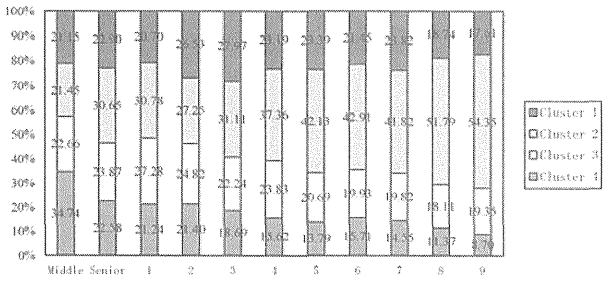


Fig. 3. The frequency ratio of each cluster by grade.

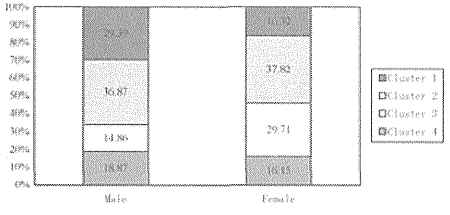


Fig. 4. The frequency ratio of each cluster by sex.

## 4. Discussion

This study was undertaken in a large sample of Japanese children by using DCDQ-J, ADHD-RS, and the New Kyoken Support to Intelligence Tests to establish relationships among coordination, ADHD tendencies, and intelligence. In this study, differences in development were evaluated, taking into consideration that motor skills increase with age and that the scores of control during movement and fine motor subclasses tend to increase linearly as the grade level increases. The general coordination changed non-linearly regardless of gender, and the scores tended to increase sharply as the grade level increased. The mean value and the development-related changes obtained in this study may be useful to study normal development of coordination and for screening of DCD in Japanese children.

When the subgroups of coordination were studied using the DCDQ-J, they were classified into 4 groups, including the poor fine motor group, the excellent coordination group, the excellent fine motor group, and the poor coordination group. Among these groups, the number of the participants in the excellent coordination group increased as the grade level increased, while those in the poor coordination group decreased. Furthermore, the poor fine motor group had more boys, while the excellent fine motor group had more girls. There were various patterns, for example, children with poor coordination were the weakest at fine motor or poor at all physical exercises, and the frequency of these patterns varied depending on their school grade and/or gender. Accordingly, special attention should be paid to children with clumsiness to determine the kind of movement that is their weak point, in consideration of their school grade and gender.

**Table 3**
Relationship between Developmental Coordination Disorder Questionnaire and intelligence quotient or attention-deficit hyperactivity disorder-rating scale.

| | DCDQ | | | |
|---|---|---|---|---|
| | Control during movement | Fine motor | General coordination | DCDQ total |
| IQ | .12*** | .14*** | .11*** | .14*** |
| ADHD-RS | | | | |
| Inattention | −.26*** | −.46*** | −.48*** | −.43*** |
| Hyperactive-Impulsive | −.19*** | −.36*** | −.35*** | −.33*** |
| ADHD total | −.24*** | −.45*** | −.45*** | −.41*** |

*** $p < 0.001$.

The DCDQ-J was related to the ADHD tendencies in children. Previous studies have mention that DCD is associated with ADHD, and that children with ADHD present clumsiness (Fox & Lent, 1996; Kopp et al., 2010; Lingam et al., 2010). In this study as well, all subscales and total scores of the DCDQ-J were significantly associated with the Japanese version ADHD-RS, which suggested that children with poor coordination more frequently showed inattention and hyperactivity in some situations. On the other hand, there was almost no relationship between scores of the DCDQ-J and the IQ. The correlation between the subscales and the total score of the DCDQ-J and their IQ ranged from 0.1 and 0.2, and children with poorer coordination tended to have lower IQs, but the relationship was very weak. Considering that the IQ should be within the normal limit in the diagnosis criteria of DCD by DSM-IV (2000), this study indicates that the DCDQ-J has some degree of validity and may be a useful screening tool for DCD in Japan.

## 5. Limitation and perspectives

Only the questionnaire survey was done in this study, which was not intended to provide a medical diagnosis of DCD. In countries other than Japan, the cutoff value of the DCDQ is set in terms of the medical diagnosis as well as other batteries of tests (Schoemaker et al., 2006; Tseng, Fu, Wilson, & Hu, 2010; Wilson et al., 2000, 2009). Therefore, the predictive validity of the DCDQ-J should be studied in Japan in the future.

## Conflict of interests

The authors have no conflict of interests to declare.

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巻頭言

# 「療育とは…」再考

## —環境の中で身体が脳を創り，運動がこころを創る—

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療育とは単に「医療」「治療」と「養育」「保育・教育」を合わせたものではなく，療育の父と呼ばれる高木憲次先生の造語であるとされています．高木先生は『療育とは，現代の科学を総動員して不自由な肢体を出来るだけ克服し，それによって幸にも恢復したら『肢体の復活能力』そのものを（残存能力ではない）出来る丈有効に活用させ，以て自活の途の立つように育成することである．』（昭和26年『療育』第1巻第1号）と定義しています．

その後，高松鶴吉先生は，医療モデルに近いこの概念を社会モデルとしてさらに発展させ，「療育とは，現在のあらゆる科学と文明を駆使して，障害をもった子どもの自由度を拡大しようとするもので，それは優れた「子育て」でなければならない．」としています．学生さんの講義ではこれらをご紹介していたのですが，療育の現場に深く携わる機会を得ることができて，今改めてその意味を考えています．

福井県こども療育センターでも，AAC（augmentative and alternative communication）を含めた様々なアシスティブ・テクノロジー（支援技術）や取り組みが療育に取り入れられています．特に，自らでは移動できない程度の障害をもつ子でも様々なmobility instrumentsを用いて，motivationをもって移動するという経験が認知機能の発達を促進するというEBMに基づき，子ども達がセンター内を楽しそうに動き回っている様子は感動的です．今後，乳児用の電動車椅子，パワースーツなどロボット工学を含めた最新の「科学と文明」が療育に寄与していけるのではと感じています．さらに，今では当たり前になったBrain–Machine Interface（BMI）である人工内耳ですが，今後，人工眼など機能代償型BMIやDeep Brain Stimulationに加え，脳内の情報を解読し，会話や書字などコミュニケーションとして出力する認知型BMIにより，障害をもった子ども達の社会参加が進むことが期待されます．

一方，周産期医療の進歩に伴い増え続けるいわゆる早産児の療育を行っていると，筋緊張の問題はもちろんですが，どこが自分の脇腹か？　自分の足がどこにあるのか？　など身体図式（Body Scheme）の形成が未成熟な子ども達，感覚の過敏や鈍麻など入力の問題を抱える子ども達がとても多いことに気づかされます．そして，これらのわずかな歪みに対する適切なポジショニングやハンドリングにより，認知発達がどんどん促進されていくことにも驚かされます．身体図式は発達の過程での様々な感覚の入力により形成され，ヒトの運動の基盤となり，その障害は認知能力に影響すると言われています．発達障害の発生メカニズムは未だ明らかではありませんが，遺伝的素因と環境との相互作用と考えられています．近年の認知発達ロボティクスの知見からも，例えば子宮と羊水という拘束された環境の中で胎児は自分自身の身体マッピングを含め経験・学習しており，その際には筋骨格系や感覚などの身体性が大きな役割を果たしていることが示唆されています．また，NICU graduatesの学童期の高次脳機能の発達についての知見が蓄積されるにつれ，自閉症スペクトラム障害やAD/HD，学習障害などに似た発達の問題があることが数多く報告されるようになってきています．自閉症スペクトラム障害の乳児期早期には粗大運動や協調，感覚など身体機能の問題がむしろ大きいことも注目されています．このように考えていくと，従来，innateと思われていた新生児模倣や顔選好性，Penfieldらの一次体性感覚野・運動野のホムンクルスなども胎児期からの子宮内での経験・学習の関与が大きいのではないか，それが十分でない時期に外界へでてきた子ども達には周産期医療のminimal handlingの原則との中で，これらの経験・学習をいつ，どのように提供するのかという神経発達行動脳科学的アプローチによる新しい療育のあり方も今後重要な課題となるのではと感じています．これらの観点は是非NICUで働くことを目指す，あるいは携わっている若い方々にも，療育との関わりをもつ機会を通じて考えていただき，また，NICUでの医療へフィードバックしていただければと願っています．

これら，「あらゆる科学と文明」を駆使して子ども達の療育方法を開発していくには学際的・大型研究の推進が必要ですが，これら障害をもつ子ども達やその家族に最も身近に寄り添っている小児科医・日本小児神経学会がイニシアティブをとって進めていければと考えています．

ところで，私はこのような発達障害における身体性，特に協調運動の発達について取り組んでいますが，研究を進める中で，子ども達の不器用さ・発達性協調運動障害を評価・スクリーニングする国際的評価尺度が我が国にないことに気づき，まずそこから始めています．福井のような地方都市，また，療育センターのような研究施設でないところでも現在カナダ，オランダ，イスラエル，イギリスと4つの国際共同研究を行っています．環境問題でよく使われる"Think globally, Act locally"という言葉がありますが，私は「世界的な視野で考え，目の前の子ども・地域のために働く」ことはもちろん，逆に，"Think locally, Act globally"「目の前の子ども・地域のことを考えれば，世界的に行動せざるを得ない」の両方を信念に活動しています．

いろいろと妄想まがいのことを書き連ねてしまいましたが，最後に，高松鶴吉先生の「療育とは情念であり，思想であり，科学であり，システムである」という，私のもうひとつの大好きな言葉をご紹介して終わりたいと思います．

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Research in Autism Spectrum Disorders

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# Validation of an interview-based rating scale developed in Japan for pervasive developmental disorders

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ABSTRACT

The pervasive developmental disorders (PDDs) Autism Society Japan Rating Scale (PARS), an interview-based instrument for evaluating PDDs, has been developed in Japan with the aim of providing a method that (1) can be used to evaluate PDD symptoms and related support needs and (2) is simpler and easier than the currently used "gold standard" instruments such as the Autism Diagnostic Interview-Revised (ADI-R). We examined the reliability and validity of PARS on the basis of data from 572 participants (277 PDD patients and 295 nonclinical controls). Inter-rater reliability was sufficient at both the item and scale level. Factor analysis extracted four subscales, for which internal consistency was found to be high. The sub and total scores of PARS showed correlations with the domain and total scores of ADI-R, in line with theoretical prediction, indicating the convergent validity of PARS. A receiver operating characteristic analysis showed that PARS has good discriminative validity in differentiating between PDD patients and nonclinical controls, regardless of intellectual capacity. Considering that PARS can be easily implemented by professionals with appropriate knowledge regarding PDDs, PARS may be superior to the existing instruments in terms of cost performance.



## 1. Introduction

Over the course of many years, several instruments have been developed for the diagnosis, evaluation, and screening of pervasive development disorders (PDD). In recent years, the Autism Diagnostic Interview-Revised (ADI-R; Le Couteur et al., 1989; Lord, Rutter, & Le Couteur, 1994) has been broadly accepted as a standardized interview-based diagnostic instrument

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for PDD. The Autism Diagnostic Observational Schedule (ADOS; Lord et al., 2000, 1989) is also widely used as an observation-based diagnostic instrument. These instruments have a high level of discriminative validity with respect to the differentiation of PDD from non-PDD and are useful in reaching a definitive diagnosis; however, their implementation requires special training and significant time, leading to the development of numerous simpler evaluation scales in recent years.

The Modified Checklist for Autism in Toddlers (M-CHAT; Robins, Fein, Barton, & Green, 2001), which has been broadly accepted as a screening instrument, is a unique tool that comprises a combination of questionnaires, telephone interviews, and structured follow-up interviews. Although it is a highly useful tool, its use is limited to toddlers because it was developed with the aim of early identification of PDD. In countries such as Japan and other Asian countries lacking the medical and governmental services for PDD that exist in the United States and Europe, it is believed that many people with undiagnosed PDD exist in a broad age group. In fact, Kawamura, Takahashi, and Ishii (2008) reported that in Toyota City, Japan, where a new systematic PDD screening system has been implemented, there were 11 times more detections of PDD compared with that observed in a survey done 20 years ago. However, few regions in the world have an adequate PDD detection system of this kind. Considering this, the development of a simple and practical evaluation scale that can be applied to a wide age group is an important and pressing issue.

The Autism Spectrum Screening Questionnaire (ASSQ; Ehlers, Gillberg, & Wing, 1999), Autism Screening Questionnaire (ASQ; Berument, Rutter, Lord, Pickles, & Bailey, 1999), and Social Responsiveness Scale (Constantino et al., 2003) have been developed as PDD evaluation scales that can be applied to a relatively broad age group. As all of these evaluation tools are in the format of a questionnaire that can be evaluated by parents or teachers, they have the advantage of being fairly easy to implement. However, in most cases, parents lack the specialized knowledge needed to understand PDD, so the standards for rating individual items can vary greatly depending on the individual conducting the evaluation, possibly leading to a deterioration of the reliability of evaluation results. Furthermore, though teachers generally have more PDD-related knowledge than do parents, they have less specific knowledge of each individual child; hence, their evaluations tend to be less reliable than those of parents. In practice, the sensitivity (true positive rate) and specificity (one minus false positive rate) of the ASSQ in distinguishing PDD and non-PDD was .91 and .77, respectively, for the parent evaluation and .90 and .58, respectively, for the teacher evaluation (Ehlers et al., 1999). Considering that the sensitivity and specificity of the ADI-R were 1.00 and .90, respectively (Lord et al., 1997), the level of accuracy of the ASSQ in distinguishing PDD from non-PDD was insufficient in the hands of both parents and teachers. Furthermore, in a simultaneous comparison conducted by Charman et al. (2007), sensitivity and specificity in identifying autistic spectrum disorders was .86 and .78, respectively, for the ASQ and .78 and .67, respectively, for the SRS, thereby indicating its insufficient precision in practical use.

To resolve this dilemma between accuracy and simplicity, the PDDs Autism Society Japan Rating Scale (PARS) has been developed in Japan as an instrument for evaluating PDDs (Adachi et al., 2006; Kamio et al., 2006; Tsujii et al., 2006). This scale was developed with the aim of providing an instrument that is simpler to use than the ADI-R and ADOS; is applicable to any age group, unlike the M-CHAT; and has better reliability and validity than questionnaire scales such as the ASSQ and ASQ. While PARS uses an interview format similar to ADI-R, the procedures, which are briefly summarized in the manual, can be implemented after simple training. Furthermore, because the criteria for rating each item is clearly defined in PARS, a more reliable and valid evaluation is possible than with questionnaire scales. In order to ease the rating process and shorten the evaluation time, the evaluator assigns values at three levels—none (0 points), somewhat apparent (1 point), and apparent (2 points)—for the 34 items listed as typical behavioral symptoms of PDD. This innovation ensures that the time required to implement PARS is kept to 30–90 min, depending on the interviewer's proficiency and the target's age and symptoms.

There is no international literature on the psychometric properties of PARS, although PARS is now widely used in Japan. This study examined the reliability and validity of PARS and involved a study population of 628 test subjects that included 302 people with PDD and 326 people without PDD. Specifically, we evaluated the inter-rater reliability, factor structure, internal consistency, correlation with the ADI-R, and the ability to distinguish subjects with PDD from a nonclinical sample.

## 2. Methods

### 2.1. PARS

The PARS instrument has been developed (Adachi et al., 2006; Kamio et al., 2006; Tsujii et al., 2006) and published (PARS Committee, 2008) in Japan. It involves the evaluation of PDD symptoms through a semi-structured interview conducted with a parent or family member of the subject as the target. This tool can be used to assess not only the risk of PDD but also the need for support pertaining to administrative and medical services. PARS comprises both an evaluation of symptoms when they were most pronounced during infancy (named the peak symptoms scale) and an evaluation of current symptoms (named the current symptoms scale). The former is used mainly to an assessment of PDD risk, and the latter is mainly used in assessment of actual support needs. The peak symptoms scale, which comprises 34 items, is the same for subjects of all age groups, whereas the current symptoms scale, which comprises 57 items, has 3 versions targeting different age groups: preschoolers, primary schoolers, and adolescents/adults. This study reports on data obtained from the peak symptoms scale.

The PARS peak symptoms scale comprises 34 items that describe the characteristic behavioral symptoms of PDDs during the preschooler phase. The items were selected by a panel of eight child psychiatrists and a developmental clinical psychotherapist who were specialized in autism research and clinical practice with more than 10 years of expertise. They compiled behavioral characteristics shown by children with PDD and classified them into eight categories—Interpersonal

Relationship, Communication, Restricted Interests, Stereotyped Behavior, Resistance, Hypersensitivity, Clumsiness, and other complications. From these, 34 items relating to symptoms that are specific to PDD, as well as items relating to nonspecific symptoms with high need for either clinical or administrative support, were selected. Twenty-two out of the 34 items corresponded to diagnostic features for PDD in the *Diagnostic and Statistical Manual 4th Edition, Text Revision* (DSM-IV-TR; American Psychiatric Association, 2000), and 8 corresponded to associated features. Symptoms described in the remaining four items (items 15, 27, 28, and 32) were not listed in the DSM-IV-TR, but since they are often present in PDD children seen in everyday clinical experience, they were included in the scales.

The evaluation of each item in PARS is based on a 30-page manual (PARS Committee, 2008). This manual includes detailed explanations of the questioning and rating standards for each item. For example, for item 1 of the peak symptoms scale (not making eye contact), a sample question "has the child ever had difficulty making eye contact?" is presented, and the rating standards are listed in detail: "0: made eye contact always," "1: had some difficulty making eye contact (made eye contact when requesting or showing interest in something but not otherwise; sometimes made eye contact and sometimes did not; made eye contact only with the parents but not with others)," and "2: rarely made eye contact (did not make eye contact with parents; avoided eye contact)." In this way, evaluation based on subjective criteria of the interviewer is avoided, and a more objective evaluation is possible.

### 2.2. Sample

The 572 subjects of the main sample comprised two broad groups: a PDD group made up of 277 subjects and a nonclinical control group made up of 295 subjects (Table 1).

Participants in the PDD group were diagnosed as having PDD or subordinate disorders based on the DSM-IV by experienced psychiatrists of medical and educational facilities in 28 areas throughout Japan. The diagnoses were made by integrating data from parental interviews; developmental and medical information; records provided by parents, other caregivers, and teachers; and direct observations of and interactions with the children. Subjects were referred to the facilities due to developmental concerns and randomly recruited for the study by examiners belonging to the facilities. Among these, 175 subjects underwent full-scale IQ tests using intelligence scales such as the Wechsler (Japanese WISC-III Publication Committee, 1998; Shinagawa, Kobayashi, Fujita, & Maekawa, 1990), Binet (Tanaka Institute for Educational Research, 2003), and K-ABC scales (Kaufman, Nadeen, & Kaufman, 1993). Of the 175 subjects, 51 were considered mentally retarded (IQ < 70), while 118 were not (IQ ≥ 70). To evaluate the correlation between PARS and the ADI-R, an ADI-R interview was additionally administered to 74 subjects (mean age = 14.0 years; SD = 3.6; range = 7–24 years; mean IQ = 86.2; SD = 24.7; range = 40–135) from the PDD group.



**Table 1**
Characteristics of the main sample.

| | Age | | | IQ | | | Gender | | |
|---|---|---|---|---|---|---|---|---|---|
| | *M*[a] | *SD*[b] | Range | *M* | *SD* | Range | Male | Female | Total |
| All age groups | | | | | | | | | |
| PDD[c] group | 12.5 | 5.8 | 3–39 | 81.6 | 29.2 | 19–142 | 233 | 44 | 277 |
| Without MR[d] (IQ[e] ≥ 70) | 12.7 | 5.5 | 4–39 | 97.2 | 16.8 | 70–142 | 105 | 13 | 118 |
| With MR (IQ < 70) | 12.3 | 4.9 | 5–31 | 43.6 | 15.7 | 18–69 | 44 | 13 | 57 |
| IQ unknown | 12.4 | 6.3 | 3–32 | – | – | – | 84 | 18 | 102 |
| Nonclinical control group | 10.8 | 7.6 | 3–38 | – | – | – | 153 | 142 | 295 |
| Preschoolers (age, 3–6 years) | | | | | | | | | |
| PDD group | 5.1 | 1.0 | 3–6 | 74.1 | 24.5 | 22–121 | 27 | 12 | 39 |
| Without MR (IQ ≥ 70) | 5.4 | 0.8 | 4–6 | 87.7 | 13.6 | 70–121 | 9 | 5 | 14 |
| With MR (IQ < 70) | 5.9 | 0.4 | 5–6 | 47.0 | 17.8 | 22–68 | 3 | 3 | 6 |
| IQ unknown | 4.5 | 1.0 | 3–6 | – | – | – | 15 | 4 | 19 |
| Nonclinical control group | 4.8 | 1.0 | 3–6 | – | – | – | 69 | 63 | 132 |
| Primary schoolers (age, 6–12 years) | | | | | | | | | |
| PDD group | 9.9 | 1.8 | 6–12 | 80.9 | 31.9 | 18–140 | 94 | 15 | 109 |
| Without MR (IQ ≥ 70) | 10.2 | 1.7 | 7–12 | 99.6 | 16.2 | 71–140 | 46 | 5 | 51 |
| With MR (IQ < 70) | 9.2 | 2.0 | 6–12 | 40.5 | 13.5 | 18–65 | 16 | 5 | 21 |
| IQ unknown | 10.0 | 1.7 | 7–12 | – | – | – | 32 | 5 | 37 |
| Nonclinical control group | 9.2 | 1.8 | 6–12 | – | – | – | 34 | 33 | 67 |
| Adolescents and adults (age, 12–39 years) | | | | | | | | | |
| PDD group | 17.3 | 5.2 | 12–39 | 77.4 | 31.2 | 19–142 | 112 | 17 | 129 |
| Without MR (IQ ≥ 70) | 17.1 | 5.5 | 12–39 | 97.9 | 16.9 | 70–142 | 50 | 3 | 53 |
| With MR (IQ < 70) | 15.9 | 3.7 | 12–31 | 44.9 | 16.7 | 19–69 | 25 | 5 | 30 |
| IQ unknown | 17.8 | 5.0 | 12–32 | – | – | – | 37 | 9 | 46 |
| Nonclinical control group | 20.1 | 6.0 | 13–38 | – | – | – | 50 | 46 | 96 |

[a] Mean.
[b] Standard deviation.
[c] Pervasive development disorders.
[d] Mental retardation.
[e] Intelligence quotient.



Participants in the nonclinical control group were recruited from the local communities by individual examiners at locations such as schools, daycare centers, universities, offices, parents' circles, and neighborhood organizations. Individuals were excluded from the nonclinical control group if they had a clinical diagnosis of any psychiatric disease. IQs were not recorded for the nonclinical control group because they did not have histories of any psychiatric problems or special needs education and were considered to have normal intellectual ability.

Furthermore, separate from the main sample, data from 56 participants (mean age = 9.2 years; SD = 5.8; range = 3–26 years) diagnosed as having PDD by experienced psychiatrists were analysed to evaluate the inter-rater reliability of PARS.

The protocol of this study was approved by the institutional review board of Hamamatsu University School of Medicine.

### 2.3. Procedure

Psychiatrists, clinical psychologists, and graduate students involved in the service for developmental disorders administered the PARS interview by referring to the manual. They had undergone a brief training, which had the following agenda: (a) a lecture on psychiatric features of individuals with PDD; (b) instructions on the rating criterion of each item of PARS; and (c) open completion, scoring, and discussion of the interview. They conducted the PARS interview with the informants (many of whom were parents) after obtaining the appropriate informed consent. The interviewers were not completely blind to the probands' diagnosis because some of them recruited participants themselves. For some participants, an additional ADI-R interview was implemented by Japanese interviewers who had undergone a three-day long ADI-R training workshop in the United States to learn the implementation and scoring methods of ADI-R (Lord et al., 1994). They created a Japanese translation of the ADI-R and received permission from the original author and the publisher to use it through a validation process based on Japanese sample (Tsuchiya et al., submitted for publication). The ADI-R generates algorithm scores for each of the three subdomains; (a) qualitative impairments in reciprocal social behavior; (b) delays in language development; and (c) restricted range of interest and/or stereotypic behaviors. The item composition of the subdomain of delays in language development differs depending on whether or not a subject can use language. We implemented ADI-R only for subjects who can use language.

For the sample used for evaluation of inter-rater reliability, PARS was administered independently to each informant by two interviewers (one experienced specialist and one less experienced trainee).

### 2.4. Statistical analyses

A comprehensive examination of the reliability and validity of PARS was conducted in five steps. First, to consider the inter-rater reliability of PARS, the correlation coefficient between the scores recorded by the two interviewers of the same subject was calculated. Second, to examine the factor structure of PARS, exploratory factor analysis (mean-adjusted weight least-square estimation with promax rotation) was performed based on the PDD group data, and four subscales were extracted. As the score for each item was considered as an ordered categorical variable of three values, factor analysis was carried out using the polychoric correlation coefficient (see Holgado-Tello, Chacon-Moscoso, Barbero-Garcia, & Vila-Abad, 2010). Third, the $\alpha$ coefficient was calculated based on data of the PDD group to examine the internal consistency of the overall scale and four subscales. Fourth, to examine convergent validity, correlation of PARS scores with the ADI-R algorithm scores was considered using Pearson's coefficient.

Fifth, to consider how well PARS distinguishes between PDD and non-PDD, *t*-tests and receiver operating characteristic (ROC) analysis (Swets, 1988) were performed. ROC analysis plots the curve (ROC curve) of the true positive rate (sensitivity) vs. the false positive rate (one minus specificity) as the discrimination cutoff value is varied. The larger the area under the ROC curve (AUC), the higher the discriminative power of the scale. In general, sensitivity and specificity are in a trade-off relationship, and the two cannot be simultaneously maximized. In the present study, the cutoff value was set at the point where the sum of sensitivity and specificity was the largest, and sensitivity and specificity for that point were reported. Further analysis including the presence of mental retardation (MR) as a variable was conducted to consider whether the discriminative power of PARS is influenced by IQ level.

Before initiating the abovementioned analyses, we examined the difference in the scale scores for the 3 age groups because previous studies (Adachi et al., 2006; Kamio et al., 2006; Tsujii et al., 2006) have examined the scale properties of the PARS separately for each age group. One-way ANOVA showed that the total PARS score did not significantly differ for the 3 age groups, both in the PDD group, $F(2, 280) = .41$, $p = .66$, and in the control group, $F(2, 315) = 2.49$, $p = .08$. Therefore, we decided to perform the analyses without any distinction between the age groups.

Significance levels of statistical tests were set at 5% and 1%. Mplus (Muthén & Muthén, 1998–2007) was used for factor analysis, and SPSS 15.0J (SPSS Inc., 2006) was used for other analyses.

## 3. Results

### 3.1. Inter-rater reliability

Spearman's rank correlation coefficients between the scores of two interviewers were significant for all items ($p < .05$ in item 27; $p < .01$ in remaining items), with an average value of .68 (SD = .11). For the total score, the Pearson's correlation coefficient between the scores of the interviewers was $r = .78$ ($p < .01$).

**Table 2**
Corrected item-total correlations and factor loadings.

| No. | Item | I-T corr.[a] | Factor loading | | | |
|---|---|---|---|---|---|---|
| | | | F1 SC[b] | F2 SD[c] | F3 SB[d] | F4 RI[e] |
| 5 | Does not communicate interest by pointing | .70 | **.83** | .17 | .01 | −.20 |
| 6 | Verbal development is delayed | .71 | **.82** | −.29 | .00 | .09 |
| 7 | Conversation does not continue | .79 | **.81** | −.22 | .03 | .29 |
| 4 | Does not bring items to show | .67 | **.79** | .16 | .08 | −.23 |
| 1 | Does not make eye contact | .74 | **.69** | −.01 | .06 | .04 |
| 2 | Is not interested in other children | .74 | **.62** | .23 | −.02 | −.05 |
| 9 | Does not play with other children | .79 | **.57** | .08 | .15 | .06 |
| 3 | Does not look back when name is called | .70 | **.53** | .02 | .20 | .06 |
| 28 | Becomes unstable bringing back to unpleasant memories | .53 | −.20 | **.82** | −.06 | −.01 |
| 26 | Becomes confused when everyday situations or routines changes | .69 | .06 | **.67** | −.12 | .06 |
| 33 | Suddenly cries or becomes upset | .60 | .12 | **.62** | .02 | .05 |
| 32 | Is very scared over nothing | .54 | −.10 | **.60** | −.06 | .18 |
| 34 | Show self-injurious action like banging head on wall or chewing hands | .46 | .01 | **.41** | .26 | −.15 |
| 27 | Cannot maintain personal independence due to disrupted lifestyle | .41 | −.17 | **.40** | .25 | −.19 |
| 30 | Disturbed by particular sounds | .63 | −.03 | **.37** | .19 | .21 |
| 24 | Does not like to be touched | .58 | .14 | **.37** | .20 | .10 |
| 31 | Is either insensitive or oversensitive to pain, heat, etc. | .62 | −.15 | **.36** | .28 | .03 |
| 20 | Does not like to be held | .56 | .18 | **.25** | .16 | .17 |
| 22 | Turns pages or crumples paper repeatedly in the same way | .54 | −.03 | −.14 | **.67** | .23 |
| 19 | Eats or swallows nonfood items | .37 | .00 | −.05 | **.66** | −.22 |
| 14 | Likes watching things that revolve | .59 | .03 | −.05 | **.66** | .13 |
| 18 | Is hyperactive and may go anywhere if left unattended | .62 | .05 | −.20 | **.65** | −.02 |
| 17 | Walks on tiptoes | .47 | −.01 | −.01 | **.60** | −.18 |
| 23 | Moves entire or part of the body repeatedly in the same pattern | .56 | .03 | .07 | **.54** | .06 |
| 12 | Becomes immersed in sensory play | .61 | .15 | −.05 | **.51** | .06 |
| 15 | Looks at things from the corner of eye or from extremely close | .62 | .15 | −.03 | **.48** | .23 |
| 11 | Repeats the words of commercials, etc. | .61 | −.08 | −.06 | .00 | **.81** |
| 10 | Parrot-like repetition stands out | .68 | .37 | −.10 | −.08 | **.68** |
| 13 | Loves road signs, logos, numbers, and letters | .59 | −.13 | .09 | .06 | **.60** |
| 8 | Speaks only one way to say what he/she wants | .70 | .09 | .04 | −.06 | **.51** |
| 21 | Repeatedly watches specific scenes of videos | .62 | −.11 | .15 | .14 | **.49** |
| 25 | Persistently asks the same question | .48 | −.28 | .19 | .00 | **.38** |
| 16 | Becomes immersed lining up toys and bottles | .61 | .05 | .21 | .03 | **.34** |
| 29 | Extremely unbalanced diet, eats very few food items | .57 | .03 | .18 | .11 | **.24** |
| | | | Interfactor correlations | | | |
| | | | F1 | F2 | F3 | F4 |
| | | F2 | .25 | | | |
| | | F3 | .45 | .50 | – | |
| | | F4 | .27 | .42 | .33 | – |

Bold loadings indicate grouping in sub-scales.
[a] Corrected item-total correlation.
[b] Social Communication.
[c] Sensitivity/Difficulty.
[d] Stereotyped Behavior.
[e] Restricted Interests.

### 3.2. Factor structure and internal consistency

Table 2 shows the corrected item-total correlation for each item and the results of factor analysis. Based on a scree plot (9.25, 3.76, 2.36, 2.02, 1.68, 1.62, ...) that showed a leveling-off of eigenvalues after the fourth factor (cf. Cattell, 1966) and perceived interpretability, a four-factor solution was employed. The four factors explained 42.27% of the variability of the total score, and each factor was named in decreasing order according to the factor loading of the items grouped in the factor, starting with Social Communication, Sensitivity/Difficulty, Stereotyped Behavior, and Restricted Interests. The $\alpha$ coefficient based on data of the PDD group was .84 for the communication scale (8 items), .74 for the sensitivity/difficulty scale (10 items), .72 for the stereotyped behavior scale (8 items), and .70 for the Restricted Interests scale (8 items). The $\alpha$ coefficient for all scales was .86. All of the individual item-to-total score correlations were positive and mainly substantial, in the range of .37–.79 (29 of the 34 exceeding .50). The mean values for each subscale and the total score for each group are shown in Table 3.

### 3.3. Correlation with the ADI-R

The correlation of PARS subscores and total score with ADI-R domain scores and total score is shown in Table 4. The score of Qualitative Abnormalities in Reciprocal Social Interaction in ADI-R showed moderate correlation with the score of Social





**Table 3**
Means and standard deviations of PARS total score and subscores.

| | Social Communication | | Sensitivity/ Difficulty | | Stereotyped Behavior | | Restricted Interest | | Total sore | |
|---|---|---|---|---|---|---|---|---|---|---|
| | M[a] | SD[b] | M | SD | M | SD | M | SD | M | SD |
| PDD[c] group | 10.03 | 4.62 | 7.36 | 4.61 | 6.12 | 4.02 | 7.96 | 4.09 | 31.46 | 12.52 |
| Without MR[d] (IQ ≥ 70) | 8.83 | 4.37 | 7.04 | 4.99 | 5.46 | 3.68 | 8.11 | 4.23 | 29.45 | 13.00 |
| With MR (IQ < 70) | 12.66 | 3.18 | 7.83 | 4.39 | 8.21 | 4.12 | 8.45 | 4.17 | 37.14 | 11.55 |
| Nonclinical control group | 0.38 | 1.19 | 0.43 | 1.05 | 0.54 | 1.07 | 0.88 | 1.50 | 2.23 | 3.64 |

[a] Mean.
[b] Standard deviation.
[c] Pervasive development disorders.
[d] Mental retardation.

**Table 4**
Correlations between the ADI-R and PARS.

| PARS | ADI-R | | | |
|---|---|---|---|---|
| | Social Interaction[a] | Communication[b] | Stereotyped Behavior[c] | Total score |
| Social Communication | .48** | .43** | .07 | .48** |
| Sensitivity/Difficulty | .17 | .03 | .37** | .20 |
| Stereotyped Behavior | .03 | .27* | .42** | .25* |
| Restricted Interest | .07 | .10 | .41** | .19 |
| Total score | .27** | .31** | .46** | .41** |

[a] Qualitative abnormalities in reciprocal social interaction.
[b] Qualitative abnormalities in communication.
[c] Restricted, repetitive, and stereotyped patterns of behavior.
* $p < .05$.
** $p < .01$.

Communication in PARS. Furthermore, the score of Qualitative Abnormalities in Communication in the ADI-R showed moderate correlation with the score of Social Communication in PARS, and weak correlation with the score of Stereotyped Behavior and the total score in PARS. The score of Restricted, Repetitive, and Stereotyped Patterns of Behavior in the ADI-R showed weak correlation with the score of Sensitivity/Difficulty in PARS and moderate correlations with the score of Stereotyped Behavior and Restricted Interests and the total score in PARS. The total score of the ADI-R showed a moderate correlation with the score of Social Communication and the total score in PARS and a weak correlation with Stereotyped Behavior.

### 3.4. Discriminative validity

Table 5 and Fig. 1 shows the results of the *t*-test and ROC analysis between the PDD groups (whole group and without MR group) and the nonclinical control group. Three main points can be concluded from the table and figure. First, PARS shows high discriminative power even when the presence or absence of MR is controlled. Second, for either comparison, the total score has more discriminative power than the subscores. This is a general trend seen in other evaluation instruments such as

**Table 5**
Discriminative validity of the total and subscores of PARS.

| | t[a] | AUC[b] | Cutoff point | Sensitivity | Specificity |
|---|---|---|---|---|---|
| *PDD vs. nonclinical control* | | | | | |
| Social Communication | 33.9 | .973 | 3 | .929 | .959 |
| Sensitivity/Difficulty | 24.6 | .961 | 2 | .921 | .902 |
| Stereotyped Behaviors | 22.5 | .928 | 2 | .896 | .851 |
| Restricted Interests | 27.2 | .953 | 3 | .875 | .902 |
| Total score | 37.6 | .991 | 9 | .975 | .956 |
| *PDD without MR vs. nonclinical control* | | | | | |
| Social Communication | 20.8 | .964 | 3 | .908 | .959 |
| Sensitivity/Difficulty | 14.3 | .949 | 2 | .882 | .902 |
| Stereotyped Behaviors | 14.4 | .921 | 2 | .882 | .851 |
| Restricted Interests | 18.2 | .952 | 3 | .882 | .902 |
| Total score | 22.5 | .990 | 9 | .975 | .956 |

[a] All *t* values are significant at the 1% level.
[b] Area under the curve.

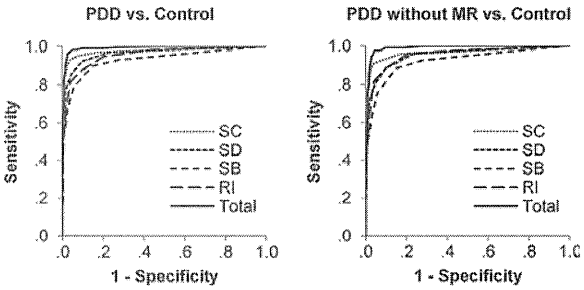


Fig. 1. Receiver operating characteristic curves for discrimination between normal control group and whole PDD (left) and PDD without MR group (right). SC, Social Communication; SD, Sensitivity/Difficulty; SB, Stereotyped Behaviors; RI, Restricted Interests.

the ADI-R (Lord et al., 1997) and ASQ (Berument et al., 1999). Third, the desired cutoff values are not affected by the presence or absence of MR.

## 4. Discussion

The objective of this study was to validate PARS, a scale developed for (1) the evaluation of PDD symptoms in a simpler manner than "gold standard" instruments, such as the ADI-R and ADOS, and (2) more objective evaluation than questionnaire scales, such as the ASSQ and ASQ. As long as the interviewer has a certain level of expertise pertaining to PDDs, PARS can be used after brief training and can be administered in an hour on an average by simplifying and structuring the interview procedure as much as possible and by using simple and clear terms in the manual. In this study, we administered PARS to individuals with PDD and nonclinical controls in order to examine its reliability and validity.

The rating scores recorded by two different interviewers of the same subject showed a sufficient correlation for individual items as well as for the overall score, demonstrating the inter-rater reliability of PARS. The developers of questionnaire scales have often criticized the form of the interview method, stating "the severity of each assessed behavior is rated by the interviewer 'second-hand' on the basis of the parent's answers" (Constantino et al., 2003). This criticism is based on the belief that the interview process produces random or systematic measurement error due to its "second-hand" nature. However, the PARS interview's high inter-rater reliability indicates that it produces little random error, probably because of each item's clearly defined rating criteria. We believe that a semi-structured interview conducted by specialists in treatment of developmental disorders will provide a more accurate measurement than a questionnaire scale based on the subjective judgments of people who lack specialized knowledge, as long as rating criteria are clearly defined and sufficient inter-rater reliability of the evaluation instrument is maintained.

Factor analysis extracted four subscales: Social Communication, Sensitivity/Difficulty, Stereotyped Behaviors, and Restricted Interests. The Social Communication scale corresponds to the "reciprocal social interaction skills" and "communication skills" criteria of the DSM-IV-TR (American Psychiatric Association, 2000), and the Stereotyped Behavior scale and the Restricted Interests scales correspond to the DSM-IV-TR's "presence of stereotyped behavior, interests, and activities." While there is no clear correspondence of the Sensitivity/Difficulty scale with the DSM-IV-TR criteria, it addresses many peripheral symptoms such as sensory over-responsibility and problematic behavior, which are thought to be important in practical support for PDD patients. Through these four scales, PARS not only covers core PDD symptoms but also covers a wide variety of peripheral symptoms. Each subscale and the overall scale showed an $\alpha$ coefficient greater than .70, which demonstrated sufficient internal consistency.

Correlation with the ADI-R clearly duplicated the correspondence relationships with DSM-IV stated above, demonstrating the convergent validity of PARS. Furthermore, the Sensitivity/Difficulty scale showed a correlation with the ADI-R's Restricted, Repetitive, and Stereotyped Patterns of Behavior domain. This might show that the limited interest or fixation on specific things or objects may be the root cause of peripheral symptoms included in the Sensitivity/Difficulty scale.

Through the ROC analysis of the ability of PARS to distinguish between PDD and non-PDD, PARS showed high discriminative power regardless of the intellectual capacity of the patient. The total score demonstrated a higher discriminative power than the subscores, similar to the case with the ADI-R (Lord et al., 1997) and ASQ (Berument et al., 1999). Considering its ease of implementation, PARS may be superior to the ADI-R or ADOS in terms of cost performance. Furthermore, the ROC analysis indicated that the selected cutoff value of PARS is relatively stable regardless of the intellectual capacity of the patient. The fact that a fixed cutoff level can be employed regardless of the nature of the interview subjects is considerably important in terms of convenience and utility in practical use.





One limitation of the study is that the interviewers were not completely blind to the probands' diagnosis. This factor might have a positive influence on the result of discriminative power analysis. Thus, the conclusion about our measurement technique's discriminative power is limited. However, it is unlikely that this problem systematically affects the result of our other analyses (i.e., factor analysis, reliability analysis, and correlation analysis), because the lack of blindness might uniformly raise the score of the PDD group and lower the score of the control group. Such uniform changes do not affect these kinds of analyses.

Finally, we discuss future issues. First, although this study examined the discriminative power of PARS in differentiating between PDD patients and the general population, there is a need to examine its discriminative power in other developmental disorders, such as attention deficit hyperactivity disorder, which shows somewhat similar symptoms to PDD (Hattori et al., 2006), or in other mental disorders, including schizophrenia, depression, and anxiety disorder, which often occur together with PDD. Second, the effectiveness of PARS in distinguishing subordinate diagnoses of PDD, which was not included among the objectives of this study, also needs to be considered. By appropriately combining the four subscales extracted in the factor analysis, PARS might be able to distinguish among subordinate diagnoses. We believe this is also an important issue with respect to the versatility of PARS. Third, an English version needs to be developed if PARS is to be used internationally. Currently, PARS is published in Japan and is being used by many clinical and research institutions (Yamada et al., 2007), but it cannot be used overseas as the Japanese version is the only one that exists. Since PARS is simpler than the ADI-R or ADOS and has sufficient reliability and validity, it can be an extremely useful instrument worldwide.

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## Book review

**The Neurological Examination of the Child with Minor Neurological Dysfunction, third ed., Mijna Hadders-Algra. Mac Keith Press (2010), ISBN-10: 1898683980, ISBN-13: 978-1898683988.**

The 3rd edition of this book was written by Mijna Hadders-Algra, Professor of Developmental Neurology at the Department of Neurology, University of Groningen, and is one of the "A Practical Guide from Mac Keith Press" series. The 1st and 2nd editions were published in 1970 and 1979, respectively, and this 3rd edition has been substantially revised and expanded to incorporate recent findings. However, it upholds the principles of pediatric developmental neurology by Bert C.L. Touwen and Heinz F.R. Prechtl, who wrote the 1st edition, because Hadders-Algra, together with Touwen, Prechtl and colleagues, has examined thousands of pediatric patients since the early 1980s.

In this book, she described the details of the examinations to notice and detect a possible neurobiological basis for behavioral, learning, and motor coordination problems in a child. These neurological examinations are clinically very important in the assessment of children with various developmental disorders, such as attention-deficit hyperactivity disorder (AD/HD), autism spectrum disorder (ASD), learning disabilities (LD) and developmental coordination disorder (DCD).

The author emphasized in this book that a child with behavioral and learning difficulties should be assessed neurologically because the brain is involved in generating his behavior and the neurological assessment enables the examiner to evaluate at lease part of the integrity of the brain.

The book consists of 10 chapters and contains an abundance of references.

The authors, including Touwen and Prechtl, have proposed the concept of minor neurological dysfunction (MND), instead of minimal brain dysfunction (MBD), a term that has not been used in recent years.

The 1st and 2nd chapters describe the histories of these two terms and summarize the importance of evaluating so-called 'soft neurological signs' in clinical practice in order to diagnose developmental disorders. The 'soft neurological signs' is termed variously by other researchers, such as 'equivocal signs' (Kennard, 1960), 'soft signs' (Hertzig, 1981), or 'subtle signs' (Denckla, 1985). In any case, it is persuasive, these days, that the pediatric developmental neurological examinations of the quality of motor behavior are powerful and sensitive tools for the evaluation of brain function.

The 3rd chapter introduces the Groningen assessment with the reliability and validity of its psychometric properties. This assessment was originally developed in the 1960s by Touwen and Prechtl, and was expanded in the 1970s by Touwen, respectively. The most items are consisted by the assessment of sensorimotor function, such as posture, muscle tone, reflexes, involuntary movement, coordination, fine manipulative ability, associated movement, and the cranial nerves. The author stressed that it is important that single signs, or abnormal reflex in the absence of other neurological signs have no clinical significance. These signs only have significance when they co-occur with other signs within a functional domain or cluster.

The 4th and following chapters illustrate in detail the methods of assessment of pediatric patients who are sitting, standing, walking, or lying down. This is followed by information on the effects of age on assessment and performance, and details of scoring.

This book contains an abundance of photographs and figures to reinforce the reader's visual and practical understanding of the subject area. The demonstration of a complete set of patient examination techniques in the accompanying DVD will help with further understanding of the concept. In particular, a comparison between normal functions and those in MND makes it easier for a beginner to distinguish the typical findings. In addition, the tables of age-related changes in typical performance in each chapter are easy to understand and highly practical.

The final, 10th, chapter, *Interpretation of Findings*, refers to the concept of disabilities in the International Classification of Functioning, Disability, and Health: Children and Youth Version (ICF-CY 2007) proposed by the World Health Organization (WHO). The authors largely classify MND into simple MND and complex MND. Complex MND is more strongly associated with learning, behavioral, and motor problems than simple MND, and she suggested that the distinction between two forms of MND is clinically useful. The most interesting idea is that they also divide MND into several subtypes on the basis of the results of close examinations of the cases they have dealt with. She proposed specific types of MND, such as (1) Dysfunctional posture and muscle tone regulation, (2) Dysfunctional reflex activity, (3) Mild dyskinesia, (4) Mild problems in coordination, (5) Mild problems in fine manipulative ability, (6) Excessive associated movements, (7) Mild cranial nerve dysfunction, and finally, Mild sensory dysfunction. Further developmental neurological studies, including brain imaging, of the differences between the various types of MND are expected to be done in future. However, as she describes, these neurological findings may assist the understanding of etiology and facilitate tailor-made guidance for the child.

There are only a few standardized methods of systematically viewing these soft neurological signs in clinical settings. This book is therefore quite useful for medical students and residents, as well as for pediatricians.

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Original article

# Focal EEG abnormalities might reflect neuropathological characteristics of pervasive developmental disorder and attention-deficit/hyperactivity disorder

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**Abstract**

Neurophysiological characteristics in electroencephalograms (EEG) were investigated for patients with pervasive developmental disorder (PDD) and for patients with attention-deficit/hyperactivity disorder (AD/HD). This study examined 64 PDD children and 22 AD/HD children with no history of epilepsy or progressive neurological or psychiatric disorder. We used multivariate analysis to compare EEG abnormalities, clinical symptoms, and intelligence levels between PDD and AD/AD patient groups. Paroxysmal discharges at the frontopolar–frontal (Fp–F) brain regions and background EEG abnormalities tended to be detected preferentially in the PDD group, although paroxysmal discharges at central–temporal (C–T) regions tended to be detected preferentially in the AD/HD group. The paroxysmal discharges observed in patients expressing persistence and impulsivity are apparently localized respectively in the Fp–F and C–T regions. A combination of EEG abnormalities, including background EEG abnormalities and paroxysmal discharges at Fp–F and C–T regions, might be useful diagnostic hallmarks to distinguish PDD with AD/HD from AD/HD alone using a logistic regression model. The dysfunction of specific brain areas associated with EEG abnormalities might explain characteristics of clinical symptoms observed in PDD and AD/HD patients.


*Keywords:* Pervasive developmental disorder; Attention-deficit/hyperactivity disorder; Electroencephalogram abnormality; Paroxysmal discharges



## 1. Introduction

According to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria, pervasive developmental disorder (PDD) can be discriminated from attention-deficit/hyperactivity disorder (AD/HD). The nosology, which does not accept the existence of dual diagnoses of PDD and AD/HD, assigns priority to the diagnosis of PDD, not AD/HD [1]. Practically, however, clinicians often encounter patients with a spectrum of these two disorders, which could be diagnosed as overlapping PDD and AD/HD rather than as a variant of PDD [2].

Numerous reports have described higher rates of prevalence of epilepsy and electroencephalographic abnormalities in children diagnosed as having PDD or AD/HD than in normal school-aged children. The respective prevalence rates of children with PDD and AD/HD showing EEG abnormalities have been reported as 21–86% and 18–30% [3–13]. Whether PDD and AD/HD have distinctive and intrinsic EEG abnormalities remains unknown. This study analyzed and compared the respective relations between EEG abnormalities and either PDD or AD/HD. We then assessed the clinical utility of EEG in the differential diagnosis of these disorders.

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## 2. Patients and methods

This study examined 86 children (12 female and 74 male) with PDD ($n = 64$) or AD/HD ($n = 22$) who had been referred to the Hiratani Clinic for Developmental Disorders of Children during January 2004–December 2008 for evaluation of their development and for diagnosis and treatment of their challenging behaviors. The author (M.H.), a pediatric neurologist at the clinic, checked up and diagnosed all subjects according to DSM-IV criteria. Patients with IQ of 70 or less (Wechsler Intelligence Scale for Children, Third Edition; WISC-III), and those with comorbid epilepsy, progressive neurological or psychiatric disorders were excluded. Informed consent was obtained from the subjects and their guardians. The ethical committee of the University of Fukui approved the project.

Each participant's EEG was recorded for at least 30 min under awake and natural sleep conditions. The 10–20 international electrode placement method was used with a time constant 0.3 and a 100 Hz high-frequency filter. The EEG abnormalities included background EEG abnormalities (slowed rhythmicity or laterality of basic waves) and paroxysmal discharges. "Slowed rhythmicity" was defined as an occipital basic rhythm of which the frequency was at least 1 Hz or slower than that of the age-matched standard basic rhythm, and "laterality of basic waves" was defined as asymmetrical occipital amplitude of not less than 50% [15,16]. Paroxysmal discharges were classified as either "diffuse" or "localized". The localized discharges were divided into three groups according to the respective dominantly affected regions: Fp–F, frontopolar to frontal regions; C–T, central to temporal regions; and P–O, parietal to occipital regions. "Lateralization of paroxysm" was defined as paroxysmal discharges detected only in a unilateral hemisphere. The presence of rolandic spikes (RS), which was one of C–T localized paroxysm, was also examined.

Medical records related to the characteristic symptoms of PDD and AD/HD including delayed language development in early childhood, persistence, impulsivity, temper tantrums, clumsiness, and hypersensitivity were obtained for this study. The intelligence level was assessed using the Wechsler Intelligence Scale for Children, Third Edition (WISC-III).

Statistical analyses were conducted using software (SPSS ver. 13.0 J; SPSS Inc., Tokyo, Japan). Statistical significance was inferred for $p < .05$. Univariate and multivariate associations among various clinical parameters, including symptoms and EEG findings, and the diagnosis were tested using logistic regression analysis. The Press Q statistic was used to evaluate the discriminatory power of the classification matrix produced by a logistic regression model when compared with a chance model.

Data are expressed as the mean ± SD or the median and range. Differences between two groups were analyzed using unpaired *t*-tests, Fisher's exact test, and $\chi^2$-tests.

## 3. Results

### 3.1. Clinical characteristics of patients

Subjects enrolled in this study were 8.6 ± 2.2 years old. The EEG and intelligence assessments were examined at similar ages of both PDD and AD/HD groups. Among the clinical symptoms, delayed language development in early childhood, persistence, and hypersensitivity perception were more prevalent in patients with PDD than in those with AD/HD (Table 1). No significant difference was found in the prevalence of impulsivity, temper tantrums, or clumsiness between the PDD and AD/HD groups, or in their IQ values.

### 3.2. Relation between clinical entities and EEG abnormalities

Background EEG abnormalities were observed more frequently in the PDD patient group than in the AD/HD patient group (22% vs. 9%) (Table 2). The total incidences of paroxysmal discharges were not significantly different between the PDD and AD/HD groups (52% vs. 41%). Paroxysmal discharges with foci at the Fp–F brain region, RS, and diffuse ones tended to be more detected in the PDD group, whereas paroxysmal discharges with foci in C–T and P–O regions tended to be more detected in the AD/HD group. However, univariate analysis showed no statistically significant differences. No significant difference in the laterality of paroxysmal discharges was found between PDD and AD/HD groups. The patients who had been sub-classified into the inattention subtype of AD/HD exhibited no EEG abnormality. No differences among subgroups of PDD were apparent in terms of the prevalence of each EEG abnormality. Fig. 1 presents examples of characteristic EEG abnormalities.

### 3.3. EEG abnormalities are associated with clinical symptoms but not with intelligence levels

Patients with delayed language development in the early childhood exhibited more background EEG abnormalities (32%, $\chi^2$-tests $p < .01$) than patients with other clinical symptoms (15–21%) (Table 3). Paroxysmal discharges observed in patients expressing persistence or

Table 1
Patient data.

| Subtype | PDD ($n = 64$)<br>Autistic disorder: 15<br>Asperger disorder: 32<br>PDD-NOS: 17 | AD/HD ($n = 22$)<br>Inattentive: 5<br>Hyperactive impulsive: 0<br>Combined: 17 | $p$-Value |
|---|---|---|---|
| Gender (female/male) | 10/54 | 2/20 | n.s. |
| Age when EEG was recorded | 8.7 ± 2.3 years | 8.4 ± 1.9 years | n.s. |
| Age when IQ was assessed | 8.6 ± 2.2 years | 8.4 ± 2.0 years | n.s. |
| Clinical presentation | | | |
| Delayed language development | 23 (36%) | 2 (9%) | <.05 |
| Persistence | 61 (95%) | 4 (18%) | <.01 |
| Impulsivity | 44 (69%) | 18 (82%) | n.s. |
| Temper tantrums | 46 (72%) | 17 (77%) | n.s. |
| Clumsiness | 48 (75%) | 12 (55%) | n.s. |
| Hypersensitivity | 42 (66%) | 5 (23%) | <.01 |
| WISC-III | | | |
| Full-scale IQ | 95 ± 14 | 96 ± 13 | n.s. |
| Verbal IQ | 93 ± 15 | 94 ± 13 | n.s. |
| Performance IQ | 99 ± 15 | 100 ± 15 | n.s. |

Mean ± SD; PDD, pervasive developmental disorder; AD/HD, attention-deficit/hyperactivity disorder; PDD-NOS, pervasive developmental disorder not otherwise specified; WISC-III, Wechsler Intelligence Scale for Children, Third Edition; n.s., not significant.

Table 2
Relation between EEG abnormalities and clinical entities.

| | PDD | | | | | AD/HD | | |
|---|---|---|---|---|---|---|---|---|
| | Autistic disorder | Asperger disorder | PDD-NOS | PDD with AD/HD[a] | Total | Combined type | Inattention type | Total |
| Number | 15 | 32 | 17 | 51 | 64 | 17 | 5 | 22 |
| Background abnormalities | 5 (33%) | 7 (22%) | 2 (12%) | 12 (24%) | 14 (22%) | 2 (12%) | 0 | 2 (9%) |
| Paroxysmal discharges | 8 (53%) | 19 (59%) | 6 (35%) | 26 (51%) | 33 (52%) | 9 (53%) | 0 | 9 (41%) |
| Diffuse | 4 (27%) | 11 (34%) | 5 (29%) | 15 (29%) | 20 (31%) | 4 (24%) | 0 | 4 (18%) |
| Foci at Fp–F | 3 (20%) | 10 (31%) | 3 (18%) | 15 (29%) | 16 (25%) | 3 (18%) | 0 | 3 (14%) |
| C–T | 3 (20%) | 9 (28%) | 2 (12%) | 12 (24%) | 14 (22%) | 8 (47%) | 0 | 8 (36%) |
| P–O | 2 (13%) | 5 (16%) | 3 (18%) | 7 (14%) | 10 (16%) | 5 (29%) | 0 | 5 (23%) |
| RS | 1 (7%) | 1 (3%) | 1 (6%) | 2 (4%) | 3 (5%) | 0 | 0 | 0 |
| Laterality Rt | 3 (20%) | 9 (28%) | 1 (6%) | 10 (20%) | 13 (20%) | 3 (18%) | 0 | 3 (14%) |
| Lt | 1 (7%) | 1 (3%) | 2 (12%) | 4 (8%) | 4 (6%) | 3 (18%) | 0 | 3 (14%) |

PDD, pervasive developmental disorder; AD/HD, attention-deficit/hyperactivity disorder; PDD-NOS, pervasive developmental disorder not otherwise specified; Fp–F, frontopolar–frontal region; C–T, central–temporal region; P–O, parietal–occipital region; RS, rolandic spikes; Rt, right side dominant; Lt, left side dominant.
[a] Cases of PDD fulfilled the diagnostic criteria for AD/HD.

hypersensitivity were most detected in Fp–F brain regions, whereas those observed in patients expressing impulsivity were most in the C–T region. Neither background EEG abnormalities nor the presence of paroxysmal discharges showed a significant correlation with intelligence level, including full scale IQ, performance IQ, and verbal IQ values, irrespective of the clinical entity (Table 4).

### 3.4. EEG abnormalities according to the age in PDD and AD/HD

Paroxysmal discharges and background abnormalities were detected most frequently in patients aged 6–8, and those aged 9–12, respectively (Table 5). Moreover, significant differences of the positive rate of EEG abnormalities with age were not found between groups (Table 5).

### 3.5. Usefulness of EEG findings to distinguish PDD and AD/HD

We evaluated the clinical usefulness of EEG findings to distinguish PDD and AD/HD as an auxiliary diagnostic means (Table 6). First, the following variables were analyzed as univariate diagnostic criteria to differentiate PDD from AD/HD: impulsivity, temper tantrums, clumsiness, background EEG abnormalities,





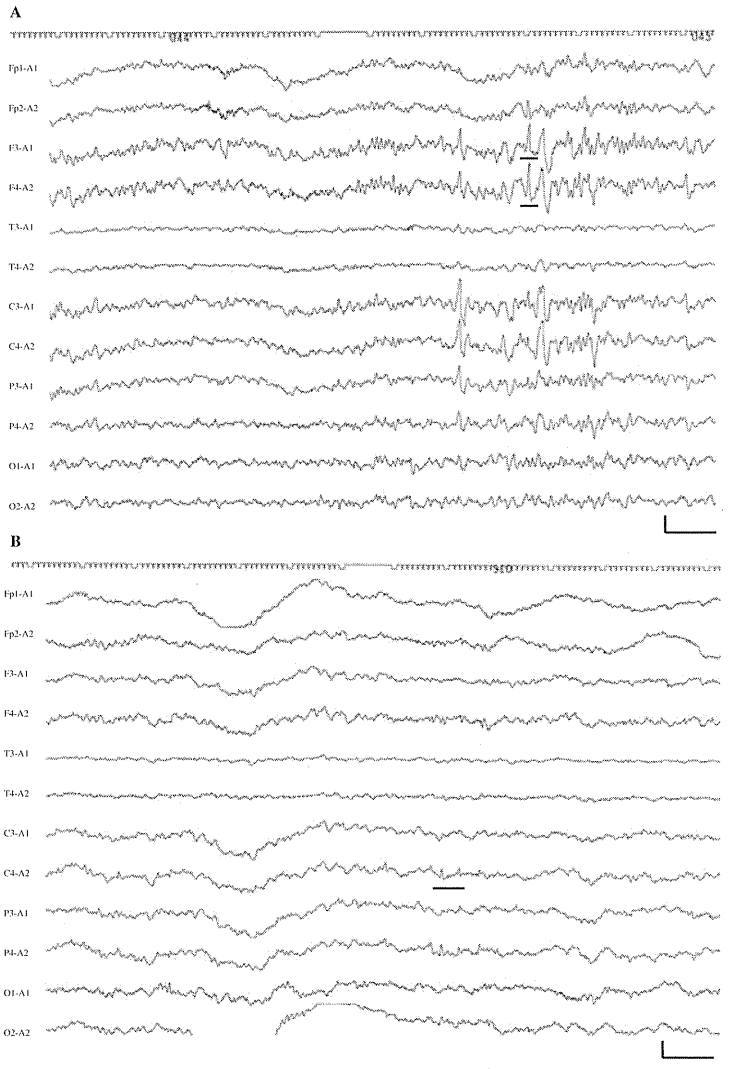


Fig. 1. Examples of characteristic EEG abnormalities. (A) This EEG record during sleep periods of an 8-year-old boy with PDD shows a spike wave on the bilateral frontal region (underline). (B) This EEG record during sleep periods of a 6-year-old boy with AD/HD shows small spike waves on the bilateral central region (underline). Calibration, 50 V, 1 s.

and diffuse, Fp–F, or C–T paroxysmal discharges. Delayed language development and persistence are important criteria for the diagnosis of PDD according to the DSM-IV. Therefore, we excluded these two factors from logistic analysis. Although each criterion alone is not a significant discriminating factor, when

Table 3
Relation between clinical symptoms and EEG abnormalities.

| Presentation | Delayed language development | | Persistence | | Impulsivity | | Temper tantrums | | Clumsiness * | | Hyper-sensitivity | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Diagnosis | PDD | AD/HD | PDD | AD/HD | PDD | AD/HD | PDD | AD/HD | PDD | AD/HD | PDD | AD/HD |
| Number | 23 | 2 | 61 | 4 | 44 | 18 | 46 | 17 | 48 | 12 | 42 | 5 |
| Background abnormalities | 8 | 0 | 13 | 0 | 10 | 2 | 9 | 1 | 8 | 1 | 9 | 1 |
| Paroxysmal discharges | 13 | 0 | 32 | 1 | 22 | 8 | 23 | 5 | 23 | 5 | 23 | 3 |
| Diffuse | 8 | 0 | 19 | 0 | 14 | 4 | 14 | 2 | 14 | 2 | 13 | 3 |
| Foci at Fp–F | 3 | 0 | 16 | 0 | 11 | 3 | 8 | 3 | 11 | 2 | 11 | 1 |
| C–T | 5 | 0 | 13 | 1 | 10 | 7 | 8 | 4 | 10 | 4 | 8 | 2 |
| P–O | 5 | 0 | 9 | 0 | 8 | 4 | 9 | 4 | 7 | 3 | 7 | 1 |
| RS | 2 | 0 | 2 | 0 | 1 | 0 | 2 | 0 | 3 | 0 | 1 | 0 |
| Laterality Rt | 3 | 0 | 13 | 0 | 11 | 2 | 8 | 3 | 9 | 2 | 9 | 1 |
| Lt | 3 | 0 | 4 | 0 | 3 | 3 | 3 | 1 | 4 | 1 | 3 | 0 |

PDD, pervasive developmental disorder; AD/HD, attention-deficit/hyperactivity disorder; Fp–F, frontopolar–frontal region; C–T, central–temporal region; P–O, parietal–occipital region; RD, rolandic discharge; Rt, right side dominant; Lt, left side dominant. *Two patients' clumsiness was not assessed.

Table 4
Relation between IQ levels and EEG abnormalities.

| Diagnosis | VIQ* | | PIQ* | | FIQ* | |
|---|---|---|---|---|---|---|
| | PDD | ADHD | PDD | ADHD | PDD | ADHD |
| Number | 60 | 22 | 60 | 22 | 60 | 22 |
| Background abnormalities | 93 ± 12 (13) | 98 ± 26 (2) | 98 ± 15 (13) | 123 ± 9 (2) | 95 ± 12 (13) | 111 ± 21 (2) |
| Paroxysmal discharges | 92 ± 14 (30) | 94 ± 15 (9) | 96 ± 16 (30) | 99 ± 17 (9) | 93 ± 13 (30) | 95 ± 15 (9) |
| Diffuse | 91 ± 16 (18) | 92 ± 17 (4) | 97 ± 18 (18) | 103 ± 24 (4) | 94 ± 14 (18) | 97 ± 20 (4) |
| Foci at Fp–F | 89 ± 12 (16) | 90 ± 18 (3) | 93 ± 17 (16) | 101 ± 11 (3) | 90 ± 13 (16) | 95 ± 13 (3) |
| C–T | 91 ± 13 (13) | 95 ± 16 (8) | 93 ± 16 (13) | 100 ± 18 (8) | 92 ± 11 (13) | 97 ± 15 (8) |
| P–O | 89 ± 15 (10) | 97 ± 19 (5) | 101 ± 13 (10) | 110 ± 15 (5) | 94 ± 13 (10) | 104 ± 14 (5) |
| RS | 96 ± 10 (3) | None | 93 ± 12 (3) | None | 94 ± 14 (3) | None |
| Laterality Rt | 86 ± 15 (13) | 89 ± 16 (3) | 95 ± 19 (13) | 94 ± 11 (3) | 90 ± 15 (13) | 91 ± 6 (3) |
| Lt | 90 ± 12 (57) | 90 ± 18 (3) | 92 ± 8 (57) | 106 ± 12 (3) | 90 ± 7 (4) | 95 ± 15 (3) |

VIQ, verbal IQ; PIQ, performance IQ, FIQ, full scale IQ; PDD, pervasive developmental disorder; AD/HD, attention-deficit/hyperactivity disorder; PDD-NOS, pervasive developmental disorder not otherwise specified; Fp–F, frontopolar–frontal region; C–T, central–temporal region; P–O, parietal–occipital region; RD, rolandic discharge; Rt, right side dominant; Lt, left side dominant. *Mean ± SD (cases with EEG abnormalities).

Table 5
Paroxysmal discharges and background abnormalities according to the age in PDD and AD/HD.

| | PDD ($n = 64$) | | AD/HD ($n = 22$) | |
|---|---|---|---|---|
| | Paroxysmal discharges | Background abnormalities | Paroxysmal discharges | Background abnormalities |
| Number (positive rate) | 33 (52%) | 14 (22%) | 9 (41%) | 2 (9%) |
| 6–8 years | 25/36 (69%) | 8/36 (22%) | 7/12 (58%) | 1/12 (8%) |
| 9–12 years | 7/22 (32%) | 6/22 (27%) | 2/9 (22%) | 1/9 (11%) |
| 13–15 years | 1/6 (17%) | 0/6 (0%) | 0/1 (0%) | 0/1 (0%) |

PDD, pervasive developmental disorder; AD/HD, attention-deficit/hyperactivity disorder.

analyzed with all criteria as confounding factors, the absence of C–T paroxysmal discharges and the presence of Fp–F paroxysmal discharges seems to support the diagnosis of PDD rather than AD/HD. Of note, the presence of Fp–F paroxysmal discharges might affirm the opposite diagnosis depending on co-evaluation of the presence of C–T paroxysmal discharges. Finally, using a stepwise regression method, the final model comprising the presence of background abnormalities and Fp–F paroxysmal discharges was produced. The absence of C–T paroxysmal discharges is apparently useful for the diagnosis of PDD. Cases that were





Table 6
Multivariate analysis of clinical parameters and EEG findings to discriminate PDD from AD/HD.

| Clinical parameters | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | Un-adjusted OR | 95% CI | $p$-Value | Adjusted OR | 95% CI | $p$-Value |
| *Clinical presentation* | | | | | | |
| Impulsivity | 0.49 | 0.15–1.63 | 0.25 | 0.57 | 0.15–2.21 | 0.42 |
| Temper tantrums | 0.75 | 0.24–2.34 | 0.62 | 0.53 | 0.13–2.19 | 0.38 |
| Clumsiness | 2.00 | 0.69–5.76 | 0.20 | 2.79 | 0.84–9.29 | 0.10 |
| *EEG* | | | | | | |
| Background abnormalities | 2.80 | 0.58–13.46 | 0.20 | 4.77 | 0.74–30.53 | 0.099 |
| Diffuse paroxysmal discharges | 2.05 | 0.61–6.83 | 0.25 | 2.13 | 0.50–9.08 | 0.31 |
| Fp–F paroxysmal discharges | 0.47 | 0.12–1.81 | 0.28 | 6.27 | 0.87–45.44 | 0.069 |
| C–T paroxysmal discharges | 0.49 | 0.17–1.40 | 0.18 | 0.13 | 0.022–0.70 | 0.018 |
| *Regression model based on EEG findings* | | | | | | |
| Background abnormalities | | | | 5.29 | 0.86–32.55 | 0.073 |
| Fp–F | | | | 5.04 | 0.92–27.73 | 0.063 |
| C–T | | | | 0.15 | 0.034–0.68 | 0.013 |

OR, odds ratio; 95% CI, 95% confidence intervals; Diffuse, diffuse paroxysms; Fp–F, focal paroxysms at the frontopolar to frontal region; C–T, focal paroxysms at the central to temporal region. Unadjusted and adjusted OR and 95% CI were calculated using logistic regression analysis. Presence and absence of parameters were converted, respectively, to 1 and 0. Diagnoses of PDD and AD/HD were converted, respectively, to 1 and 0.

Table 7
Multivariate analysis of clinical parameters and EEG findings to discriminate PDD with AD/HD from AD/HD.

| Clinical parameters | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | Un-adjusted OR | 95% CI | $p$-Value | Adjusted OR | 95% CI | $p$-Value |
| *Clinical presentation* | | | | | | |
| Impulsivity | 0.59 | 0.17–2.04 | 0.40 | 0.74 | 0.18–3.09 | 0.68 |
| Temper tantrums | 0.64 | 0.20–2.05 | 0.46 | 0.40 | 0.09–1.76 | 0.22 |
| Clumsiness | 1.95 | 0.65–5.82 | 0.23 | 2.63 | 0.75–9.26 | 0.13 |
| *EEG* | | | | | | |
| Background abnormalities | 3.08 | 0.63–15.10 | 0.17 | 6.19 | 0.82–46.51 | 0.077 |
| Diffuse paroxysmal discharges | 1.88 | 0.54–6.48 | 0.32 | 2.24 | 0.44–11.27 | 0.33 |
| Fp–F paroxysmal discharges | 0.16 | 0.68–10.27 | 0.16 | 9.38 | 1.09–80.50 | 0.041 |
| C–T paroxysmal discharges | 0.54 | 0.18–1.59 | 0.26 | 0.09 | 0.01–0.72 | 0.023 |
| *Regression model based on EEG findings* | | | | | | |
| Background abnormalities | | | | 7.54 | 1.01–42.55 | 0.049 |
| Fp–F | | | | 6.76 | 1.08–42.55 | 0.042 |
| C–T | | | | 0.12 | 0.02–0.66 | 0.015 |

OR, odds ratio; 95% CI, 95% confidence intervals; Diffuse, diffuse paroxysms; Fp–F, focal paroxysms at the frontopolar to frontal region; C–T, focal paroxysms at the central to temporal region. Unadjusted and adjusted OR and 95% CI were calculated using logistic regression analysis. Presence and absence of parameters were converted, respectively, to 1 and 0. Diagnoses of PDD with AD/HD and AD/HD were converted, respectively, to 1 and 0.

classified correctly by the final regression model were 76.7%. The Press Q statistic was $24.6 > 6.63$, which is the critical value at a significance level of .01, indicating that the predictions were significantly better than could be expected by chance. The logistic regression models showed that VIQ, PIQ, and FIQ were not significant independent criteria (data not shown).

As a practical matter, discriminating PDD with AD/HD from AD/HD alone is difficult. We re-evaluated the usefulness of EEG findings to distinguish PDD with AD/HD from AD/HD alone using a logistic regression analysis. As Table 7 shows, similar results were obtained. The presence of background EEG abnormalities, Fp–F, and C–T paroxysmal discharges were identified by statistically significant discriminating factors in the final models. The hit ratio of the final regression model was 74%. The Press Q statistic was 16.78, indicating that the classification results are significantly better than could be expected by chance.

## 4. Discussion

According to DSM-IV criteria, PDD and AD/HD are classified as distinct clinical entities. However, many cases show difficulty in discriminating PDD with AD/HD from AD/HD alone, according to the clinical symptoms and

developmental history [2]. The usefulness of EEG examination for diagnosis of PDD and AD/HD has remained controversial. Our data show that a combination of EEG findings, including background EEG abnormalities, and paroxysmal discharges at Fp–F and C–T brain regions might be a useful diagnostic hallmark that is useful to distinguish PDD with AD/HD from AD/HD alone, and that focal EEG abnormalities might reflect their neurophysiological characteristics cooperatively.

Patients with PDD or AD/HD are known to present epilepsy and EEG abnormalities in many cases [8–13]. The detected prevalence of EEG abnormalities among patients with PDD or AD/HD varies depending on the study design. Few studies have examined the qualitative differences in the EEG findings between these patient groups. Limitations to interpretation of the results of the previous studies are applicable for the following reasons. First, some studies adopted different diagnostic criteria, such as DSM III-R, or specified none [3,7,9]. Second, the enrolled subjects in the studies differ in age and level of intellectual development. Tuchman et al. reported a significant association between severe language deterioration and EEG abnormalities in a minority of PDD patients [4]. Several studies have demonstrated a correlation between low IQ level and EEG abnormalities [5,6]. Because the patients enrolled in this study were diagnosed with PDD or AD/HD according to the DSM-IV criteria, with neither mental disability (full scale IQ $< 70$), severe language deterioration, nor epilepsy, we were able to exclude influences of mental disability and epileptic seizures on the subjects' EEG findings. In fact, this study revealed no significant relation between the IQ level and EEG abnormality.

Kawasaki et al. [3] reported that paroxysmal discharges at the frontal brain regions emerged in a patient with PDD during middle childhood and adolescence. Yasuhara et al. [6] demonstrated that 85.9% of children with PDD suffer from epileptic seizure discharges, which more frequently developed from the frontal part (40.5%) and fronto pole (12.5%) than from other brain regions (<11%). Consistent with these findings, paroxysmal discharges at the Fp–F region are apparently detected preferentially in PDD patients and are associated with "persistence", a necessary criterion for the diagnosis of PDD. The presence of paroxysmal discharges at frontal brain regions might support the PDD diagnosis.

The paroxysmal discharges at the P–O region are apparently more associated with "Temper tantrums" than with other clinical symptoms. "Temper tantrums" is a clinical symptom observed in patients with combined type of AD/HD as well as those with PDD. Consequently, unlike the presence of paroxysmal discharges at the Fp–F region, those at the P–O region cannot be regarded as a discriminating factor between PDD and AD/HD by logistic regression analysis.

Holtmann et al. reported that the prevalence of RS in children with AD/HD is significantly higher than that expected from epidemiologic studies and that some AD/HD children with RS tended to exhibit more hyperactive-impulsive symptoms [11,14]. Although RS were not detected in the EEG of AD/HD patients in the present study, the presence of other forms of paroxysmal discharged at C–T regions is more likely to be associated with impulsivity and is apparently a predisposing factor to AD/HD. Dysfunction of C–T brain areas might impair executive functions, leading to impulsive behaviors in AD/HD patients.

Several functional brain imaging studies have revealed a relation between clinical symptoms analyzed in this study and specific brain regions [17–20]. According to these studies, persistence and temper tantrums are related to the frontal lobe, although impulsivity is related to the frontal lobe, basal ganglia, and thalamus [17–19]. A discrepancy exists in the cerebral localization of impulsivity between EEG finding in this study and the results of brain imaging. Additional studies must be undertaken to elucidate the pathophysiological effects of localized paroxysmal discharges on clinical symptoms.

Two main developmental models of developmental disturbance including AD/HD, the maturational lag model [21] and the developmental deviation model [22], have been proposed based on results from electrophysiological studies. In this study, paroxysmal discharges and background abnormalities decreased with age in both groups. Moreover, no significant difference between groups in the positive rate of EEG abnormalities with age was found. Our results are supportive of maturational lag as the neurophysiological theory in PDD and AD/HD, although no long-term longitudinal data of individual subjects exist.

We acknowledge several limitations to our study, mainly attributable to the small sample size of patients from a single clinic and a university hospital. Particularly, patients with inattention type and hyperactive-impulsive type of AD/HD are few. For that reason, characteristics of EEG findings and clinical parameters of the AD/HD group might not be representative of the entire AD/HD population.

In conclusion, we suggest a reevaluation of the diagnosis utility of conventional EEG findings in PDD and AD/HD as independent variables in logistic regression models. Additional studies must be undertaken to elucidate the relation between the foci of paroxysmal discharges and clinical symptoms.

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# A nationwide survey on quality of life and associated factors of adults with high-functioning autism spectrum disorders

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**Abstract**
The psychosocial outcomes of individuals with high-functioning autism spectrum disorder (HFASD) appear to be diverse and are often poor relative to their intellectual or language level. To identify predictive variables that are potentially ameliorable by therapeutic intervention, this study investigated self-reported psychosocial quality of life and associated factors for adults with HFASD. All participants (n = 154) had a diagnosis of autism spectrum disorder, were over 18 years of age, lived in the community, and had used one or more support services during the survey period. The results demonstrated that psychosocial quality of life was lower than that of the general Japanese adult population. Environmental factors, such as mother's support and early diagnosis, were associated with better quality of life, and aggressive behaviors were associated with poorer quality of life, while expressive language level at preschool years, a conventional outcome predictor, did not predict quality of life. These results emphasize that quality of life measures should be included as outcome indicators in treating individuals with HFASD.

**Keywords**
high-functioning autism spectrum disorder, quality of life, adult, outcome, early diagnosis

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## Introduction

Because autism spectrum disorder (ASD) is a life-long developmental disorder characterized by social and communication impairments and repetitive/stereotyped behaviors, therapeutic intervention for individuals with ASD and their families should be planned for and provided throughout the life span. According to previous outcome studies of autism/ASD, long-term outcomes have repeatedly been shown to be relatively poor when measured by conventionally used indicators, such as employment or independent living, and IQ or expressive language levels during the preschool years, have been thought to be powerful predictors of long-term outcomes (Kobayashi et al., 1992; Howlin et al., 2004; Mawhood et al., 2000). A growing body of literature indicates that children with ASD can be reliably diagnosed in the second year of life (Johnson et al., 2007; Landa, 2008). Furthermore, there is accumulated evidence that early detection and intervention focusing on communication development can lead to substantially better prognosis (Landa, 2008).

Although individuals with high-functioning ASD (HFASD) usually have good intellectual or language development from a very early age, their long-term outcomes are not necessarily desirable and are rather diverse (Kamio et al., 2011). Recent studies have discovered an HFASD subgroup with comorbid psychiatric conditions, which may lead to poor long-term outcomes (Howlin et al., 2004; Tsatsanis, 2003). Counter-examples are also found; some who would have been predicted to do poorly as adults based on their modest intellectual or language development were found to be leading satisfactory lives (Persson, 2000; Ruble and Dalrymple, 1996). Given such diversity in the long-term outcomes of individuals with ASD, it is important to measure long-term outcomes more comprehensively, including subjective aspects such as quality of life (QoL) (Renty and Roeyers, 2006; Ruble and Dalrymple, 1996), and to identify predictive variables that can be changed by therapeutic intervention.

The QoL concept is increasingly being introduced into the health-related science field for children with psychiatric disorders (Bastiaansen et al., 2004). According to the World Health Organization (WHO; The WHOQOL Group, 1995), QoL is defined as 'the individual's perception of their position in life, in the context of culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns', ranging from the person's physical health, psychological state, level of independence, social relationships, personal beliefs, and their relationship to salient features of their environment.

Several studies have investigated QoL during adulthood for people with ASD. Most studies evaluated QoL by proxy (Gerber et al., 2008; Saldaña et al., 2009) or through indirect measures (Persson, 2000) for adults with both intellectual disabilities and ASD, and Renty and Roeyers (2006) investigated self-reported QoL of 58 adults with HFASD. These results showed that the QoL of HFASD populations largely depends on the nature of support services currently being received, suggesting that QoL can be improved by changing environmental factors. Furthermore, Renty and Roeyers (2006) demonstrated that although support characteristics were significantly related to QoL in adults with HFASD, disability characteristics such as IQ or severity of autism were not. This result emphasizes the importance of an available supportive social network, individual needs assessment, and effective professional support for adults with HFASD as well as for ASD adults with intellectual disabilities. However, in the study by Renty and Roeyers (2006) neither informal nor formal support was correlated with QoL, and perceived informal support was positively correlated with it.

In Japan, a new regulation took effect in April 2005 that aims to establish multidisciplinary service systems to improve the function and social participation of individuals with high-functioning autism, Asperger syndrome, and other developmental disorders. Currently, the majority of people with HFASD were not diagnosed as children and only a few people received adequate formal or informal support throughout childhood (Kamio and Inokuchi, 2009). Moreover, mental health

professionals have become increasingly aware of undiagnosed adults with HFASD seeking psychiatric treatment for their comorbid psychiatric symptoms.

The first aim of the present study was to determine the QoL of adults with HFASD living in the community in Japan. The second aim was to identify factors associated with QoL, both in the present and the past. We predicted that ongoing support from early childhood to adulthood is associated with a better QoL in adulthood.

## Methods

In January 2009, we conducted a nationwide survey by mailing questionnaires to 192 specialized facilities that provide consultation and daycare services for local residents with developmental disorders, and to prefectural centers that provide welfare and primary mental healthcare services for local residents. These facilities consisted of 61 Support Centers for Persons with Developmental Disorders, 65 Institutions for Persons with Autism, and 66 Centers for Mental Health and Welfare Services throughout Japan. Clinical staff at each facility helped identify and enroll study participants. Participants were eligible for the study if they had a diagnosis of ASD, were 18 years of age or older, and used any services provided by the facilities during the period 13 January to 13 February 2009. Among 1103 individuals who were identified as eligible, questionnaires were given to the 402 individuals who were willing to participate in the study and whose parents were also willing to participate. By the end of March 2009, 321 questionnaires had been collected from participants at 63 facilities (a response rate of 79.9%).

The protocol of this study was approved by the ethics committee of the National Center of Neurology and Psychiatry in Japan. Written informed consent to participate in our study was obtained from a parent or a guardian, and also from each participant where possible.



### *Participants*

Out of 202 respondents who returned questionnaires with the self-report portions completed, the final study sample consisted of 154 respondents (123 males and 31 females) with complete information provided by the respondents themselves, their parents, and facility staff who knew the respondents well. For seven ASD participants, information was obtained not from parents but from facility staff who knew the respondents well. Because the self-report questionnaires were distributed only to ASD participants whom facility staff thought could understand and respond appropriately, these participants should be considered to be relatively high-functioning. Although we could not confirm their functioning levels with cognitive test data, this assignment appears to be supported by the fact that 136 of the 154 participants (88.3%) received mainstream education and completed higher education without any support, and that only four participants (2.6%) received special education throughout grades 1 to 12. The mean age of the 154 service user participants was 27.6 years (SD 6.5 years, range 18–49 years), and their characteristics based on the parent-supplied information are outlined in Table 1. In decreasing order of frequency, clinical ASD diagnoses ranged from Asperger syndrome, pervasive developmental disorders, high-functioning autism, autism, to pervasive developmental disorders not otherwise specified (PDD-NOS). Table 2 outlines the past history of the ASD service user participants as completed by the parents.

### *Survey questionnaires*

The survey questionnaires comprised the following: parent (or staff)-rated items of the ASD service user's demographic information (listed in Table 1), past history (listed in Table 2), and performance



**Table 1.** Characteristics of ASD participants (N = 154)

| Characteristics | N (%) |
|---|---|
| Gender | |
| Male | 123 (79.9) |
| Female | 31 (20.1) |
| Age categories (years) | |
| 18–24 | 61 (39.6) |
| 25 + | 93 (60.4) |
| Residential status | |
| Independent living | 11 (7.1) |
| Living with family | 142 (92.2)[e] |
| Supported living (group home) | 1 (0.6) |
| Marital status | |
| Married/partnered | 9 (5.8) |
| Unmarried | 145 (94.2) |
| Education | |
| ≤high school[a] | 92 (59.7) |
| Further higher education[b] | 62 (40.3)[f] |
| Employment | |
| Employed[c] | 37 (24.0) |
| Unemployed[d] | 115 (74.7) |
| Homemaker | 2 (0.1) |
| Comorbid with other medical conditions | |
| Physical conditions | 16 (10.4) |
| Psychiatric conditions (other than ASD) | 58 (37.7) |
| Challenging behaviors | |
| Self-injurious behaviors | 14 (9.1) |
| Aggressive behaviors | 45 (29.2) |

[a]The category '≤high school' includes secondary high school, high school, and special schools for handicapped children.
[b]The category 'further higher education' includes college, polytechnic junior college, and graduate school.
[c]The category 'employed' includes part-time job, full-time job, and self-employed.
[d]The category 'unemployed' includes no occupation, during vocational training, and during leave.
[e]A majority of unmarried Japanese men (70.3%) and women (76.4%) (18-34 years) live with parents according to National Institute of Population and Security Research (2009).
[f]68.6% of new graduates from high school proceed to higher education according to Ministry of Education, Culture, Sports, Science and Technology (2009).

in his/her current environment (described below); self-rated QoL (nine items across two domains); and for staff only, several items concerning current family support.

*Performance in the current environment.* Parent participants were asked to rate the extent of difficulty that the ASD service user participant experienced when doing things related to general tasks and demands, communication, mobility, self-care, domestic life, interpersonal interactions, and relationships in his/her current environment. Those questions were based on WHO's International Classification of Functioning, Disability, and Health (ICF), and the definition of 'current environment' includes assistive devices or personal assistance whenever the person actually uses them to perform actions or tasks. The parent participants answered questions using a 5-point rating scale (1 = complete difficulty; 2 = severe difficulty; 3 = moderate difficulty; 4 = mild difficulty; 5 = no difficulty).