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Original Article

Title

Risk factors for motor coordination problems in preschool-aged children

Running Head

Motor coordination problems

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Abstract

Background: Motor coordination problems (MCP) in children can sometimes be diagnosed as developmental coordination disorder (DCD). Early intervention for DCD is necessary because it often continues into adolescence, causing mental and physical complications. Few studies have investigated the prevalence of childhood MCP in the Japanese population and examined the risk factors for MCP. Therefore, we investigated the prenatal factors associated with MCP in preschool-aged children.

Methods: This study was based on a prospective cohort study, the Hokkaido Study on Environment and Children's Health. Mothers of 4,851 children who reached the age of 5 years within the study-period received questionnaires, including the Japanese version of the developmental coordination disorder questionnaire (DCDQ-J). We examined the risk factors associated with MCP using logistic regression analysis.

Results: Of 3,402 returned DCDQ-J questionnaires, 3,369 were answered completely. From the 3,369 children, we categorized having MCP by using two cut-off scores: that of the DCDQ'07 and the cut-off at the 5th percentile of a total DCDQ-J score. Comparing children with and without MCP, we found significant differences in the education level of the mothers, annual household income during pregnancy, maternal alcohol consumption and smoking during pregnancy, and sex and age of the children at the time of completing the DCDQ-J by both categorizations. Adjusted logistic regression analysis revealed that maternal

smoking during the first trimester of pregnancy and male sex were significantly associated with MCP.

Conclusions: Our results suggest that maternal smoking during pregnancy is the main factor associated with MCP in preschool-aged children.

Key words:

cohort study, Japan, maternal smoking, motor coordination problem, prechoolage children

Motor coordination problems (MCP) in children can sometimes be diagnosed as developmental coordination disorder (DCD), which is classified as a neurodevelopmental disorder in the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).1 Based on the DSM-5, the motor skills of children diagnosed with DCD are below the level expected for their age. This motor skill deficit significantly and persistently interferes with their daily activities, affecting their productivity in school, and their performance during prevocational, vocational, and leisure activities. Although the suggested prevalence of DCD is 5%-6% among children aged 5-11 years, 1 several studies have shown that the prevalence of DCD ranges from 1.8% to 19% among school-aged children.^{2,3} Although the cause of DCD has not yet been identified, some previous studies have suggested potential risk factors associated with DCD. Perinatal factors in children, such as very early preterm birth and very low birth weight, have shown to be associated with a risk for DCD,4-7 and male children are more likely to develop DCD than female children. 4,8 However, only a few studies have investigated perinatal and parental characteristics that may predict DCD.8-10

The symptoms of DCD can begin during the early developmental period. Children diagnosed with DCD experience difficulty in their daily activities, even at the preschool age. A previous study comparing children with and without probable DCD showed differences in developmental play age and frequency of engaging in play. Furthermore, children with DCD demonstrated heterogeneous patterns of performance and learning during childhood. Although improvements may be

observed in the long term, problems in coordination continue through adolescence in an estimated 50%–70% of children.^{1,13} These problems cause secondary physical complications, such as obesity and low cardiopulmonary endurance,^{14,15} as well as mental illnesses, such as depression and anxiety.^{16,17} This indicates the need for early prevention of DCD and the identification of children with DCD to ensure timely remedial intervention and prevention of subsequent complications.

Although a previous study reported that DCD is a common motor problem, ¹⁸ it has been described as a "hidden problem." Similarly, in Japan, DCD has been reported less often than other neurodevelopmental disorders in the *DSM-5*. In recent years, the necessity for interventions for children with DCD has been discussed, but these interventions have not been implemented in schools, particularly in kindergarten and nursery. Although several studies have investigated the prevalence of DCD, as previously mentioned, its prevalence and risk factors have not been thoroughly investigated in Asia, including Japan. Furthermore, although there are a few identified risk factors of motor coordination problems (MCP) that will enable the design of preventive measures, investigating the associated factors may be helpful for the prevention of MCP. This study aimed to examine the prenatal factors associated with MCP in Japanese preschool children.

Methods

Study Participants

This study was based on a prospective cohort study, namely the Hokkaido Study on Environment and Children's health: the Hokkaido cohort. Women in their early stages of pregnancy were enrolled from February 2003 to March 2012. They visited one of the 37 affiliated hospitals or clinics in the study area (Hokkaido Prefecture) for prenatal health care in the maternity unit. Hokkaido is in the northern region of Japan and has a population of approximately 5 million, which is 4.2% of the total population of Japan. A baseline questionnaire was completed at the time of enrollment (during the first trimester) to obtain parental information, such as demographic characteristics, medical and obstetric histories, and smoking or alcohol consumption during pregnancy. Perinatal data, such as the infant's birth weight and sex, were obtained from birth records maintained by an obstetrician.²⁰⁻²² This cohort consisted of 20,926 pregnant women, but only the 4,851 children born between April 2008 and November 2011 were included in this study. When they turned 5 years old, we sent followup questionnaires to their parents.

Measurement tool: the Japanese version of the developmental coordination disorder questionnaire

We used the Japanese version of the developmental coordination disorder questionnaire (DCDQ-J)²³ to evaluate DCD. Originally, the DCDQ 2007 (DCDQ'07) was a parent-reported measurement tool developed to assist in the

identification of DCD in children. The DCDQ-J was developed and adapted to the Japanese culture in accordance with international guidelines. The DCDQ-J consists of 15 items divided into 3 distinct factors. The first factor is "control during movement" and contains six items related to motor control during movement. The second factor, "fine motor and handwriting," contains four items related to fine motor movement and handwriting. The third factor consists of five items related to general coordination and is called "general coordination." Each item was evaluated by the parent for comparison between their child and other children on a scale ranging from 1 to 5 as follows: (i) "Not at all like your child"; (ii) "A bit like your child"; (iii) "Moderately like your child"; (iv) "Quite a bit like your child"; and (v) "Extremely like your child." The total score for the 15 items ranged from 15 to 75, and children with low scores were suspected to have DCD.

The cut-off score appropriate for age groups of children was established in the DCDQ'07.²⁵ A total score of 46 or less in children <8 years of age was considered as "indication of or suspect for DCD." Because the cut-off score has not yet been validated for the DCDQ-J, we applied two different cut-off scores: the cut-off score of the DCDQ'07 and the cut-off score at the 5th percentile. We applied the Leeds Consensus Statement in this study. In the Leeds Consensus Statement, although the 15th percentile was often used as the cut-off for monitoring children, a cut-off at the 5th percentile was recommended as both reasonable and part of custom and practice in both clinical and research settings.²⁶ Therefore, children with total DCDQ-J scores up to the 5th percentile were assigned to the MCP group in this

study.

Statistical analyses

The DCDQ-J scores were compared between sexes using either the chisquare test or the Mann–Whitney U test. We included the following maternal variables: maternal educational level, annual household income, alcohol consumption, smoking during the first trimester of pregnancy, and parity. The variables of the children were sex and age at the time of answering the DCDQ-J. We used logistic regression to evaluate the difference between the two groups of children, with or without MCP. Variables that were significantly associated with MCP were included in the multivariate logistic regression to estimate the odds ratio of having MCP. The IBM SPSS Statistics software package version 23.0 (IBM Japan, Tokyo, Japan) was used for statistical analysis. Statistical significance was set at two-sided P < 0.05.

Ethical considerations

This study was conducted with the written informed consent of all the participants. The protocol used in this study was approved by the Institutional Ethical Board at the Hokkaido University Center for Environmental and Health Sciences and Hokkaido University Graduate School of Medicine.

Results

From the 4,851 children whose mothers were sent follow-up questionnaires when their children were 5 years old, we received 3,402 answered questionnaires. Of which 3,369 were answered completely, and the response rate of the DCDQ-J was 69.45%. The mean age of the children was 64.1 months, ranging from 60 to 82 months. The study population comprised 1,701 (50.5%) boys and 1,668 (49.5%) girls. The DCDQ-J scores and the distribution of having an MCP categorized by the cut-off among the participants are shown in Table 1. The mean DCDQ-J score was 54.48, and the standard error of the mean was 10.54, with skewness and kurtosis of -0.476 and 0.122, respectively. There were significant differences in the DCDQ-J total score and the score of component factors, such as the scores for "fine motor and handwriting" and "general coordination" between boys and girls. Categorized by the cut-off score of DCDQ'07, 21.8% children had MCP, whereas 5.2% children had MCP using the cut-off score at the 5th percentile.

The characteristics of the participants are shown in Table 2. The differences between the children with and without MCP by each cut-off are shown. Using the cut-off score of the DCDQ'07, significant differences in socioeconomic statuses, such as the educational level of mothers and annual household income during pregnancy, were observed between the two groups of children. Maternal alcohol consumption and smoking during the first trimester of pregnancy were associated with MCP, but there was no significant association between paternal smoking during pregnancy and MCP. Regarding the

characteristics of the children, significant sex-related differences were observed and younger participants had a higher tendency of developing MCP than older participants did. Univariate analysis using the cut-off score at the 5th percentile showed the same significant differences.

Table 3 shows the odds ratio of having MCP as categorized by each cut-off. After adjusting for the age and sex of the children, a low educational level of the mothers and a low annual household income during pregnancy contributed to a higher odds ratio for presenting with MCP. Moreover, maternal alcohol consumption and smoking during the first trimester of pregnancy increased the odds ratio. After adjustment for maternal and children's factors, including the variables significantly associated with MCP, male children had a higher risk of presenting with MCP than females did. Regarding maternal factors, smoking during the first trimester of pregnancy was significantly associated with MCP in both categorizations.

Discussion

This study examined the factors associated with MCP in Japanese preschool children. We showed that male sex and maternal smoking during the first trimester of pregnancy are risk factors associated with MCP.

Because the cut-off score has not yet been validated for the DCDQ-J, we used two cut-off points. As shown in Table 1, when using the cut-off score of the DCDQ'07 (≦46) appropriate for the age group of the participants included in this

study, 736 children (21.8%) were categorized as "indication of or suspect for DCD." In contrast, using DCDQ-J scores ranging from 0 to the 5th percentile to classify the MCP group was a more stringent cut-off (≦36) than that used in the DCDQ'07. However, these two different cut-off scores did not change the results.

In this study, the prevalence of MCP was significantly higher among boys than girls. This result is similar to those reported in previous studies.^{4,5,8} A previous study on Japanese children aged 4–15 years also reported a sex-related difference in the total DCDQ-J score.²³

In this study, we observed that maternal smoking during pregnancy was associated with MCP. A previous study identified an association between maternal smoking during pregnancy and subtly reduced motor competence in 11-year-old children.⁹ Another study showed that maternal smoking is a risk factor for DCD in term-born children at the age of 7.8 Christensen et al. reported that they found no statistical significance when comparing children of smokers and non-smokers aged 6–9 years, except that in Greenland, children of smokers showed a lower DCDQ-score than children of non-smokers did at 8–9 years.¹⁰ Furthermore, other studies have also suggested an association between prenatal exposure to smoking and decreased motor development in children.^{27,28} There are some suggestions that explained the association between maternal smoking and MCP. However, there are no studies to clarify the causal relationship between maternal smoking and MCP.

Maternal smoking during pregnancy causes an increased level of

carboxyhemoglobin in the bloodstream and reduced uterine blood flow due to nicotine, which results in the fetus being deprived of oxygen and nutrients.²⁹ This, in turn, affects the development of the fetal brain and nervous system. However, this does not adequately explain the etiology of DCD, because there are many factors involved in the neurodevelopment of children, such as the genetic makeup and perinatal environment.

Both categorizations that we used have advantages and disadvantages. The cut-off score at the 5th percentile was more stringent, but it may be inappropriate because its use is recommended for individually administered, culturally appropriate, and norm-referenced tests according to the Leeds Consensus Statement; however, it is worth noting that a similar previous study has used this categorization.³⁰ Other studies have used the cut-off score of the DCDQ'07.³¹ However, using the DCDQ'07 cut-off, 736 children (21.8%) were categorized as having MCP in our study. Since the DCDQ'07 cut-off score was validated in Canadian children,²⁵ it is not clear whether it is also appropriate for Japanese children. Moreover, although no study has reported the prevalence of DCD in 5year-old children using lower cut-off scores, a previous study using the DCDQ'07 showed that 3.1% of Danish children aged 7 years had lower cut-off scores (≦ 46).³² Although the prevalence of DCD ranges from 1.8% to 19% among schoolaged children as reported by the previous studies, 6,8 similarly, there was a difference in the prevalence of "indication of or suspect for DCD" using the cutoff score of the DCDQ'07 for the same age group. Although this difference may be caused by the age, sex, and/or race of these children, it is necessary to evaluate the effect of these factors on the differences reported in other studies. Further studies are necessary to obtain more precise estimates of the prevalence of DCD in the Japanese population and to validate the cut-off score of the DCDQ-J by comparing with other standard scales for the evaluation of motor performance, such as the second edition of the Japanese version of the Movement Assessment Battery for Children, which is currently under development.³³

The main strength of this study is its prospective cohort design. This study showed the prevalence of having MCP among Japanese children of preschool age. However, there are some limitations. The prevalence of having MCP may not be generalizable across the entire Japanese population because the participants of this cohort study were pregnant women who had visited hospitals or clinics within the Hokkaido Prefecture. The results may apply to the entire population in the Hokkaido prefecture because the hospitals or clinics were evenly distributed throughout the prefecture, accounting for approximately 40% of institutes with delivery units in the prefecture.²² Although the factors associated with MCP among preschool children revealed in this study are not specific to the Hokkaido prefecture, it may be of benefit to investigate another area in Japan.

Some of the information on the medical history of the children, such as the presence of mental retardation and neurological diseases, were not included in the questionnaire because these disorders cause symptoms similar to those

observed in children with MCP. This information could have been useful to make a better estimation of the prevalence of DCD. This study did not involve direct interviews with the participants, rather the questionnaires were sent to them. The DCDQ-J included in the questionnaire was only used for screening, not a diagnosis, since the aim of this study was not to diagnose DCD but to examine the factors associated with MCP in preschool-aged children. We categorized the children with lower DCDQ-J scores as having MCP, but MCP was not defined in the same way as DCD is defined in the *DSM-5*. Nevertheless, the DCDQ-J may be useful for estimating DCD in children who exhibit motor deficits but have not been previously diagnosed with DCD.

In this study, we examined the factors associated with MCP in Japanese preschool-aged children, but we did not examine the influence of some environmental factors in daily life after delivery. In previous studies, an increased risk of DCD or probable DCD was shown to be associated with rented housing tenure and lower maternal socioeconomic status.² Moreover, some environmental factors after delivery, such as physical space inside the house, and engagement of a parent in games involving body parts,³⁴ influenced motor skill development. In addition, some previous studies have examined the association between DCD and prenatal environmental chemical exposure, such as perfluorinated chemicals³⁵ and dioxin.³⁶ We are conducting further studies to identify the effects of such environmental chemicals on DCD.

In conclusion, this study, which was based on a prospective birth cohort study,

shows that maternal smoking during pregnancy is a risk factor for MCP in preschool-aged children. The results of this study suggested that the public health approach towards maternal smoking during pregnancy may be helpful for the prevention of MCP.

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Disclosure

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Author Contribution

R.K. concepted and designed the study. A.A., C.M., S.I., M.M., K.Y., and N.T. conducted the research and collected data. R.K., A.A., C.M., S.I., M.M., K.Y., and N.T. critically revised the article. A.N. developed the DCDQ-J that we utilized to evaluate DCD. S.S. drafted the manuscript. K.Y. and T.S. discussed

the contents of this manuscript and supported the manuscript writing process.

All authors read and approved the final manuscript.

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Table 1. DCDQ-J score and distribution of having motor coordination problems (MCP) among the participants

		Total	Male	Female	
		(n = 3369)	(n = 1701)	(n = 1668)	
		Mean ± SD or N (%)	Mean ± SD or N (%)	Mean ± SD or N (%)	р
DCDQ-J	Total score	54.48 ± 10.54	52.94 ± 11.00	56.04 ± 9.80	<0.01
	CDM	21.39 ± 4.48	21.43 ± 4.66	21.34 ± 4.30	0.33
	FM/HD	15.16 ± 3.73	14.07 ± 3.86	16.26 ± 3.23	< 0.01
	GC	17.93 ± 4.16	17.44 ± 4.26	18.44 ± 3.99	<0.01
The cutoff score of the DCDQ'07	≦46	736 (21.8)	457 (26.9)	279 (16.7)	<0.01
The 5th percentile of the DCDQ-J score	≦36	176 (5.2)	131 (7.7)	45 (2.7)	<0.01

DCDQ-J: the Japanese version of the developmental coordination disorder questionnaire.

CDM: Control during movement, FM/HD: Fine motor/Handwriting, GC: General coordination

Table 2. Characteristics of the participants and difference between the children with and without motor coordinaiton problems (MCP) by each cut-off

	Total		The cutoff score of the DCDQ'07					The 5th percentile of the DCDQ-J sco				
			without MCP		with MCP			without MCP		with MCP		
	(n=3369 N	<u>)) </u>	<u>(n = 2</u> 0 N	633) %	(n = 7)	36) %	р	<u>(n = 3</u> N	193) %	(n = 1) N	76) %	р
Maternal characteristics	N	70		70		70	Р	- 11	70		/0	Р
Age at delivery (years, Mean ± SD)	31.42 ±	4.73	31.34	± 4.72	31.71	± 4.77	0.06	31.40	± 4.73	31.85	± 4.79	0.15
Pre-pregnancy BMI (kg/m²)												
<18.5	579 1	17.2	468	17.8	111	15.1	0.12	557	17.4	22	12.5	0.11
18.5≤, <25		70.7	1856	70.5	526	71.5		2253	70.6	129	73.3	
25≤	347 1	10.3	261	9.9	86	11.7		323	10.1	24	13.6	
Parity												
Primiparity		34.6 53.8	895	34.0 54.3	272 382	37.0 51.9	0.16	1098	34.4 54.1	69 86	39.2 48.9	0.18
Multiparity	1813 5	33.0	1431	54.5	302	51.9		1727	54.1	00	40.9	
Educational level												
<high graduate<="" p="" school=""> High school graduate</high>	106 1264 3	3.1 37.5	72 977	2.7 37.1	34 287	4.6 39.0	0.03	94 1191	2.9 37.3	12 73	6.8 41.5	0.02
High school graduate<		37.5 43.2	1157	43.9	299	39.0 40.6		1388	43.5	68	38.6	
College graduate		15.4	410	15.6	110	14.9		497	15.6	23	13.1	
Acohol consumption during												
pregnancy at the first trimester												
Yes	330	9.8	241	9.2	89	12.1	0.02	304	9.5	26	14.8	0.03
No	2952 8	87.6	2325	88.3	627	85.2		2808	87.9	144	81.8	
Smoking during pregnancy												
in the first trimester Yes	204	6.1	141	5.4	63	8.6	<0.01	182	5.7	22	12.5	<0.01
No		73.9	1966	74.7	525	71.3	10.0.	2381	74.6	110	62.5	10.0
Paternal characteristics												
Educational level												
<high graduate<="" school="" td=""><td>174</td><td>5.2</td><td>132</td><td>5.0</td><td>42</td><td>5.7</td><td>0.90</td><td>162</td><td>5.1</td><td>12</td><td>6.8</td><td>0.59</td></high>	174	5.2	132	5.0	42	5.7	0.90	162	5.1	12	6.8	0.59
High school graduate		37.5	989	37.6	273	37.1		1194	37.4	68	38.6	
High school graduate< College graduate		24.7 31.4	649 829	24.6 31.5	182 229	24.7 31.1		785 1009	24.6 31.6	46 49	26.1 27.8	
Smoking during pregnancy in the first trimester												
Yes	1620 4	48.1	1264	48.0	356	48.4	0.96	1541	48.3	79	44.9	0.39
No	1226	36.4	958	36.4	268	36.4		1157	36.2	69	39.2	
Family's characteristics												
Annual household income per year												
at pregnancy (million yen) <3	621 1	18.4	460	17.5	161	21.9	<0.01	573	17.9	48	27.3	0.02
3≤, <5		38.1	1002	38.1	283	38.5	\0.01	1222	38.3	63	35.8	0.02
5≤, <8	841 2	25.0	681	25.9	160	21.7		805	25.2	36	20.5	
8≤	248	7.4	203	7.7	45	6.1		237	7.4	11	6.3	
Mother's marital status												
Married		93.0	2459	93.4	675	91.7	0.06	2972	93.1	162	92.0	0.52
Not married	209	6.2	152	5.8	57	7.7		196	6.1	13	7.4	
Child's characteristics												
Sex Male	1701 5	50.5	1244	47.2	457	62.1	<0.01	1570	49.2	131	74.4	<0.01
Female		49.5	1389	52.8	279	37.9	30.01	1623	50.8	45	25.6	30.01
Contational ago (wooks)												
Gestational age (weeks) ≤36	173	5.1	128	4.9	45	6.1	0.19	159	5.0	14	8.0	0.11
37≤		94.9	2505	95.1	691	93.9		3034	95.0	162	92.0	
Birth weight (g)												
<2500	297	8.8	228	8.7	69	9.4	0.51	277	8.7	20	11.4	0.22
2500≤	3072	91.2	2405	91.3	667	90.6		2916	91.3	156	88.6	
Age at answering DCDQ-J	64.14 ±	5 57	64.36	+ 5 70	63 35	± 5.04	<0.01	64 22	± 5.61	62 56	± 4.54	<0.01
(months, Mean ± SD)	O 1. 17 I	0.01	57.50	_ 0.70	55.55	_ 0.0+	~0.01	J-7.22	_ 0.01	52.50		~O.O I

DCDQ-J: the Japanese version of the developmental coordination disorder questionnaire. Chi-square test or Mann-Whitney U test

Table 3. Adjusted odds ratios (OR) for motor coordination problems (MCP) by each cut-off

	The cutoff score of the DCDQ'07						The 5th percentile of the DCDQ-J score						
	Model	1		Model 2			Model	1		Model 2			
	OR	95% CI	р	OR	95% CI	р	OR	95% CI	р	OR	95% CI	р	
Mother's educational level													
<high graduate<="" school="" td=""><td>1.66</td><td>1.08 - 2.56</td><td>0.02</td><td>1.47</td><td>0.88 - 2.46</td><td>0.14</td><td>2.23</td><td>1.15 - 4.30</td><td>0.02</td><td>2.02</td><td>0.93 - 4.38</td><td>0.07</td></high>	1.66	1.08 - 2.56	0.02	1.47	0.88 - 2.46	0.14	2.23	1.15 - 4.30	0.02	2.02	0.93 - 4.38	0.07	
High school graduate	Refere	ence		Refere	Reference		Reference			Reference			
High school graduate<	0.88	0.74 - 1.06	0.19	0.91	0.72 - 1.14	0.41	0.81	0.57 - 1.14	0.22	0.87	0.56 - 1.35	0.54	
College graduate	0.90	0.70 - 1.16	0.41	1.08	0.80 - 1.47	0.61	0.73	0.45 - 1.19	0.21	0.94	0.51 - 1.74	0.85	
Mother's alcohol consumption													
during pregnancy at the first trimester		4.00 4.00	0.04	4.00		0.44		4.40	0.04				
Yes	1.41	1.09 - 1.83	0.01	1.29	0.95 - 1.77	0.11	1.74	1.12 - 2.71	0.01	1.75	1.03 - 2.95	0.04	
No	Refere	ence		Refere	nce		Refere	ence		Reference			
Mother's smoking during in the first trimester													
Yes	1.63	1.19 - 2.24	< 0.01	1.48	1.05 - 2.10	0.03	2.52	1.55 - 4.11	< 0.01	2.01	1.16 - 3.48	0.01	
No	Refere	ence		Reference			Reference			Reference			
Annual household income per year													
at pregnancy (million yen)													
<3	1.24	0.99 - 1.55	0.06	1.07	0.83 - 1.39	0.59	1.62	1.09 - 2.39	0.02	1.29	0.81 - 2.05	0.28	
3≤, <5	Refere	ence		Refere	nce		Reference			Reference			
5≤, <8	0.84	0.68 - 1.05	0.12	0.78	0.60 - 1.00	0.05	0.88	0.58 - 1.35	0.57	0.77	0.46 - 2.05	0.31	
8≤	0.80	0.56 - 1.13	0.21	0.77	0.52 - 1.15	0.21	0.93	0.48 - 1.80	0.82	0.75	0.33 - 1.28	0.50	
Sex													
Male	1.83	1.54 - 2.16	< 0.01	1.90	1.55 - 2.32	< 0.01	3.00	2.12 - 4.24	< 0.01	2.61	1.71 - 3.96	<0.01	
Female	Refere	ence		Refere	nce		Reference			Reference			

DCDQ-J: the Japanese version of the developmental coordination disorder questionnaire.

Model 1, adjusted for child's age and sex. Model 2, adjusted for the variables having a significant association with MCP in model 1 plus.