poor sensitivity; Table 5) when the analysis was limited to subjects younger than 5 years of age, suggesting that diagnostic validity was compromised in younger individuals. This finding was also consistent with our hypothesis. The compromised sensitivity for younger individuals may be rather straightforward; prior studies have been consistent with this finding, and our own results indicated compromised discriminability between AD and PDDNOS individuals below 5 years of age. However, as such compromised discriminability was not firmly upheld due to potential biases and the limited statistical power of our study sample, analysis of a larger number of individuals may have provided a higher level of sensitivity. Indeed, a recent large-scale study indicated a sensitivity for correctly diagnosing AD as high as 82.7 %, even when participants were under the age of 36 months (Risi et al. 2006). Nevertheless, it remains possible that the low level of sensitivity for those aged less than 5 years in the present study was not simply due to sample selection or the algorithm applied, but also a reflection of the difficulty of differentiating AD from PDDNOS in individuals at such young age, as was suggested by recent literature (Turner and Stone 2007).

In light of the proposed diagnosis of ASD in the forthcoming Diagnostic and Statistical Manual of Mental Disorders (version 5), research interests have increasingly focused on differentiating ASD from non-ASD individuals using ADI-R; however, there is no established cutoff for ASD in ADI-R. Attempts have been made to apply the original algorithm to ASD individuals; unfortunately, sensitivity for correctly diagnosing ASD was shown to be insufficient (Kim and Lord 2012; Risi et al. 2006). A related attempt to differentiate ASD from non-ASD individuals using ADI-R was the use of other assessment scales such as the Vineland Adaptive Behavior Scale (Sparrow et al. 1984) to improve sensitivity (Tomanik et al. 2007). Another attempt at differentiation was to relax the original, stringent algorithm for AD. For instance, in one genetic study (International Molecular Genetic Study of Autism Consortium 2001), the diagnosis of ASD was made according to ADI-R, whereby exceeding the cutoffs of three domains (A, B, C) was required for ASD diagnosis, with the exception that a score on any one of the three domains could fall one point below the threshold. We recalculated sensitivity using this relaxed criterion in the current study, resulting in an overall sensitivity of 64 %. When the same analysis was repeated for three age bands, sensitivity was 27 % for subjects aged < 5 years old, 71 % for subjects aged 5:0–9:11 years old, and 74 % for those 10 years old and older (Table not shown). At present, ADI-R-JV appears to have limited diagnostic validity with respect to detecting ASD.

Nevertheless, studies have emphasized that the use of ADOS together with ADI-R is a sensible approach, in that the combination of the two reflects consensus clinical judgments of AD as well as of ASD better than any other single instrument used alone (Le Couteur et al. 2008), even in individuals as young as 3 years old and younger (Risi et al. 2006). In this regard, evaluations of the sensitivity of both the Japanese version of ADOS and ADI-R-JV for correctly diagnosing ASD should be conducted.

It should also be noted that the sensitivity of ADI-R-JV with respect to correctly diagnosing AD among individuals with concomitant cognitive delay (IQ/DQ < 70) was 94 %, i.e., not lower than the corresponding result for individuals with an IQ of >70 (92 %); this findings was inconsistent with our expectations, as well as with a prior study (de Bildt et al. 2004). Furthermore, other studies have shown that specificity was more prone than sensitivity to be compromised when the examinee exhibited cognitive delay, and thus individuals with cognitive delay are more likely to be overdiagnosed (Lord et al. 1994; Risi et al. 2006). As regards the discrepancy with our hypothesis, the sample bias of the present study should be taken into account, because the mean IQ/DQ of individuals with AD and PDDNOS in this study was fairly high, even higher than reported in previous studies. In addition, the small number of enrolled participants with an IQ/DQ of <70 could have limited the statistical power of the study to detect any compromising effects of cognitive delay on diagnostic validity.

Limitations and Strengths

Treatment or interventions that may have affected the children enrolled in this study should also be taken into account, particularly in the assessment of diagnostic subgroups. It was a limitation of this study that we did not collect relevant data on this topic. On the other hand, ADI-R is a measure based principally on the observation of past behavior during early stages of development, and usually is employed prior to such interventions, and is not based on a patient's current status. This means that the scores we obtained were less likely to reflect intervention effects compared to the scores of instruments that assess current behaviors, such as ADOS. In addition, we observed good to excellent inter-rater reliability, discriminant validity, and diagnostic validity of ADI-R-JV even without considering treatment effects that would have been observed among clinically referred individuals. Considering that statistical tests are generally biased toward null hypotheses (no difference), an adjustment allowing for treatment effects, when examined, would increase the validity of the ADI-R-JV.

In the present study, clinically referred and control individuals were enrolled according to different protocols. If caregiver motivation to participate in this study differed

for the two groups of individuals examined, the difference may have been a substantial source of sample bias. The most likely scenario related to this issue would be that a caregiver of a control individual was highly motivated to participate in the study when there was a concern that the child may have had an undiagnosed psychiatric disorder such as ASD. Indeed, such motivation might have been reflected in high proportions of non-ASD psychiatric disorders; 2 out of 16 control individuals in the reliability study (Table 1) and 4 out of 82 control individuals had such a diagnosis. Parental education and socioeconomic status, when available, may have provided some insight into the extent of this problem, but unfortunately we did not collect such data, which might otherwise have helped to refute this scenario. However, if such a motivation to participate in the study had indeed been the case, it is likely that a number of individuals with ASD would have been detected among control individuals, yet there was not a single case of undiagnosed ASD (i.e., later detected as such) among individuals initially enrolled as controls (Table 1 and Appendix Table 2 in supplementary materials). To minimize this ambiguity, confirmatory studies will be necessary.

Consensus clinical diagnoses were obtained through clinical assessments and case reviews of all of the available information, albeit outside the context of the administration of ADI-R-JV. This approach might have led to a lack of information for optimizing the diagnosis, but it ensured the independence of the administration of the ADI-R-JV. Moreover, ADI-R-JV was administered in a blinded fashion without any reference to the clinical consensus diagnosis, which could also be considered as a strength of the present study.

When we finalized our consensus clinical diagnosis, it might have been helpful to facilitate diagnosis derived from ADOS. It may also have been helpful to adopt this protocol as an external criterion for estimating the validity of ADI-R-JV. Indeed, the Japanese translation of ADOS has been available to those who established the research reliability of ADOS (i.e., since 2010). Our research team consists of very experienced clinicians and clinical researchers, and among the 8 team members involved in establishing a consensus clinical diagnosis, 4 had already established, and 2 were planning to establish, the research reliability of the ADI-R; 3 had already established, and 3 were planning to establish, the research reliability of ADOS; and each member had participated in at least one research training session on either ADI-R or ADOS. Thus, all the team members involved in establishing a consensus clinical diagnosis were fully knowledgeable about the current diagnosis of ASD in a research setting.

Conclusions

ADI-R-JV is a reliable tool, and has sufficient ability to discriminate between individuals with AD and other diagnoses, as well as between individuals with AD and those with no psychiatric diagnosis. The sensitivity for correctly diagnosing AD was generally high (92 %), but appeared to be compromised (55 %) when the tool was used to assess children younger than 5 years of age. The specificity of ADI-R-JV was consistently high, regardless of the age and cognitive level of the examinee.

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References

American Psychiatric Association. (2000). *Task force on DSM-IV. Diagnostic and statistical manual of mental disorders: DSM-IV-TR*. Washington, DC: American Psychiatric Association.

Baron-Cohen, S., Scott, F. J., Allison, C., Williams, J., Bolton, P., Matthews, F. E., et al. (2009). Prevalence of autism-spectrum conditions: UK school-based population study. *British Journal of Psychiatry, 194*, 500–509.

Cicchetti, D. V. (1994). Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology. *Psychological Assessment, 6*, 284–290.

Cicchetti, D. V., Lord, C., Koenig, K., Klin, A., & Volkmar, F. R. (2008). Reliability of the ADI-R: Multiple examiners evaluate a single case. *Journal of Autism and Developmental Disorder, 38*, 764–770.

Cicchetti, D. V., & Sparrow, S. A. (1981). Developing criteria for establishing interrater reliability of specific items: applications to assessment of adaptive behavior. *American Journal of Mental Deficiency, 86*, 127–137.

Cicchetti, D. V., Volkmar, F., Klin, A., & Showalter, D. (1995). Diagnosing autism using ICD-10 criteria: a comparison of neural networks and standard multivariate procedures. *Child Neuropsychology, 1*, 26–37.

Cox, A., Klein, K., Charman, T., Baird, G., Baron-Cohen, S., Swettenham, J., et al. (1999). Autism spectrum disorders at 20 and 42 months of age: stability of clinical and ADI-R diagnosis. *Journal of Child Psychology and Psychiatry, 40*, 719–732.

de Bildt, A., Sytema, S., Ketelaars, C., Kraijer, D., Mulder, E., Volkmar, F., et al. (2004). Interrelationship between autism diagnostic observation schedule-generic (ADOS-G), autism diagnostic interview-revised (ADI-R), and the diagnostic and statistical manual of mental disorders (DSM-IV-TR)

classification in children and adolescents with mental retardation. *Journal of Autism and Developmental Disorder, 34*, 129–137.

Fleiss, J. L., & Cohen, J. (1973). The equivalence of weighted kappa and the intraclass correlation coefficient as measures of reliability. *Educational and Psychological Measurements, 33*, 613–619.

Fombonne, E. (2009). Epidemiology of pervasive developmental disorders. *Pediatric Research, 65*, 591–598.

Gilchrist, A., Green, J., Cox, A., Burton, D., Rutter, M., & Le Couteur, A. (2001). Development and current functioning in adolescents with Asperger syndrome: a comparative study. *Journal of Child Psychology and Psychiatry, 42*, 227–240.

Gray, K. M., Tonge, B. J., & Sweeney, D. J. (2008). Using the autism diagnostic interview-revised and the autism diagnostic observation schedule with young children with developmental delay: Evaluating diagnostic validity. *Journal of Autism and Developmental Disorder, 38*, 657–667.

Hill, A., Bolte, S., Petrova, G., Beltcheva, D., Tacheva, S., & Poustka, F. (2001). Stability and interpersonal agreement of the interview-based diagnosis of autism. *Psychopathology, 34*, 187–191.

International Molecular Genetic Study of Autism Consortium. (2001). A genomewide screen for autism: Strong evidence for linkage to chromosomes 2q, 7q, and 16p. *American Journal of Human Genetics, 69*, 570–581.

Kawamura, Y., Takahashi, O., & Ishii, T. (2008). Reevaluating the incidence of pervasive developmental disorders: impact of elevated rates of detection through implementation of an integrated system of screening in Toyota, Japan. *Psychiatry and Clinical Neurosciences, 62*, 152–159.

Kim, Y. S., Leventhal, B. L., Koh, Y. J., Fombonne, E., Laska, E., Lim, E. C., et al. (2011). Prevalence of autism spectrum sisorders in a total population ample. *American Journal of Psychiatry, 168*, 904–912.

Kim, S. H., & Lord, C. (2012). New autism diagnostic interview-revised algorithms for toddlers and young preschoolers from 12 to 47 months of age. *Journal of Autism and Developmental Disorder, 42*, 82–93.

Kočovská, E., Biskupstø, R., Carina Gillberg, I., Ellefsen, A., Kampmann, H., Stora, T., et al. (2012). The rising prevalence of autism: A prospective longitudinal study in the Faroe Islands. *Journal of Autism and Developmental Disorder,*. doi: 10.1007/s10803-012-1444-9.

Koyama, T., Osada, H., Tsujii, H., & Kurita, H. (2009). Utility of the Kyoto scale of psychological development in cognitive assessment of children with pervasive developmental disorders. *Psychiatry and clinical neurosciences, 63*, 241–243.

Lampi, K. M., Sourander, A., Gissler, M., Niemela, S., Rehnstrom, K., Pulkkinen, E., et al. (2010). Validity of finnish registry-based diagnoses of autism with the ADI-R. *Acta Paediatrica, 99*, 1425–1428.

Le Couteur, A., Haden, G., Hammal, D., & McConachie, H. (2008). Diagnosing autism spectrum disorders in pre-school children using two standardised assessment instruments: The ADI-R and the ADOS. *Journal of Autism and Developmental Disorder, 38*, 362–372.

Lord, C., & Jones, R. M. (2012). Annual research review: Re-thinking the classification of autism spectrum disorders. *Journal of Child Psychology and Psychiatry, 53*, 490–509.

Lord, C., Risi, S., DiLavore, P. S., Shulman, C., Thurm, A., & Pickles, A. (2006). Autism from 2 to 9 years of age. *Archives of General Psychiatry, 63*, 694–701.

Lord, C., Risi, S., Lambrecht, L., Cook, E. H., Jr., Leventhal, B. L., DiLavore, P. C., et al. (2000). The autism diagnostic observation schedule-generic: a standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorder, 30*, 205–223.

Lord, C., Rutter, M., & Le Couteur, A. (1994). Autism diagnostic interview-revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorder, 24*, 659–685.

Lord, C., Storoschuk, S., Rutter, M., & Pickles, A. (1993). Using the ADI-R to diagnose autism in preschool children. *Infant Mental Health Journal, 14*, 234–252.

McGovern, C. W., & Sigman, M. (2005). Continuity and change from early childhood to adolescence in autism. *Journal of Child Psychology and Psychiatry, 46*, 401–408.

Mildenberger, K., Sitter, S., Noterdaeme, M., & Amorosa, H. (2001). The use of the ADI-R as a diagnostic tool in the differential diagnosis of children with infantile autism and children with a receptive language disorder. *European Child and Adolescent Psychiatry, 10*, 248–255.

Parner, E. T., Schendel, D. E., & Thorsen, P. (2008). Autism prevalence trends over time in Denmark: Changes in prevalence and age at diagnosis. *Archives of Pediatrics and Adolescent Medicine, 162*, 1150–1156.

Risi, S., Lord, C., Gotham, K., Corsello, C., Chrysler, C., Szatmari, P., et al. (2006). Combining information from multiple sources in the diagnosis of autism spectrum disorders. *Journal of the American Academy of Child and Adolescent Psychiatry, 45*, 1094–1103.

Rutter, M., Le Couteur, A., & Lord, C. (2003). *ADI-R: Autism diagnostic interview revised. WPS edition manual.* Los Angeles, CA: Western Psychological Services.

Saemundsen, E., Magnússon, P., Smári, J., & Sigurdardóttir, S. (2003). Autism diagnostic interview-revised and the childhood autism rating scale: Convergence and discrepancy in diagnosing autism. *Journal of Autism and Developmental Disorder, 33*, 319–328.

Sparrow, S. S., Balla, D., & Cicchetti, D. V. (1984). *Vineland adaptive behavior scales (VABS).* Circle Pines, MN: American Guidance Service.

Tanaka Institute of Education. (1987). *Tanaka-Binet intelligence scale.* Tokyo: Taken Publisher.

Tomanik, S. S., Pearson, D. A., Loveland, K. A., Lane, D. M., & Bryant Shaw, J. (2007). Improving the reliability of autism diagnoses: Examining the utility of adaptive behavior. *Journal of Autism and Developmental Disorder, 37*, 921–928.

Turner, L. M., & Stone, W. L. (2007). Variability in outcome for children with an ASD diagnosis at age 2. *Journal of Child Psychology and Psychiatry, 48*, 793–802.

Ventola, P. E., Kleinman, J., Pandey, J., Barton, M., Allen, S., Green, J., et al. (2006). Agreement among four diagnostic instruments for autism spectrum disorders in toddlers. *Journal of Autism and Developmental Disorder, 36*, 839–847.

Waterhouse, L. (2008). Autism overflows: Increasing prevalence and proliferating theories. *Neuropsychology Review, 18*, 273–286.

Wechsler, D., Golombok, S., & Rust, J. (1992). *Wechsler intelligence scale for children—Third edition (WISC-IIIUK).* London, UK: The Psychological Corporation.

Williams, J. G., Higgins, J. P., & Brayne, C. E. (2006). Systematic review of prevalence studies of autism spectrum disorders. *Archives of Disease in Childhood, 91*, 8–15.

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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

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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.

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 χ^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%, χ^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 ($n = 64$) Autistic disorder: 15 Asperger disorder: 32 PDD-NOS: 17	AD/HD ($n = 22$) Inattentive: 5 Hyperactive impulsive: 0 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,

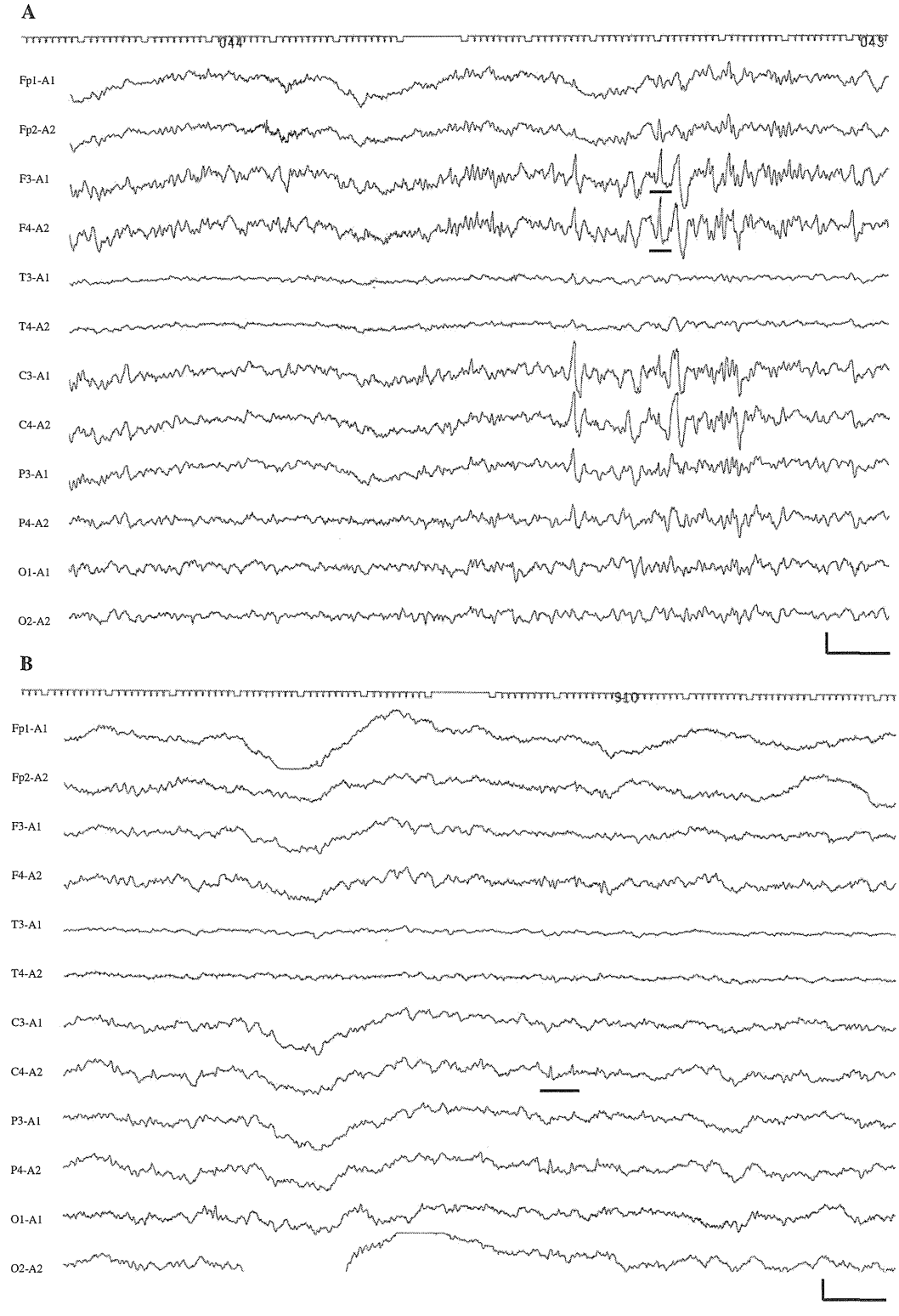

Fig. 1. Examples of characteristic EEG abnormalities. (A) This EEG record during sleep periods of an 8-year-old boy with PDD shows a spike wave on the bilateral frontal region (underline). (B) This EEG record during sleep periods of a 6-year-old boy with AD/HD shows small spike waves on the bilateral 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 Diagnosis	Delayed language development		Persistence		Impulsivity		Temper tantrums		Clumsiness *		Hyper-sensitivity	
	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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References

[1] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: APA; 1994.

[2] Kawatani M, Nakai A, Mayumi M, Hiratani M. Retrospective analysis of pervasive developmental disorder patients initially diagnosed with attention deficit/hyperactivity disorder. No to Hattatsu (Tokyo) 2009;41:11–6, [in Japanese].

[3] Kawasaki Y, Yokota K, Shinomiya M, Shimizu Y, Niwa S. Brief report: electroencephalographic paroxysmal activities in the frontal area emerged in middle childhood and during adolescence in a follow-up study of autism. J Autism Dev Disord 1997;27:605–20.

[4] Tuchman RF, Rapin I. Regression in pervasive developmental disorders: seizures and epileptiform electroencephalogram correlates. Pediatrics 1997;99:560–6.

[5] Hara H. Autism and epilepsy: a retrospective follow-up study. Brain Dev 2007;29:486–90.

[6] Yasuhara A. Correlation between EEG abnormalities and symptoms of autism spectrum disorder (ASD). Brain Dev 2010;32:791–8.

[7] Nomura Y, Nagao Y, Kimura K, Hachimori K, Segawa M. Epilepsy in autism: a pathophysiological consideration. Brain Dev 2010;32:799–804.

[8] Hughes JR, DeLeo AJ, Melyn MA. The electroencephalogram in attention deficit-hyperactivity disorder: emphasis on epileptiform discharges. Epilepsy Behav 2000;1:271–7.

[9] Williams J, Schulz EG, Griebel ML. Seizure occurrence in children diagnosed with ADHD. Clin Pediatr (Phila) 2001;40:221–4.

[10] Richer LP, Shevell MI, Rosenblatt BR. Epileptiform abnormalities in children with attention-deficit-hyperactivity disorder. Pediatr Neurol 2002;26:125–9.

[11] Holtmann M, Becker K, Kentner-Figura B, Schmidt MH. Increased frequency of rolandic spikes in ADHD children. Epilepsia 2003;44:1241–4.

[12] Ishii T, Takahashi O, Kawamura Y, Ohta T. Comorbidity in attention deficit-hyperactivity disorder. Psychiatry Clin Neurosci 2003;57:457–63.

[13] Silvestri R, Gagliano A, Calarese T, Aricò I, Cedro C, Condurso R, et al. Ictal and interictal EEG abnormalities in ADHD children recorded over-night by video-polysomnography. Epilepsy Res 2007;75:130–7.

[14] Holtmann M, Matei A, Hellmann U, Becker K, Poustka F, Schmidt MH. Rolandic spikes increase impulsivity in ADHD – a neuropsychological pilot study. Brain Dev 2006;28:633–40.

[15] Lindsley DB. A longitudinal study of the occipital rhythm in normal children. J Genet Psychol 1939;55:197–213.

[16] Smith JR. The frequency growth of the human alpha rhythm during normal infancy and childhood. J Psychol 1941;11:177–98.

[17] Dawson G, Webb S, Schellenberg GD, Dager S, Friedman S, Aylward E, et al. Defining the broader phenotype of autism: genetic, brain, and behavioral perspectives. Dev Psychopathol 2002;14:581–611.

[18] Sonuga-Barke EJ. The dual pathway model of AD/HD: an elaboration of neuro-developmental characteristics. Neurosci Biobehav Rev 2003;27:593–604.

[19] Quirk GJ, Beer JS. Prefrontal involvement in the regulation of emotion: convergence of rat and human studies. Curr Opin Neurobiol 2006;16:723–7.

[20] Peyron R, Laurent B, Garcia-Larrea L. Functional imaging of brain response to pain. A review and meta-analysis. Neurophysiol Clin 2000;30:263–88.

[21] Clarke AR, Barry RJ, McCarthy R, Selikowitz M. Age and sex effect in the EEG: differences in two subtypes of attention-deficit/hyperactivity disorder. Clin Neurophysiol 2001;112:815–26.

[22] Chabot RJ, Serfontein G. Quantitative electroencephalographic profiles of children with attention deficit disorder. Biol Psychiatry 1996;40:951–63.

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