Title:

Prevalence estimates of neurodevelopmental disorders in Japan: A community sample questionnaire study

Running title: Neurodevelopmental disorders in Japan

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Abstract

Aim: The prevalence estimates of neurodevelopmental disorders have been calculated by questionnaire surveys scored by a single rater, which introduces inherent rater biases. The present study aimed to estimate the prevalence and comorbidity rates of four neurodevelopmental disorders based both on parent and teacher rating scales.

Methods: We performed a community sample survey recruiting 3852 children aged 6–9 years. Both parents and teachers evaluated clinical conditions in children using questionnaire-style scales. These scales with the cut-off values were used to estimate the prevalence and comorbidity rates of attention deficit / hyperactive disorder, autism spectrum disorder, specific learning disorder (or developmental dyslexia), and developmental coordination disorder.

Results: The prevalence estimates were separately confirmed according to the raters. Some estimates were higher than those in the previous studies conducted in other countries. We also found a large disagreement between the parent and teacher rating scores. Moreover, the degree of agreement between two raters varied depending on the severity of clinical condition in the child.

Conclusion: These estimates are the first findings based on evaluating children by two raters. The prevalence and comorbidity estimates are informative to the researchers and clinicians of pediatric neurology. The disagreement between two raters raises questions about previous estimates of neurodevelopmental disorders.

1. Introduction

Prevalence estimates of neurodevelopmental disorders are indispensable in pediatric medicine. The estimates usually affect medical/welfare policy decisions for neurodevelopmental disorders and provides the fundamentals for progression of pediatric researches. According to previous studies, the estimates of major disorders are below: attention deficit / hyperactive disorder (ADHD) = 7.2 – 9.5% [1, 2]; autism spectrum disorder (ASD) = 0.7 – 2.2% [3-6]; specific learning disorder (or developmental dyslexia) (SLD/DD) = 1.2 – 24.0% [7, 8]; developmental coordination disorder (DCD) = 1.4 – 19.0% [9, 10]. Critical concerns about the estimates, such as variability and validity, are common among the previous studies. The estimates vary across ages, within and between countries. There is currently disagreement on one specific estimate due to the methodological differences, like surveys on administrative data (medical / educational / welfare) and national/regional surveys based on certain reports (medical doctor / parents / teacher). As such, systematic reviews will be one of the best solution to this problem [1,2]; however, another concern with previous research is that almost all of these studies have focused on a specific disorder.

Most previous studies have not estimated the prevalence rates of several disorders all together, and failed to report co-occurrence rates among the disorders. For example, a couple of the surveys reported the prevalence estimate of ASD and also provided the rates of comorbidity between ASD and other disorders [11 ,12]. The comorbidity rates were estimated while centering on ASD, so that other overlaps without ASD were not reported in these studies like the comorbidity between ADHD and SLD. Both of researchers and clinicians have certainly known that some patients have two or three neurodevelopmental disorders. Moreover, it might be that different disorders become clinically evident with age when the targeted disorders are hidden in some patients [13, 14]. Most studies have focused on one specific disorder and we did not fully understand how much each disorder exists alone either

overlaps with others among the major neurodevelopmental disorders, which requires us to estimate the prevalence rates of these disorders all together.

A national survey, one of the few studies that have targeted multiple disorders at a time, called "Research about children/students with probable developmental disabilities who need educational support in regular class" was conducted by a ministry in Japan [15]. This survey was carried out by the teacher-rating questionnaires that focused on ADHD, ASD, and SLD. While it counted the number of children suspected to have these disorders using a unique cut-off point to each questionnaire, the rates of co-occurrence among the disorders were calculated, for example, approximately 0.4% of children are suspected of having ADHD, ASD, and SLD. It is considered of value in assessing the disorders all together; however, it can be hard to avoid the rater biases [16-18] because the questionnaires were filled solely by the elementary-school teacher. Usually, moderate differences are expected between parent and teacher rating scales [16], and children suspected of having disorders by teacher rating scales might be seen as typically developing children by parents. Thus, both parents and teachers should evaluate the same children, and the prevalence estimates would be provided based on each of parent and teacher rating scales. This would help us to think which clinical conditions can be more easily considered as a disorder by teachers or parents.

Moreover, these surveys will not be completed without reliable and validated scales for all neurodevelopmental disorders. Although the surveys based on the certain questionnaires cannot investigate the number of patients having the medical diagnosis, due to lack of administrative data, the advantages of the surveys are that they can evaluate potential patients who did not get the diagnosis or either refused to visit the hospital. Thus, the scales determine the quality of the estimates, and most studies have been very careful when they introduce the scales and cut-off points [19-21]. Here, we introduced reliable and valid scales

to our surveys that have been used as tools to aid medical diagnosis in the field of pediatric neurology.

The present study aimed to estimate the prevalence rates of major neurodevelopmental disorders such as ADHD, ASD, SLD, and DCD. The prevalence rate of oppositional defiant disorder (ODD) was also estimated due to high comorbidity with ADHD [22], and both of them can strongly affect school adaption in children [23]. As a community sample survey using questionnaires, both parents and teachers evaluated the same children which provides two types of the prevalence estimates depending on raters and differences between raters. Additionally, we provide the rates of comorbidities among these disorders without centering on a specific disorder. Few previous studies have been performed under these conditions, and the present findings are informative for pediatric neurology both in the clinical and research fields.

2. Methods

2-1. Participants

We recruited participants from a community with a population of 3852 children aged 6 – 9 years (i.e., 1st through 3rd grade) in 2015. The community was selected because the total population was approximately 148,000, which is equivalent to the average population of a city in Japan (i.e., 142,000), and age distribution of the population was similar to the average distributions in Japan. Sixteen elementary schools were enrolled in the community study. All schools had regular classes from 1st through 6th grades. The questionnaire packs were delivered to both parents and teachers via each school in which their children were enrolled. We collected 2461 and 866 packs from parents and teachers, respectively (response rate = 63.9 % and 22.5%). Prior to engagement in the study, we provided sufficient explanations about the study to the school principals, children, and their parents, and then obtained school

approval and informed consent from all schools and parents, respectively, prior to study participation. The research protocol was approved by the ethics committee at National Center of Neurology and Psychiatry (Tokyo, Japan; approval number A2015-004).

2-2. Measures

2-2-1. Scale for Attention Deficit Hyperactive Disorders and Oppositional Defiant Disorder

Symptoms of ADHD and Oppositional Defiant Disorder (ODD) in children were assessed by a Japanese version of the Swanson, Nolan, and Pelham Rating Scale-IV (SNAP-IV) [24]. The SNAP-IV has high reliability and validity in several countries including Japan [24, 25] and the original version was used as a primary outcome measure in the Multimodal Treatment of Attention Deficit Hyperactivity Disorder (MTA) study [26]. The SNAP-IV is a 26-item questionnaire comprised of three factors: Inattention, Hyperactivity–Impulsivity, and ODD. Each item is measured on a four-point Likert scale ranging from 0 (''not at all'') to 3 (''very much''), and each factor score is calculated by taking the mean of the items. Higher scores on the factors reflect more severe symptoms. We set cut-off values for Inattention, Hyperactivity–Impulsivity, and ODD as 2.56, 1.78, and 1.88, respectively, meaning that children with results over these cut-offs are suspect of having these diagnoses [26] though some of them might not have medical diagnoses confirmed by medical doctors.

2-2-2. Scale for Autism Spectrum Disorders

The Social Responsiveness Scale Second Edition (SRS-2) was introduced as a scale for evaluating children's social behavior related to ASD. Both reliability and validity were confirmed in the original version of the SRS-2 [27], and it has been used to measure autistic symptom severity in several countries [28, 29]. The SRS-2 is a 65-item questionnaire that has a total and five subcategory scores: Social Awareness, Social Cognition, Social

Communication, Social Motivation, and Restricted Interests and Repetitive Behavior. Raters were asked to respond to each item using a four-point Likert scale ranging from 1 (''not true'') to 4 (''always true''). Scores were translated into T scores (M=50, SD=10) based on the conversion tables depending on types of raters (parent / teacher) and child's gender. We set cut-off points of T scores ≥ 76. Children rated about the cut-off have severe impairments in social interactions and are strongly suspected to meet diagnostic criteria of ASD. Again, their probable diagnoses were not always confirmed by medical doctors and we might miss diagnosed children who scored under the cut-off points.

2-2-3. Scale for Specific Language Disorder (Developmental Dyslexia)

We assessed dyslexic symptoms in children via the Reading and Writing Clinical Checklist (RWC). The RWC is used as a diagnostic procedure for Japanese developmental dyslexia [30, 31]. The RWC is statistically confirmed to have adequate reliability and validity, with which we can detect children with developmental dyslexia from normal children with good sensitivity and the specificity. The RWC is a 30-item questionnaire (15 items for reading and 15 items for writing). We used ten of the 15 reading and writing items to provide insight into kana literacy (total = 20 items) because 1st-grade children had not learned enough Japanese kanji at the time of the present survey. Each item is measured on a five-point Likert scale ranging from 0 (''not at all'') to 4 (''always true''), and each factor score (Reading / Writing) is calculated by summing the item scores. Higher scores on the factors reflect more severe symptoms. We also counted the number of items with a score of three and above (i.e., positive items), and set the cut-off points for Reading and Writing disabilities as 7 or more positive items which are in line with the diagnostic procedure for Japanese developmental dyslexia [28].

2-2-4. Scale for Developmental Coordination Disorder

The Movement Assessment Battery for Children-Second Edition Checklist (MC) [32] was used as a scale for evaluating motor skills of children. The assessment battery and MC have been widely used in several countries for assessing symptoms of DCD in children [33, 34]. The original version of the MC has adequate reliability and validity confirmed in the UK [32] though no data has been provided based on Japanese samples. Thus, the MC was purchased from the publisher (Pearson Assessment, Oxford, UK) and then translated from English to Japanese. The five examiners and researchers verified the precision and reliability of the translated MC prior to the study. The MC is composed of 30 question items, and each item is rated on a four-point Likert scale ranging from 0 ('very well") to 4 (''not close''). Total score is calculated by summing the item scores, with higher scores indicating greater difficulty in movement. We used original cut-off points for identifying the children suspected of having DCD, which have been established based on the UK samples [32]. The cut-off points have not been standardized by Japanese sample [35].

2-3. Data analyses

We excluded sample data which had at least one missing value in each questionnaire and did not conducted any data imputation (i.e., pairwise deletion). This preprocessing required us to remove many samples, which lead to different numbers of statistical samples depending on questionnaire and raters. First, we calculated the prevalence rates of disorders using each cut-off point of the questionnaire depending on the raters. The chi square (χ^2) tests were performed to examine the differences of the prevalence rates between teacher and parent rating scales. Second, the comorbidity rates among the disorders were estimated. The comorbid-child was defined as one that exceeded the cut-off values of two or more questionnaires by each rater. Finally, we investigated how much the parent and teacher rating

of clinical conditions in children agreed using samples when both succeeded in evaluating the same child. We calculated indices of agreement between the two raters such as κ coefficients and a prevalence-adjusted and bias-adjusted kappa (PABAK) [36], while generating Bland-Altman plots of each disorder to assess the trends of differences between the two raters. Statistical analyses were conducted using R version 3.3.3 [37].

3. Results

3-1. Prevalence Rates of Each Disorder

The prevalence rates of ADHD were 6.3% and 6.5% based on parent and teacher rating scores of SNAP-IV, respectively. The rates were not significantly different between the two raters (p = .87, see Table 1 for χ^2 statistics and 95% confidence intervals); however, the rate of children having diagnosable inattention symptoms was significantly higher in the parent rating scale than in the teacher rating (p = .03) while the opposite trends were confirmed about the hyperactivity–impulsivity (p = .001), and ODD (p < .001). The parent rating SRS-2 reported 1.9% as the prevalence rate of ASD, which was significantly lower than the teacher-rating SRS-2 (p < .001). As for the developmental dyslexia, the rates were significantly higher in the teacher rating RWC than in the parent rating, and these differences were also found in each factor like Reading and Writing (all p < .001). Approximately one-third of children were evaluated as having DCD based on the parent rating MC and half of the children having the disorder based on the teacher rating MC. These incredible rates were produced by the UK's cutoff values that did not seem appropriate for the Japanese samples. Thus, we decided to exclude the MC data from further analyses.

3-2. Comorbidity Rates Among the Disorders

Table 2 presents the comorbidity rates among the three disorders. The rates of comorbidity between ADHD and other disorders were 1.1% (with ASD) and 0.6% (with SLD) based on the parent rating scales. These rates were not significantly different from those based on the teacher-rating scales like 2.1% (ADHD × ASD) and 1.2% (ADHD × SLD) (p = .09 and .23, respectively). The comorbidity rates of ASD with SLD were lower in the parent rating scales than in the teacher rating (p < .001). As for the triple comorbidity, 0.2% of children were considered to have three disorders by their parents, which is lower than when evaluated by their teachers (p < .001).

3-3. Agreements Between Parent and Teacher Rating Scales

We found moderate agreements between the parent and teacher rating of clinical conditions in children based on the PABAKs from .78 to .90 (Table 3); however, these agreement rates are drastically decreased when we focused only on children considered to have disorders by their parents and/or teachers. Only two of 35 children were identified as having ASD by both parents and teachers (i.e. agreement rate = 6%) while others were identified either by parents or by teachers. All agreement rates about suspected children were low such (range of 6% to 16%). The Bland-Altman plots showed the details of these disagreements between the two raters (Figure 1). Based on the plots, strong fixed biases were not found in all disorders because the averaged score differences between the raters was almost 0 (i.e., teacher rating scores minus parent rating scores). On the other hand, proportional biases were confirmed as significant in all disorders (Pearson's r = .09 - 42, all ps < .05). That is, when clinical conditions in children are severe (i.e., averaged scores of teacher and parents are high), teachers considered the conditions as more severe, but parents considered the conditions less severe (i.e., the score gaps between the raters got wider).

4. Discussion

The present study performed a community sample survey to estimate the prevalence rates of several neurodevelopmental disorders all together. This survey enabled us to draw a Venn diagram about the rates, indicating how much each disorder exists alone and overlaps with others. Interestingly, these rates estimated by teacher rating scales were different from those by parent rating. Additionally, the agreement between the two raters varied depending on the severity of clinical condition in the children. These are the first findings based on the Japanese sample, which help us to interpret the present results with epidemiological findings in other countries.

The present prevalence estimates of ADHD were lower than those calculated by the previous systematic review, indicating 7.2% [1]. Previous studies reported the geographical differences of the prevalence estimates of ADHD, and the estimates in Asian countries are often 2% lower compared to the North America [1, 2]. The present estimates seem to be in line with the previous findings based on the Asian characteristics; however, the estimates of subtypes in ADHD were not always consistent with the other reports. Usually, the number of patients with inattentive types of ADHD is two or three times as much as those with hyperactive-impulsive types [38]. The present estimates based on the teacher rating scales were exactly opposite to these findings. This inversion pattern of the estimates partly reflected unique viewpoints of teachers. In Japanese schools, hyperactive-impulsive behaviors are noticeable by teachers beyond necessity because children were often required to keep quiet [39]. Thus, teachers may over-identify these behaviors. Teacher rating characteristics were also confirmed in the estimate gaps between the teacher and parents rating scales.

On the other hand, the prevalence estimates of ASD was slightly higher than those in previous studies [3-6]. Over the last three decades, we have noticed the increasing prevalence of ASD involving autistic disorder or pervasive developmental disorders [3]. A recent study

has reported the estimates of 1.68% from the population-based survey using administrative data [3]. Despite the trend of the times, the estimates in the present study still seem high, especially the estimates based on the teacher rating questionnaires indicating 9.3%. Differences between the present and other studies come from survey style. The present study calculated prevalence rates using the questionnaire data whose distribution is continuous. These rates would be drastically changed when we slide the cut-off value by just one point [27, 40]. Thus, the present estimates based on the teacher rating scales might count the number of the patients with subthreshold autistic conditions. We have to carefully make a judgement whether or not the patients above the cut-off values in the preset study will also be diagnosed with ASD by medical doctors using well-known standardized tests such as Autism Diagnostic Observation Schedule, Second Edition [41].

In contrast with ASD and ADHD, the number of patients with developmental dyslexia drastically varies with linguistic area. Approximately one or two in ten people are affected with dyslexia in Denmark [42], as one of the countries whose prevalence rates of dyslexia are highest in the world. The prevalence rates in English-speaking courtiers usually range from 5% to 12% in the UK and USA [43, 44]. Japanese children are more rarely affected with dyslexia, at a rate of 0.98% [45]; however, the prevalence rate has not been estimated for about 50 years due to the absence of the diagnostic guideline for dyslexia [30]. These differences would be derived from linguistic characteristics like grapheme–phoneme correspondences and letter-styles. Still, the prevalence rates based on the present teacher rating scales is higher than those in the previous studies. The high prevalence rates from teacher rating scales might contain the number of children with "learning difficulties" other than "learning disorders". Some of the teachers have considered the children as dyslexic when they have poor academic achievement, even if they are not diagnosed. The perception gaps between disorder and poor academic achievement in teachers can be reduced with enhanced

awareness of dyslexia, and prevalence rates in the future are expected to be lower than current rates.

The present study also enabled us to calculate prevalence of disorder alone and overlap with other disorders. Interestingly, the number of children with ASD alone was higher than with comorbidities between ASD and other disorders. For example, based on the parent rating scale, the rates of ASD alone is 0.3%, while the sum of the comorbidity rates is 1.5% (ADHD × ASD =1.1%; ASD × SLD =0.2%; ADHD × ASD × SLD =0.2%). This also happened in teacher rating when some prevalence rates were higher than those in the parent rating. Several previous studies examined the comorbidity of ASD and ADHD; however, the comorbidity rates were not consistent among studies (37% - 85%) [46]. The present study also revealed the high potential risk of comorbidity of ASD and SLD, which is not well established in previous studies. These results suggested that most school-age children with ASD have severe difficulties in attention, inhibition, and learning in addition to social interaction limitations, but some only have social impairments and/or restricted interests and repetitive behavior. Thus, pediatric neurologists need to consider the possibility of comorbidity when the patients are diagnosed with ASD.

Prevalence rates calculated here were estimated based on questionnaires evaluated by both teacher and parent raters, which gives us interesting information about the agreement rates between the raters. The agreement rates were quite low. Moreover, the Bland-Altman plots indicated that the rating gaps between the teacher and parents increased when the clinical condition in children became more severe, even though it was impossible to confirm which ratings would be more appropriate for evaluation of children's clinical condition. The disagreement of two raters and rater effects have been reported in previous studies regarding the ADHD scale [17, 47], but few studies have found trends in score gap depending on severity in clinical condition. Based on the present findings, parents would overestimate small

issues in children while they would underestimate or ignore the severe difficulties in their children whose conditions are diagnosable. Our findings also raise a question about the results of a Japanese national survey only using teacher questionnaires [15]. Nation-wide surveys would be necessary for estimating the prevalence rates based both on teacher and parent rating scales.

Some limitations exist in the present study and should be addressed in future studies. First, we did not calculate the number of diagnosed children confirmed by medical doctors. The present study performed a questionnaire survey in a community sample. The questionnaire survey enables us to find children who have not visited the hospital, despite their diagnosable condition. On the other hand, this methodology can overestimate or underestimate the prevalence rates due to rater biases. We must introduce administrative data, including medical diagnoses, and examine the differences of prevalence rates between survey types. Another limitation is the quality of rating scale for DCD. The present study adopted the MC to estimate rates of DCD because the original assessment battery of MC (i.e., Movement Assessment Battery for Children second edition) has been used as a diagnostic tool for DCD worldwide [32-34]; however, the results of MC indicated that half of Japanese children have DCD, which overestimates the prevalence rates compared to the descriptions from the general diagnostic manual [48]. This is partly because the cutoff values for DCD were set based on the UK's sample [32] and this cutoff may not fit Japanese samples. Thus, the rating scale for DCD, including the cutoff values, should be standardized in Japan for future studies. Moreover, the response rates from teachers were relatively low. These were partly attributed to teacher's workload stress to answer the questionnaire because they were requested to evaluate 10 to 35 children by themselves. Thus, some of the teachers decided to answer it only for specific children without evaluating whole children in their classes, which could lead

to the biased results. Further studies should improve the response rates and adjust non-response bias [49].

In conclusion, the present study estimated the prevalence rates of several neurodevelopmental disorders. The comorbidity rates among the disorders were calculated based both on teacher and parent rating scales. Moreover, we found details regarding disagreements between the two raters which have not been fully addressed in previous studies. These results could be used for future research regarding neurodevelopmental disorders.

Disclosure statement

The authors have no conflicts of interest to declare.

Author Contributions

YK, FA, and MI: conception and design of the study; acquisition and analysis of data; drafting the manuscript or figures.

Figure legends

Figure 1. The Bland-Altman plots generated by parent and teacher rating scales. (a) SNAP-IV: Inattention (b) SNAP-IV: Hyperactivity-Impulsivity (c) SNAP-IV: ODD (d) SRS-2 (e) RWC: Reading (f) RWC: Writing

***: $p < .001$, **: $p < .01$, *: $p < .05$

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Table 1 Prevalence estimates of each disorder

		Parent Rating		Teacher Rating		χ^2 values
		% [95% CI]	N	% [95% CI]	N	
ADHD		6.3 [5.4-7.4]		6.5 [4.8-8.5]		0.03[ns]
subtypes	Inattention	5.0 [4.2-6.0]	2343	3.2 [2.0-4.7]	756	4.53[*]
	Hyperactivity–Impulsivity	2.8 [2.2-3.6]		5.3 [3.8-7.1]		10.59[**]
ODD		1.2 [0.8-1.8]		7.3 [5.5-9.4]		79.00[***]
ASD		1.9 [1.3-2.5]	2085	9.3 [7.2-11.8]	666	78.98[***]
SLD(DD)		3.0 [2.3-3.8]		11.2 [9.0-13.7]		79.12[***]
subtypes	Reading	1.9 [1.4-2.6]	2248	8.0 [6.1-10.2]	740	62.01[***]
	Writing	2.2 [1.6-2.9]		9.6 [7.6-11.9]		79.41[***]
DCD		31.9 [29.9-33.8]	2240	50.0 [45.5-54.5]	484	57.40[***]

***: $p < .001$, **: $p < .01$, *: $p < .05$

ADHD: attention deficit / hyperactive disorder, ODD: oppositional defiant disorder, ASD: autism spectrum disorder, SLD (DD): specific learning

disorder (or developmental dyslexia), DCD: developmental coordination disorder

Table 2 Comorbidity rates among disorders

	Parent Rating (N=1775)	Teacher Rating (N = 430)	χ^2 values
ADHD only	3.9 [3.1-5.0]	2.3 [1.1-4.2]	2.59[ns]
ASD only	0.3 [0.1-0.7]	3.0 [1.6-5.1]	29.22[***]
SLD only	1.7 [1.1-2.4]	6.7 [4.6-9.5]	33.95[***]
ADHD×ASD	1.1 [0.6-1.7]	2.1 [1.0-3.9]	2.89[ns]
ADHD×SLD	0.6 [0.3-1.1]	1.2 [0.4-2.7]	1.42[ns]
ASD×SLD	0.2 [0.1-0.6]	2.8 [1.5-4.8]	31.62[***]
ADHD×ASD×SLD	0.2 [0.1-0.6]	2.1 [1.0-3.9]	20.60[***]

***: $p < .001$, **: $p < .01$, *: $p < .05$

ADHD: attention deficit / hyperactive disorder, ASD: autism spectrum disorder, SLD: specific learning disorder

Table 3 Agreement between parent and teacher rating scales

	ADHD (Total)	ADHD (Inattention)	ADHD (Hyperactivity–Impulsivity)	ODD	ASD	SLD (Total)	SLD (Reading)	SLD (Writing)
κ	.15	.13	.18	.10	.08	.17	.25	.22
PABAK	.78	.84	.87	.89	.85	.84	.90	.87
N (suspected)	71	49	41	33	35	50	32	41
by parents	46	39	18	5	8	14	8	11
by teacher	17	6	18	26	25	30	19	24
by both	8	4	5	2	2	6	5	6
N (normal)	501	523	531	539	415	486	504	495

PABAK: a prevalence-adjusted and bias-adjusted kappa

ADHD: attention deficit / hyperactive disorder, ODD: oppositional defiant disorder, ASD: autism spectrum disorder, SLD: specific learning

disorder

Figure 1