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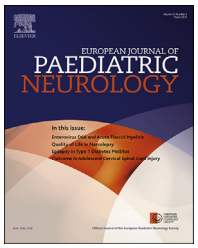

Original article

Risk of Developmental Coordination Disorder in Italian very preterm children at school age compared to general population controls

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ABSTRACT

Background: Developmental Coordination Disorder (DCD) is a neurodevelopmental disorder that involves difficulties in goal-directed motor coordination, with ineffective control of fine and gross motor movements in the absence of sensory impairment or neurological condition. DCD is frequently reported in children born very preterm (VP) who survive without CP.

Aims: To measure the risk of DCD at school age in a large area-based cohort of VP children and general population controls, adjusting for gender, birth weight by gestational age and age at assessment.

Methods: VP children (N = 608) were part of a prospective cohort study in Italy. Controls (N = 370) were participants in the DCDQ-Italian validation study in the same age range. The Italian version of Developmental Coordination Disorder Questionnaire (DCDQ-Italian) was used to measure the performances in motor coordination during ordinary activities from the parental point of view. Multivariable regression analysis was used to obtain adjusted risk ratios of screening positive for DCD.

Results: VP children had scores significantly lower than peers, and about 30% of them appeared at risk of DCD using the 15th percentile cut-off of the Italian validation study.

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Birth-weight <10th percentile for gestational age and male gender were significant predictors. A slight trend effect was present, with extremely preterm children (<28 weeks gestation) showing the highest risk.

Conclusions: Our study confirmed the higher DCD risk in VP children, particularly when males and SGA.

1. Introduction

Survival of very preterm (VP, i.e. < 32 weeks of gestation) infants has increased over the past three decades in high-income countries due to improvements in obstetrical and neonatal care[1,2] but the rates of adverse neurodevelopmental outcomes among survivors remain high.[3] While major neurological disorders such as cerebral palsy (CP) appear decreasing both in frequency[4] and severity,[5] minor motor dysfunctions (abnormalities in posture, muscle tone, strength, coordination or balance), are becoming more relevant.[6,7] Developmental Coordination Disorder (DCD) is a neurodevelopmental disorder characterised by a level of performance in activities requiring motor coordination substantially below that expected for age and cognitive abilities.[8] It includes difficulties with balance, gross and fine motor control and visual-motor integration that manifest as lack of agility, clumsiness in running, jumping and climbing, as well as in actions requiring competence with objects such as ball games. Writing, drawing, and small objects manipulation may be affected, together with self-care abilities including autonomous feeding and dressing. Over time, physical inactivity may lead to overweight or obesity.[9] The consequences of DCD on daily life, social relations and academic achievement are increased in case of comorbidities such as attention deficit and hyperactivity disorder (ADHD), language or learning specific disorder,[10–12] and may be long-lasting.[13] Several studies have reported persistent psychosocial problems and anxiety in adolescence[14,15] and increased incidence of psychiatric disorders in later life.[16] Learning new skills, such as driving or playing sports, may remain problematic into adulthood.[17,18]

About 5–6% of school-aged children in the general population are affected by DCD, but rates as low as 1.8% and as high as 25% have been reported, depending also on the diagnostic instrument and cut-off level adopted.[19,20] Rates have been reported to be higher in VP or very low birth weight (VLBW, birthweight <1500 gr) children,[21–23] but studies carried out in Italy are lacking.

Many studies found increased prevalence of DCD in males[23–25] while others did not.[26,27] The reason for such inconsistency is unknown. Males may be more likely to be diagnosed with DCD because expectations regarding motor performance are higher in boys than in girls, depending on national and social context.[28,29] According to Zwicker[30] the inconsistency might be due to the different sample composition of the various studies, and specifically to the proportion of VP children included.

We used the Italian version of the Developmental Coordination Disorder Questionnaire (DCDQ)[31,32] to measure the risk of DCD in a prospective area-based cohort of VP children in three Italian regions and compare the results with those from the general population sample of the Italian validation study.[27]

2. Materials and methods

2.1. Study population

2.1.1. Very preterm children

The ACTION (Accesso alle Cure e Terapie Intensive Ostetrico-Neonatali - Access to Intensive Obstetrical and Neonatal Care) follow-up project is an area-based prospective cohort study including all infants born at 22–31 completed weeks of gestational age (GA) during 2003–2005 in six Italian regions.[33] In three of these regions (Friuli-Venezia-Giulia, FVG-, Toscana and Lazio) children were followed up to school age (8–11 years) for cognitive and neuropsychological evaluation (N = 804, response rate 73.4%).

2.1.2. General population controls

Controls were a sub-group (N = 373) of participants in the DCDQ-Italian validation study[27], selected in the same age range (8–11 years) of the VP children.

The validation sample was recruited at the primary and lower secondary schools in two Italian cities, Roma in Lazio and Pavia in Lombardy. Children diagnosed with developmental delay, intellectual deficit, neurological disorder (i.e. cerebral palsy, muscular dystrophy) or autism spectrum disorder were excluded.

2.2. Ethics

In accordance with the Declaration of Helsinki, written parental informed consent and approval by the Ethics Committees of the relevant institutions were obtained both for the ACTION follow-up and for the validation study.

2.3. Measures

2.3.1. The Italian version of Developmental Coordination Disorder Questionnaire (DCDQ-Italian)

The Developmental Coordination Disorder Questionnaire[31] is a 15-item parent report tool developed to assist in the identification of specific motor challenges that a child may

experience in daily life. The original instrument has been translated and validate in several countries including Italy. The Italian version yields high internal consistency (Cronbach coefficient alpha 0.89) and stability.[32]

The questionnaire explores motor function in 3 separate areas. The area "Control during Movement" includes items related to motor control while the child or an object (e.g. a ball) are in movement. The second area concerns 'Fine Motor/ Handwriting' and the third 'General Coordination'. Parents are asked to provide their responses according to a five-point Likert scale (from 1, "not at all similar to your child", to 5 "completely similar to your child") using as comparison other children of the same age. The individual item scores are added to provide sub-scores and a total score (range 15–75), with higher values indicating no suspect of DCD. Based on the total score, each child can be classified as falling below the 5th, 15th or 25th percentile cut-off for being "indicated, or suspected, DCD" versus "probably not DCD," according to three age groups (for 5–7, 8–9 and 10–15 completed years).[27]

2.3.2. *Other measures and data collection*

For VP children, perinatal and neonatal data were abstracted from clinical records using a standardized data collection form with agreed definitions. GA was recorded as the best obstetrical estimate using information on the last menstrual period and ultrasound measures.

Follow-up at school age assessed the presence and severity of cerebral palsy, useful vision and hearing, and use of aids. Diagnoses of neurodevelopmental disorders (including Attention Deficit/Hyperactivity Disorder -ADHD-, specific learning disorder, language, and autism-spectrum disorders) were recorded on the basis of parental report and, when available, of clinical documentation. We used the Kaufman Assessment Battery for Children, second edition (KABC-II)[34,35] to measure cognitive development (Mental Processing Index, MPI). Parental questionnaires, including the DCDQ-Italian, were used to investigate other aspects of child development.

For the validation study, the parents of potential participants were informed about the aims and methods by researchers and teachers through meetings at school and/or individual contacts. Upon agreement to participate, they were asked to complete the DCDQ-Italian together with a questionnaire on child development, including questions on diagnosed specific neurodevelopmental disorders (such as language and learning disorders, ADHD).[27]

2.4. *Data management and analysis*

For the purpose of this study, we excluded from the VP sample cases of cerebral palsy or other movement limiting conditions such as asymmetrical lower limbs and feet malformations (N = 58 and 6 respectively), severe vision or hearing problems (N = 18 and 7 respectively) and cognitive disability (N = 37 with cognitive score <70 and N = 7 with diagnosed autism spectrum disorder). In 63 cases the DCDQ-Italian was missing or incomplete. Thus, the final sample included N = 608 VP children. In the general population sample, we excluded 3 VP children who, being born outside the ACTION regions, did not belong to the original VP cohort recruited at birth.

Using the joint VP and controls database, we computed means, standard deviations (SD) and ranges of the DCDQ total and subscales scores by levels of covariates, and tested the associations using one-way analysis-of-variance. We then applied the age-specific cut-offs derived from the DCD-Q Italian validation study[27] for the 5th, 15th and 25th percentiles respectively to compute the risks of DCD in the VP children and controls and to check for optimal cut-off points. Univariable differences were tested using the Chi-squared test.

We carried out multivariable modified Poisson regression analysis[36] to obtain adjusted Risk Ratios and 95% CI intervals of scoring DCDQ-positive at the 15th percentile for VP children compared to general population controls (GA 32–42). Models were adjusted for infant sex, age at assessment (8–9 vs 10–11 years) and SGA status (<10th percentile). Birth weight percentiles were computed using the intrauterine references developed according to the method proposed by Gardosi and based on Hadlock's fetal growth equation, and adapted to the Italian population using the national sex-specific mean and standard deviation of birth weight at 40 weeks gestation.[37] We did not adjust for ADHD, specific learning and language disorders as these are considered comorbidities of DCD rather than risk factors.

Interactions between gestational age (coded as 22–27, 28–31 for VP children and 32–42 for controls) and covariates were tested at a $p = 0.10$ level. Additionally, to test the hypothesis that the effect of gender on DCDQ scores varies by GA, we included in the multivariable models the interaction term between GA and infant sex, and performed post-hoc comparisons.

Data analysis was performed with STATA 14.0 SE (Stata Corporation, College Station, Texas).

3. Results

Table 1 shows the demographic characteristics of the study population and the reported presence of known comorbidities of DCD. As expected, VP children were significantly more likely than controls to be SGA (27.7% versus 7.9%) and to report comorbidities such as ADHD (4.8%), specific learning (7.3%) and language (7.0%) disorders. The mean age at assessment was 9.2 years for VP and 9.4 years for normative sample children ($p < 0.001$).

Table 2 shows the distribution of DCDQ-Italian scores by demographic characteristics and comorbidities. VP children had scores significantly lower than peers, indicating increased risk of DCD. SGA, presence of comorbidities and younger age at assessment (8–9 years) were also associated with lower total and sub-scale DCDQ scores. Females had significantly higher scores than males for the DCDQ total, the 'Fine/Motor Handwriting' and 'General coordination' sub-scales, while no difference was found for "Control during Movement".

VP children were significantly more likely than peers to score below the cut-offs for total and sub-scale domains (Table 3), independently from the percentile cut-off used. Based on the 15th percentile, as suggested by the European Academy of Childhood Disability,[38] 30.4% of the VP children compared to 16.2% of controls were classified as at risk for

Table 1 – Demographic characteristics and reported comorbidities for DCD in the study populations.

	Very Preterm children (N = 608)		General population controls (N = 362)	
	n	%	n	%
Gestational age, wks				
22–27	126	20.7	0	0.0
28–31	482	79.3	0	0.0
32–42	0	0.0	362	100.0
p < 0.001				
Birthweight by GA				
<10th percentile	168	27.7	22	8.0
≥10th percentile	440	72.4	253	92.0
p < 0.001				
Infant sex				
Male	336	55.3	178	49.2
Female	272	44.7	184	50.8
p = 0.066				
Age at DCDQ assessment, y				
8–9	402	66.1	171	47.2
10–11	206	33.9	191	52.8
p < 0.001				
Age, Mean (SD)	9.2 (0.71)		9.4 (1.10)	
One-way Anova: p < 0.001				
Attention Deficit/Hyperactivity Disorder (ADHD)				
No	573	95.2	201	99.5
Yes	29	4.8	1	0.5
Not recorded	–	–	160	–
p = 0.005				
Specific learning disorder				
No	556	92.7	334	95.2
Yes	44	7.3	17	4.8
p = 0.130				
Language disorder				
No	226	93.0	346	97.2
Yes	17	7.0	10	2.8
Not recorded (in 2012–13)	307	–	–	–
p = 0.015				
Region				
FVG	95	15.6	0	0.0
Lazio	314	51.6	0	0.0
Toscana	199	32.7	0	0.0
Roma	0	0.0	202	55.8
Pavia	0	0.0	160	44.2

DCD. The corresponding proportions were 14.0 and 6.2% at the 5th percentile, and as high as 44.7 and 28.1% at the 25th percentile. The results were similar for all the sub-scales.

Table 4 shows the results of multivariable analyses using the 15th percentile cut-off. The adjusted risk ratios of scoring 'DCDQ positive' ranged from 1.60 to 2.16 for VP compared to control children. We found a slight trend effect for gestational age, that was stronger for the 'General coordination" sub-scale. Age at assessment was not significantly related to outcomes apart from "Control during Movement," that appeared to be better in the older children. SGA children and males had a higher risk compared to controls, but the differences were not significant for the "Control during movement" sub-scale.

When stratified by GA, the adjusted RRs of scoring DCDQ positive for males versus females appeared significantly >1 in VP children for all scores but "Control during Movement", and a dose–response effect was noted with higher RRs at 22–27 than at 28–31 weeks (Fig. 1). No significant differences between males and females were detected among control children. However, the stratified CIs were very large for the extremely preterm children (<28 weeks GA) due to the small size of this group, and overall the interaction between sex and GA was not significant at p < 0.10 level precluding firm conclusions about sex differences in DCDQ scoring between VP and term born children.

4. Discussion

We found that in Italy the risk for school-age VP children of scoring positive at the DCD questionnaire was over two-fold higher than in general population controls. Additional risk factors were SGA status and male gender. Motor development appeared significantly better in older children as regards the "Control during Movement" sub-scale.

Similar results were reported by other studies based on parental questionnaires and on direct assessment of children. Zhu et al.[39] showed that every one-week decrease in GA before 40 weeks was associated with a 19% increased risk of screening positive at the DCDQ. A large meta-analysis on motor development in VP children, based on three different motor tests, reported an average difference of −0.57 to −0.88 SD compare to peers, and these results persisted throughout childhood.[6] More recently, a review by Edwards et al.[21] confirmed the increased risk for DCD for children born VP and/or VLBW, with a >8-fold increased likelihood of scoring below the 15th percentile at the Movement Assessment Battery for Children (MABC) compared to term-born peers.

The association with SGA is in agreement with the numerous studies pointing to intrauterine growth retardation as predictor of several adverse outcomes, including mortality and early morbidity, cognitive deficits and adverse neurological development, lending support to the Barker hypothesis on long-term consequences of intrauterine programming.[22]

The association between DCD and gender is still an open issue.[29] The Italian validation study did not find any gender difference,[27] and the same was true for other studies carried out in the general population.[40,41] The findings of the present study appear consistent with the hypothesis suggested by Zwicker,[23] who linked the male motor disadvantage found by some studies to the higher prevalence of DCD in VP infants, also in the light of the documented increased adverse neurological outcomes in VP males compared to females[42,43] After stratification for GA, we found that VP males had increased risk of DCD in all areas except "Control during Movement", and a dose–response effect was evident with highest adjusted RRs in the most preterm group. However, these results cannot be considered conclusive as overall the interaction between GA and gender was not statistically significant, and the stratified confidence intervals were wide. Larger studies with direct assessment of children are needed to clarify the issue.

We found that older children were less likely to score positive for "Control during movement" compared to their younger peers. If confirmed by longitudinal studies with direct movement assessment, this finding would provide support to

Table 2 – DCDQ scores by participants' demographic characteristics and reported comorbidities.

	DCDQ Total score (15–75)				Control during Movement (6–30)				Fine Motor/Handwriting (4–20)				General Coordination (5–25)			
	Mean	Sd	Min	Max	Mean	Sd	Min	Max	Mean	Sd	Min	Max	Mean	Sd	Min	Max
Gestational age, wks																
22–27 (n = 126)	58.8	11.8	17	75	23.5	5.2	7	30	15.9	3.5	4	20	19.4	4.6	6	25
28–31 (n = 482)	59.3	10.3	29	75	23.5	4.7	9	30	16.1	3.3	6	20	19.7	3.9	6	25
32–42 (n = 362)	63.4	8.8	30	75	25.2	3.9	7	30	17.4	2.8	9	20	20.8	3.6	8	25
	$p < 0.001$				$p < 0.001$				$p < 0.001$				$p < 0.001$			
Birthweight by GA																
<10th percentile (n = 190)	57.3	10.6	29	75	22.9	4.7	11	30	15.6	3.5	6	20	18.9	4.3	6	25
≥10th percentile (n = 693)	61.5	9.9	17	75	24.4	4.5	7	30	16.9	3.1	4	20	20.3	3.8	6	25
	$p < 0.001$				$p < 0.001$				$p < 0.001$				$p < 0.001$			
Infant sex																
Male (n = 514)	59.8	10.6	29	75	24.0	4.8	7	30	16.1	3.3	7	20	19.7	4.1	6	25
Female (n = 456)	61.8	9.5	17	75	24.2	4.4	7	30	17.1	3.0	4	20	20.5	3.7	6	25
	$p = 0.002$				$p = 0.501$				$p < 0.001$				$p = 0.002$			
Age at DCDQ assessment, y																
8–9 (n = 573)	59.5	10.5	17	75	23.6	4.7	7	30	16.3	3.3	4	20	19.6	4.1	6	25
10–11 (n = 397)	62.6	9.4	31	75	25.0	4.3	7	30	17.0	3.0	8	20	20.6	3.5	9	25
	$p < 0.001$				$p < 0.001$				$p = 0.001$				$p < 0.001$			
ADHD																
No (n = 774)	60.6	10.1	17	75	24.1	4.6	7	30	16.6	3.2	4	20	20.0	3.9	6	25
Yes (n = 30)	50.3	10.9	29	71	21.2	5.1	12	30	12.9	3.4	6	20	16.2	4.2	6	25
	$p < 0.001$				$p < 0.001$				$p < 0.001$				$p < 0.001$			
Specific learning disorder																
No (n = 890)	61.5	9.8	17	75	24.4	4.5	7	30	16.9	3.1	4	20	20.3	3.8	6	25
Yes (n = 61)	51.5	11.4	29	72	21.5	5.3	9	30	13.0	3.4	6	20	17.0	4.2	6	25
	$p < 0.001$				$p < 0.001$				$p < 0.001$				$p < 0.001$			
Language disorder																
No (n = 572)	62.2	9.3	30	75	24.7	4.3	7	30	17.0	3.0	8	20	20.5	3.6	8	25
Yes (n = 27)	55.1	12.1	30	74	22.2	5.6	9	30	14.7	3.5	8	20	18.3	4.5	10	25
	$p < 0.001$				$p = 0.004$				$p < 0.001$				$p = 0.002$			

Table 3 – Proportion of DCDQ scores below the 5th, 15th and 25th percentile cut-offs.

	<5th percentile[a]			<15th percentile[a]			<25th percentile[a]		
	N	% Pos	(95% CI)	N	% Pos	(95% CI)	N	% Pos	(95% CI)
DCDQ Total Score (15–75)									
Gestational age, wks									
22–27 (n = 126)	20	15.9	(10.0,23.4)	38	30.2	(22.3,39.0)	54	42.9	(34.1,52.0)
28–31 (n = 482)	65	13.5	(10.6,17.0)	147	30.5	(26.6,35.0)	218	45.2	(41.0,50.1)
32–42 (n = 362)	23	6.4	(4.1,9.4)	59	16.3	(12.6,20.5)	101	27.9	(23.3,32.8)
	p = 0.001			p < 0.001			p < 0.001		
Control during Movement (6–30)									
Gestational age, wks									
22–27 (n = 126)	26	20.6	(13.9,28.8)	41	32.5	(24.5,41.5)	58	46.0	(37.1,55.1)
28–31 (n = 482)	91	18.9	(15.6,22.8)	155	32.2	(28.2,36.8)	217	45.0	(40.8,49.9)
32–42 (n = 362)	27	7.5	(5.0,10.7)	63	17.4	(13.6,21.7)	111	30.7	(26.0,35.7)
	p < 0.001			p < 0.001			p < 0.001		
Fine Motor/Handwriting (4–20)									
Gestational age, wks									
22–27 (n = 126)	23	18.3	(11.9,26.1)	41	32.5	(24.5,41.5)	51	40.5	(31.8,49.6)
28–31 (n = 482)	70	14.5	(11.6,18.1)	158	32.8	(28.8,37.4)	202	41.9	(37.7,46.7)
32–42 (n = 362)	24	6.6	(4.3,9.7)	78	21.6	(17.4,26.1)	110	30.4	(25.7,35.4)
	p < 0.001			p = 0.001			p = 0.002		
General Coordination (5–25)									
Gestational age, wks									
22–27 (n = 126)	22	17.5	(11.3,25.2)	42	33.3	(25.2,42.3)	53	42.1	(33.3,51.2)
28–31 (n = 482)	59	12.2	(9.5,15.6)	125	25.9	(22.2,30.3)	192	39.8	(35.7,44.6)
32–42 (n = 362)	27	7.5	(5.0,10.7)	63	17.4	(13.6,21.7)	100	27.6	(23.1,32.5)
	p = 0.005			p < 0.001			p < 0.001		

[a] Caravale et al., age specific cutoffs for the 5th, 15th and 25th percentile.

Table 4 – Adjusted risk ratios for DCDQ-positive (<15th percentile cut-offs)[a].

	DCDQ Total Score			Control during Movement			Fine Motor/ Handwriting			General Coordination		
	aRR[a]	(95%CI)	p-value	aRR[a]	(95%CI)	p-value	aRR[a]	(95%CI)	p-value	aRR	(95%CI)	p-value
Gestational age, wks												
22–27	1.92	(1.31,2.83)	0.001	1.79	(1.24,2.57)	0.002	1.58	(1.12,2.23)	0.010	2.12	(1.46,3.07)	0.000
28–31	1.86	(1.35,2.56)	<0.001	1.73	(1.28,2.33)	<0.001	1.58	(1.19,2.08)	0.001	1.57	(1.13,2.18)	0.007
32–42 (Controls)	Ref			Ref			Ref			Ref		
Birthweight by GA												
<10th percentile	1.41	(1.11,1.78)	0.005	1.24	(0.98,1.57)	0.068	1.29	(1.03,1.62)	0.024	1.39	(1.08,1.80)	0.010
≥10th percentile	Ref			Ref			Ref			Ref		
Infant sex												
Male	1.37	(1.10,1.71)	0.005	1.09	(0.88,1.34)	0.432	1.73	(1.40,2.15)	<0.001	1.41	(1.12,1.79)	0.003
Female	Ref			Ref			Ref			Ref		
Age at DCDQ assessment, y												
8–9	Ref			Ref			Ref			Ref		
10–11	1.01	(0.81,1.27)	0.904	0.72	(0.57,0.91)	0.005	1.07	(0.87,1.31)	0.514	1.14	(0.90,1.43)	0.280

[a] The aRR are adjusted for all variables in the table. Ref. Indicates the reference category (aRR = 1). aRRs>1 indicate increased risk and aRR<1 decreased risk compared to the reference category. Adjusted risk ratios (aRR) and 95% confidence intervals (CI) were obtained from multivariable modified Poisson regression analysis.

strategies, such as task-oriented interventions, aimed at improving motor performance.

The strengths of this study are the large size and the area-based recruitment strategy of the VP cohort, as well as the availability of the participants in the Italian validation study for comparison. There are also limitations. Information on pre- and perinatal variables such as parental socio-demographic data and pregnancy complications was limited in the general population sample. The assessment of comorbidities was purely anamnestic, and data were missing for a large proportion of children in the validation and VP samples. We did not have data on rehabilitation history. Finally, no direct assessment for DCD was available for the VP children.

Nevertheless, our study confirmed the high prevalence of children screened positive at DCDQ in a large sample of Italian school age children, particularly when born SGA or at very preterm GA. Health care and educational professionals and, possibly, parents should be aware of these findings, as referral for direct assessment and early intervention may help to prevent later emotional and educational complications.[15] The

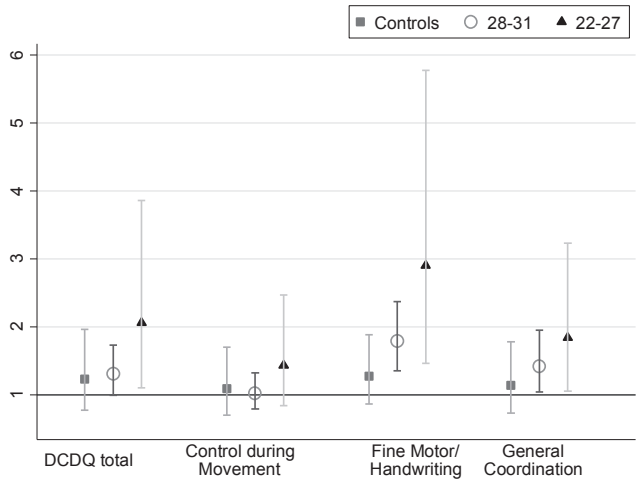

Fig. 1 – Adjusted risk ratios for scoring DCD-positive (males vs females). Note: Estimates obtained from multivariable modified Poisson Regression analysis with the interaction between GA (22–27, 28–31, term controls) and infant sex (male vs female), adjusted for age at assessment and SGA status.

DCDQ, translated and validated in several languages, may be a useful screening tool both for clinical and research purposes starting from 5 years of age, and has the added value of validating the concerns of the parents. DCDQ-positive children, and particularly those belonging to higher risk groups such as very preterm, SGA or diagnosed with other developmental disorders, should be promptly referred for early direct motor assessment and intervention.

5. Conflict of interest

The Authors have no conflict of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejpn.2019.01.002.

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