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**Association of Difficulties in Motor Skills with Longitudinal Changes in Social Skills in Children
with Autism Spectrum Disorder: Findings from the ELENA French Cohort**

Hugo Peyre^{a,b*}, Marianne Peries^{a,b}, Emmanuel Madieu^{a,b}, Aurore David^{a,b}, Marie-Christine Picot^{a,b,c},
Andrew Pickles^d, Amaria Baghdadli^{a,b,e}

^a Centre de Ressource Autisme Languedoc-Roussillon et Centre d'Excellence sur l'Autisme et les
Troubles du Neurodéveloppement (CeAND), CHU Montpellier, France.

^b Université Paris-Saclay, UVSQ, Inserm, CESP, Team DevPsy, 94807 Villejuif, France

^c Clinical Research and Epidemiology Unit Department of Medical Information, University Hospital,
CHU Montpellier, France.

^d Department of Biostatistics and Health Informatics, King's College London, UK.

^e Faculté de Médecine, Université de Montpellier, France.

*Corresponding author: Hugo Peyre, Autism Reference Centre of Languedoc-Roussillon CRA-LR,
CHU de Montpellier - SMPEA Peyre Plantade, 291 avenue du Doyen Giraud, 34295 Montpellier,
04.67.33.99.68, email: rech-clinique-autisme@chu-montpellier.fr

ORCID ID:

Hugo Peyre: 0000-0001-8757-0783

Marianne Peries: 0000-0002-6791-4419

Emmanuel Madieu: 0000-0002-8402-6149

Marie-Christine Picot: 0000-0003-4204-7299

Andrew Pickles: 0000-0003-1283-0346

Amaria Baghdadli: 0000-0002-5679-7544

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Abstract

Rational: Developmental Coordination Disorder is a frequently co-occurring condition with Autism Spectrum Disorder (ASD). Several cross-sectional studies have reported that children with difficulties in motor skills have higher severity of ASD symptoms. This study aims to examine the association of difficulties in motor skills with longitudinal changes in social skills in children with ASD. **Methods:** Participants were drawn from the ELENA cohort, a French longitudinal cohort of children with ASD. Motor skills were assessed using the Movement Assessment Battery for Children at baseline, while social skills were measured using the Autism Diagnostic Observation Schedule (ADOS-2) and the Vineland Adaptive Behavior Scales (VABS-II) at both the baseline and a follow-up assessment conducted 3 years later. A composite score of social skills was created at baseline and at both time points. Linear regression models were performed to assess the association between difficulties in motor skills and changes in social skills, considering potential confounders such as IQ, age, and gender. **Results:** The sample included 162 children with ASD. Children with difficulties in global motor skills (N=114) showed less favorable trajectories in social skills compared to those without motor difficulties. The results were consistent when examining the ADOS-2 and the VABS-II separately. **Discussion:** This study provides evidence for the negative impact of difficulties in motor skills on the longitudinal development of social skills in children with ASD. **Conclusion:** Interventions targeting motor difficulties may have broader benefits, extending beyond motor function to improve socialization.

Keywords: Autism, motor skills, longitudinal, physical activity

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Statements and Declarations

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Conflict of Interest: The authors declare that they have no conflict of interest.

Data Availability: The datasets used and analysed during the current study are available from the corresponding author upon reasonable request.

Authors' contributions: Amaria Baghdadli is the principal investigator of ELENA cohort. Hugo Peyre, Marianne Peries, Emmanuel Madieu, Marie-Christine Picot & Amaria Baghdadli contributed to the study conception and design. Marianne Peries & Hugo Peyre performed analysis. The first draft of the manuscript was written by Hugo Peyre and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethical Approval: The ELENA cohort study was performed in line with the principles of the Declaration of Helsinki. This study was approved by the Ethics Committee on the Research of Human Subjects at Marseille Mediterranean and the National Commission for Computing and Liberties (CNIL. number DR-2015-393).

Consent to participate: Signed informed consent is obtained from all participating families included in the ELENA cohort.

Clinical Trial Registration: NCT02625116

INTRODUCTION

Autism spectrum disorder (ASD) is a lifelong developmental condition defined by deficits in social skills, communication, and repetitive or restricted behaviors or interests [1]. The most recent prevalence study report that 1 in 36 (2.8%) of 8-year-old children are diagnosed with ASD in the US. A continuous increases in the prevalence of ASD has been reported in several countries [2–5]. ASD represents a heterogeneous entity at the phenotypic and etiological levels and pose a significant challenge for clinicians to determine the most appropriate treatment for each individual. The trajectories of symptom severity in ASD are also heterogeneous and the early clinical characteristics associated with these trajectories are not fully understood.

Although difficulties in motor skills are not a part of the core ASD diagnostic criteria, they are among the most common comorbid condition reported by families and medical care providers [6]. This motor incoordination can affect gross motor skills (whole-body movements like running and jumping) and/or fine motor skills (movements of the hands, like using pencils, scissors and doing up buttons). It may be part of a diagnosis of Developmental Coordination Disorder (DCD) that is usually confirmed from the age of 5 years [1]. Findings from the large Simons Foundation Powering Autism Research for Knowledge (SPARK) US study, suggest difficulties in motor skills assessed using parental questionnaires (the DCD Questionnaire) were found in about 85% of children with ASD aged 5 to 15 years [6, 7]. However, only 14% of these children received a formal diagnosis of DCD [7] and 32% received specific interventions focused on improving motor skills [6]. These results point to the lack of identification and specific interventions of this neurodevelopmental condition so frequently associated with ASD. Studies using objective measures (such as the Movement Assessment Battery for Children - M-ABC) have also reported difficulties in motor coordination in up to 80% of children with ASD [8, 9].

Several cross-sectional studies have reported that children with difficulties in motor skills have higher severity of ASD symptoms, reinforcing the evidence that these symptoms dimensions (motor skills and core ASD symptoms) are closely related. This association has been reported in studies conducted

on toddlers (N = 159, including 110 children with ASD [10]) as well as in a small sample of 6- to 15-year-old children with ASD (N = 35) even after adjusting for IQ [11]. ASD symptoms were measured in these two studies using the well-established Autism Diagnostic Observation Schedule Calibrated Severity Score (ADOS CSS [12]), the motor skills were assessed by the Mullen Scales of Early Learning [13] in the study conducted on toddlers and the Test of Gross Motor Development-2 [14] in the study conducted on 6- to 15-year-old children. These results raised the question of whether difficulties in motor skills could have a negative impact on the course of the core symptoms of ASD (MacDonald et al., 2014). In a sample of 101 children aged 10- to 14-year-old children with ASD, Green et al found a cross-sectional association of difficulties in motor skills (assessed using the Movement Assessment Battery for Children - MABC [15]) with adaptive behaviors (measured with the Vineland Adaptive Behavior Scale – VABS [16]) that wasn't maintained after adjustment for IQ [8]. This result challenges the view that motor skills make an independent contribution to the adaptive behaviors of children with ASD, suggesting a discrepancy between the results of studies conducted using direct clinical observation (ADOS) and those using indirect and ecological observation using parent interviews (VABS). Additionally cross-sectional studies are not optimal for precisely examining the complex relationships among multiple clinical dimensions. In contrast, longitudinal studies are better suited for addressing such questions, as they allow for the exploration of changes and associations over time. Only one study conducted on 13 young children with ASD has examined this association longitudinally, and found that better motor skills at age 2 was associated with better outcomes of ASD symptoms at age 4 [17] requiring further studies conducted on larger sample. To the best of our knowledge, no study conducted on children diagnosed with ASD has comprehensively investigated the association of the distinct types of difficulties in motor skills (i.e., gross motor skills, fine motor skills, or both) with outcomes of ASD symptoms.

There are complex interrelationships between social development and other areas such as motor development [18]. The main hypothesis put forward to explain the association between motor and social skills being the activity difficulties hypothesis that states that children with difficulties in motor skills may withdraw from physical activities that require a certain level of motor-skill proficiency [19]. As a consequence, their opportunities to engage in social and communication-based interactions may

be reduced, thus limiting their opportunities to practice and improve their social skills [19]. In support of this hypothesis, two pilot studies have reported benefits for social skills following interventions focused on improving motor skills [19, 20]. If this association is confirmed in longitudinal studies, it would provide further evidence for the need for motor skill-focused interventions in children and adolescents with both ASD and difficulties in motor skills, to improve their motor and social skills. However, it cannot be ruled out that difficulties in motor skills are not associated with changes in social skills, or that this association is mediated by IQ (as in the cross-sectional study by Green et al [8]).

Consequently, the present study aims to examine the association between difficulties in motor skills and longitudinal changes in social skills between the beginning and end of our prospective follow-up in the ELENA cohort, a French longitudinal cohort of children with ASD. Social skills are observed using both direct measures (ADOS-2 CSS - social domain) and indirect measures in an ecological situation (VABS-II - socialization domain). In view of the conflicting results of published cross-sectional studies using ADOS-2 CSS and VABS scores, this association will also be tested separately for these two measures. In addition, this association will be examined as a function of the type of difficulties in motor skills (gross motor skills only, fine motor skills only, or both), which has been little studied to date.

MATERIALS AND METHODS

Participants

The ELENA cohort

Participants in our sample of children with ASD were recruited from the ELENA cohort (Longitudinal Study of Children with Autism), an ongoing prospective and multiregional cohort of children with ASD [21]. In total, 876 children aged 2 to 16 years old were included in the ELENA cohort between 2013 and 2019. At inclusion, these children were assessed on their motor, social and intellectual skills,

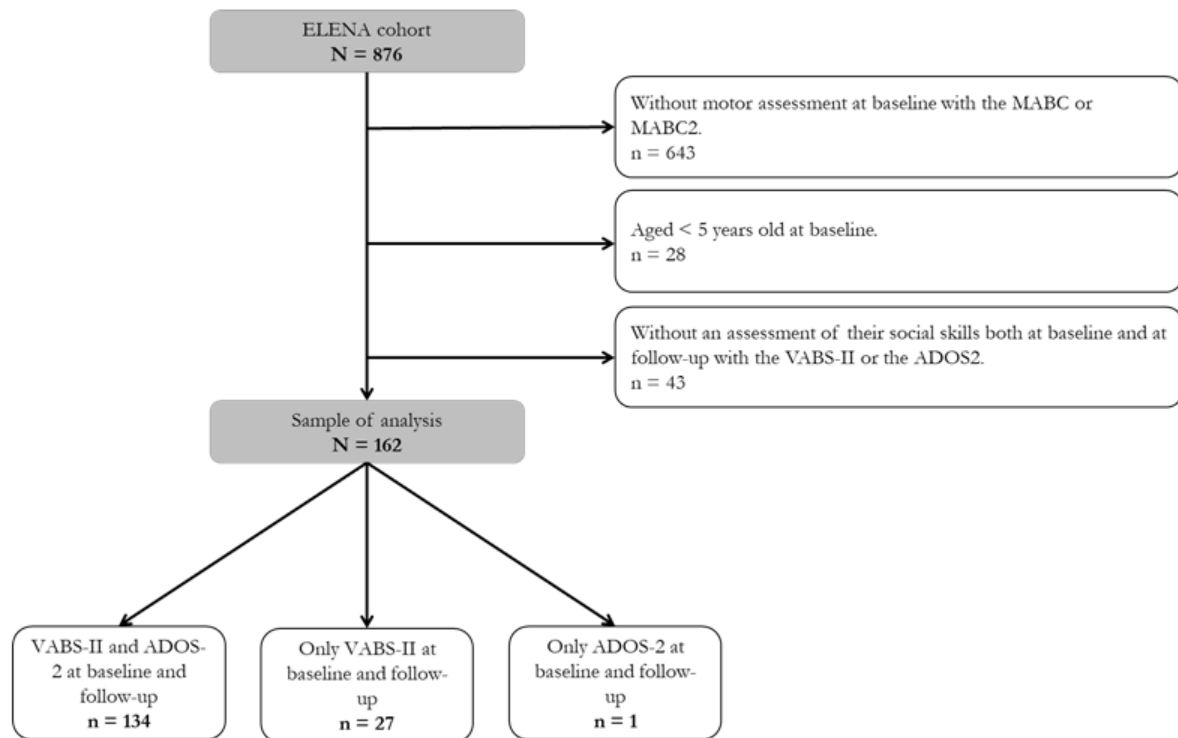
and many other socio-demographic characteristics were collected (age, gender, parental education and socioeconomic status). A follow-up was carried out at 3 years later to reassess their social skills.

All children received a clinical diagnosis of ASD according to the DSM-5 criteria, confirmed by a multidisciplinary team using a standardized process, including the ADOS-2 [22] and the ADI-Revised [23], administered by licensed and trained psychologists, a parental interview about the child's adaptive functioning using the VABS-II (Sparrow et al., 2011), and direct psychological examinations to assess cognitive level using appropriate psychometric test according to age [Wechsler scales [24–26] or K-ABC-II scale [27]].

Study sample

We include a sample of children from the ELENA cohort aged 5 years or older to identify children with persistent difficulties in motor skills. We exclude children without (i) an assessment of their motor skills with the Movement Assessment Battery for Children [15, 28] and without (ii) an assessment of their social skills both at baseline and at follow-up (either with the VABS-II or the ADOS-2 or both, (Figure 1)).

Fig 1 Flowchart



Measurements

Motor skills at baseline

Motor skills were assessed at baseline using the Movement Assessment Battery for Children (MABC [15] or MABC-2 [28]), which is one of the most widely used assessment tools for the identification and description of difficulties in motor skills of children 3–17 years. It is composed of fine and gross motor tasks which enables the assessment of each child's global motor skills compared to their peers of the same age. In children over 5 years, global scores below or equal to the 15th percentile for the MABC and 16th percentile for the MABC-2 are usually considered to indicate a motor difficulties [15, 28, 29]. Additionally, the MABC (and MABC-2) make it possible to identify children with difficulties in gross motor skills only, in fine motor skills only, or both motor areas. It is important to mention that some children may have difficulties in gross or fine motor skills only without having difficulties on the general score [30].

Social skills at baseline and follow-up

ADOS-2 : ASD symptom severity was examined using the Autism Diagnostic Observation Schedule 2 (ADOS-2) [22], a semi-structured behavioral observation protocol that assesses ASD symptomatology. At baseline and follow-up, children were assessed with the module appropriate to their age, language, and developmental level. The Calibrated Severity Scores (CSS) of the ADOS-2 can be compared across modules, over time, and across individuals [12]. The internal consistency of the CSS total score (based on symptoms of two domains: Social Affect (SA) and Restricted Repetitive Behaviors (RRB) ranges from poor to excellent ($\alpha = 0.50\text{--}0.92$), test-retest reliability was acceptable (0.64–0.88), and interrater reliability ranged from good to excellent (0.79–0.98) [12]. In the present study, we used the CSS Social Affect score which spans from 1 to 10, a higher score corresponding to greater severity of social-communication symptoms.

VABS-II: Adaptive skills were assessed using the Vineland Adaptive Behavior Scales, Second Edition (VABS-II) [31]. This standardized caregiver interview of 297 items measures adaptive behaviors in the subdomains of communication, daily living skills, and socialization. The reliability and the intra-class coefficient of the test/re-test of the VABS-II for each domain has been reported excellent [31]. In the present study, we used the standard score (mean = 100, SD = 15) for the socialization domains.

Potential confounders

Intelligence: The intellectual quotient (IQ) was calculated using standardized and validated instruments (i.e. Brunet-Lézine-R [32], BECS [33], PEP-3 [34], WPPSI-IV[25], WISC-V [24], WAIS-IV [35], K-ABC [27]) selected according to the child's age and developmental level following the approach used by Howlin et al [36].

Statistical analyses

A composite score of social skills was created at baseline and at follow-up by averaging the standardized scores of the inverted ADOS-2 Social Affect CSS (i.e., 10 - ADOS-2 Social Affect CSS non-standardized score; in order to ensure a consistent directionality with the VABS-II VABS-II) and the socialization domain of the VABS-II (when both scores were available at baseline and follow-up).

We also calculated the Spearman correlation between the ADOS-2 Social Affect CSS and the socialization domain of the VABS-II between the two time points.

Age groups have been established to correspond to the different stages of schooling in France: preschool children (under 6 years), school-age children (6 to 12 years), and adolescents (12 years and older). We described the motor, social and intellectual skills as well as the socio-demographic characteristics of our sample of analysis using means \pm SDs for continuous variables and frequencies and percentages for categorical variables. The Chi-square or Fisher's test and the ANOVA were used, as appropriate, to compare differences between children with and without difficulties in global motor skills.

We examined whether difficulties in global motor skills were associated with longitudinal changes in the composite score of social skills score between the beginning and the end points of our prospective follow-up in the ELENA cohort, using a multivariate linear regression. Models were adjusted for gender, age at baseline, IQ and Social Skills at baseline.

In the following models we tested the association parameter of the difficulties in global motor skills (binary variable).

- *Model 1. Composite_Score_Social_Skills_follow-up = Composite_Score_Social_Skills_baseline + Motor_Difficulties_Global + IQ + Gender + Age.*

This association was then tested on the ADOS-2 Social Affect CSS (model 1a) and the socialization domain of the VABS-II (model 1b) separately.

To determine whether the types of difficulties in motor skills (fine motor skills only, gross motor skills only and difficulties in both area) were more strongly associated with changes in social skills, the following models were used to test the global p-value of the association parameter of the type of motor difficulties (theses analyses were restricted to children with at least one of the three types of motor difficulties ; N = 131).

- *Model 2. Composite_Score_Social_Skills_follow-up = Composite_Score_Social_Skills_baseline + Motor_Difficulties_Type + IQ + Gender + Age.*

This association parameter was then tested on the ADOS-2 Social Affect CSS (model 2a) and the socialization domain of the VABS-II (model 2b) separately.

The previous models (2, 2a and 2b) were also performed, including children without motor difficulties to determine the effect size of the longitudinal changes in the composite social skills in the three types of difficulties in motor skills (children without motor difficulties as the reference group).

In supplementary analyses, we re-ran these analyses separately in a subsample of children who completed both the ADOS-2 Social Affect CSS and the socialization domain of the VABS-II at baseline and follow-up (N = 134). This supplementary analysis was performed because the number of missing data was imbalanced across the two measures (Figure 1).

All statistical analyses were performed using SAS Enterprise Guide V7.13 (SAS Institute Inc., Cary, NC, USA).

We used the Bonferroni correction to adjust the critical value for multiple comparisons (we set p-value threshold at 0.01).

RESULTS

Our sample included 162 children aged in mean of 8.9 years (SD = 3.0) with a male/female ratio of 134/28 (Table 1).

Table 1. Description of our analysis sample and comparison of children with and without motor difficulties at baseline

	Sample of analysis	Without difficulties in global motor skills [§]	With difficulties in global motor skills [§]	p-value
	N=162	N=48	N=114	
Children characteristics at baseline				
Chronological age (years)	8.9 (±2.99)	8.7 (±2.9)	9.0 (±3.0)	0.56
[5-6 years[28 (17.3%)	10 (20.8%)	18 (15.8%)	0.49
[6-12 years[106 (65.4%)	32 (66.7%)	74 (65.9%)	
≥12 years	28 (17.3%)	6 (12.5%)	22 (19.3%)	
Gender				
Boys	134 (82.7%)	6 (12.5%)	22 (19.3%)	0.30
Girls	28 (17.3%)	42 (87.5%)	92 (80.7%)	
Intellectual Quotient (IQ)	91.9 (±22.1)	99.2 (±16.0)	88.9 (±23.6)	0.01
Intellectual disability				
With intellectual disability (IQ<70)	26 (16.1%)	1 (2.1%)	25 (21.9%)	<0.01
Without intellectual disability (IQ≥70)	136 (83.9%)	47 (97.9%)	89 (78.1%)	
Autism Diagnostic Observation Scheduled (ADOS-2)				
Social affect: Calibrate severity scale (CSS)	6.9 (±2.1)**	6.1 (±2.3) [£]	7.2 (±1.9) [°]	0.004
Vineland Adaptative Behavior Scales (VABS-II)				
Socialization standard score	70.8 (±11.0) [£]	74.5 (±9.2)	69.2 (±11.4) [£]	<0.01
Composite score of social skills [□]	-0.04 (±0.79)	0.30 (±0.7)	-0.18 (±0.78)	<0.01
Types of deficits of motor skills				
None	23 (14.9%) ^{§§}	23 (52.3%) [§]	0 [§]	<0.01
Deficit of fine motor skills	17 (11.0%)	6 (13.6%)	11 (10.0%)	
Deficit of gross motor skills	26 (16.9%)	12 (27.3%)	14 (12.7%)	
Deficit of fine and gross motor skills	88 (57.2%)	3 (6.8%)	85 (77.3%)	
Children characteristics at follow-up				

Chronological age (years)	12.0 (\pm 3.0)	11.8 (\pm 2.9)	12.1 (\pm 3.1)	0.56
Autism Diagnostic Observation Scheduled (ADOS-2)				
Social affect: Calibrate severity scale (CSS)	7.6 (\pm 1.9)	6.9 (\pm 2.2)	7.9 (\pm 1.7)	0.01
Vineland Adaptive Behavior Scales (VABS-II)				
Socialization standard score	71.7 (\pm 10.7)	76.8 (\pm 9.0)	69.6 (\pm 10.7)	<0.01
Composite score of social skills \square	0.02 (\pm 0.8)	0.47 (\pm 0.8)	-0.18 (\pm 0.7)	<0.01
Parents characteristics				
Paternal education	N=112	N=37	N=75	
Elementary	0	0	0	0.95
Secondary (high school)	55 (49.1%)	18 (48.6%)	37 (49.3%)	
Higher qualifications (college, graduated school)	57 (50.9%)	19 (51.4%)	38 (50.7%)	
Maternal education	N=115	N=38	N=77	
Elementary	2 (1.7%)	0	2 (2.6%)	
Secondary (high school)	33 (28.7%)	11 (28.9%)	22 (28.6%)	1.0
Higher qualifications (college, graduated school)	80 (69.6%)	27 (71.1%)	53 (68.8%)	
Parental Socioeconomic status $\square\square$	N=140	N=43	N=97	
Low	51 (36.4%)	12 (27.9%)	39 (40.2%)	0.15
Middle	43 (30.7%)	12 (27.9%)	31 (32.0%)	
High	46 (32.9%)	19 (44.2%)	27 (27.8%)	

Data are given in mean (\pm SD) or n (%).

£1 missing data, \square 2missing data, **3 missing data, \$4 missing data, \$\$8 missing data.

§Global scores below or equal to the 16th percentile for the MABC and 15th percentile for the MABC-2 are usually considered to indicate motor difficulties.

\square We create a composite score of social skills at baseline and follow-up by averaging the standardized score of the inverted ADOS Social Affect CSS and the standardized score of the VABS socialization domain (when both scores were available at baseline and follow-up).

$\square\square$ Parental Socioeconomic status: Low SES: farm workers, labourers, service workers and unemployed; Medium SES: farmers, supervisors, skilled craftsmen; High SES: business owners, professionals, managers.

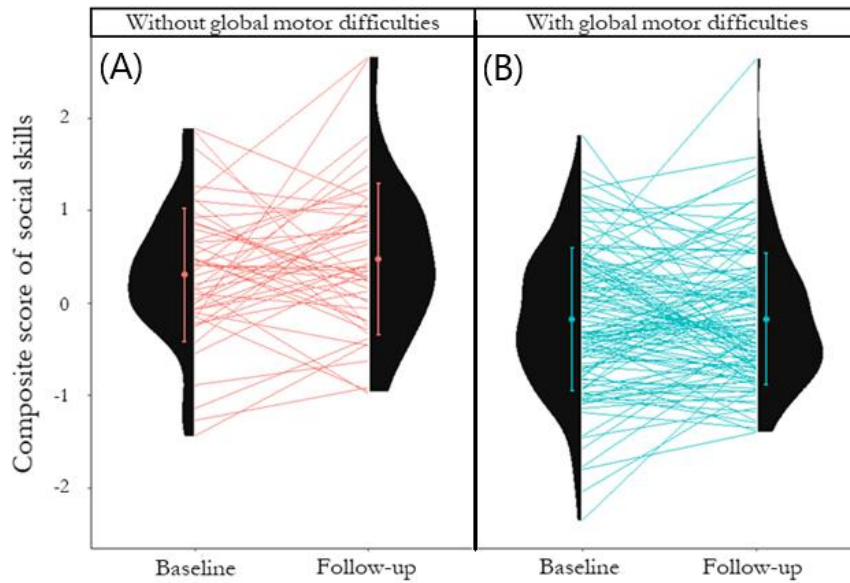
The flowchart is described in Figure 1.

Children participating in the ELENA cohort that were included in the present study (N = 162) were older (according to one of the inclusion criteria of age \geq 5 years to capture persisting difficulties in motor skills), had a higher IQ and better adaptive skills than those that were excluded (N = 714) (Online Resource 1).

Among these children, 114 had difficulties in global motor skills (70% of our sample) including 85 children with difficulties in fine and gross motor skills, 14 with difficulties in gross motor skills only and 11 with difficulties in fine motor skills. Some children without difficulties in global motor skills (23 out of 48) had difficulties in gross motor skills (N=12), difficulties in fine motor skills (N=6) or difficulties in fine and gross motor skills (N = 3).

Children with difficulties in global motor skills had lower social skills at baseline and at the 3 years' follow-up (3.1 years, SD = 0.2, Figure 2).

Fig 2 Individual trajectories of social skills between baseline and follow-up, separately for (A) children without global motor difficulties (N=48) and (B) children with global motor difficulties (N=114)



In our main linear regression model adjusted for IQ, age, and gender, the presence of difficulties in global motor skills at follow-up was associated with poorer changes in social skills (standardized $\beta = -0.42$ (95%-CI = [-0.66; -0.17], $R^2 = 0.32$, p -value < 0.01, $N = 162$, model 1, Table 2). This association was consistently found when examining separately changes in the ADOS-2 Social Affect CSS ($\beta = 0.99$, 95%-CI = [0.23; 1.75], $R^2 = 0.12$, p -value = 0.01, $N = 135$, model 1a, Table 2) and the socialization domain of the VABS-II ($\beta = -4.09$, 95%-CI = [-7.17; -1.01], $R^2 = 0.36$, p -value = 0.01, $N = 161$, model 1b).

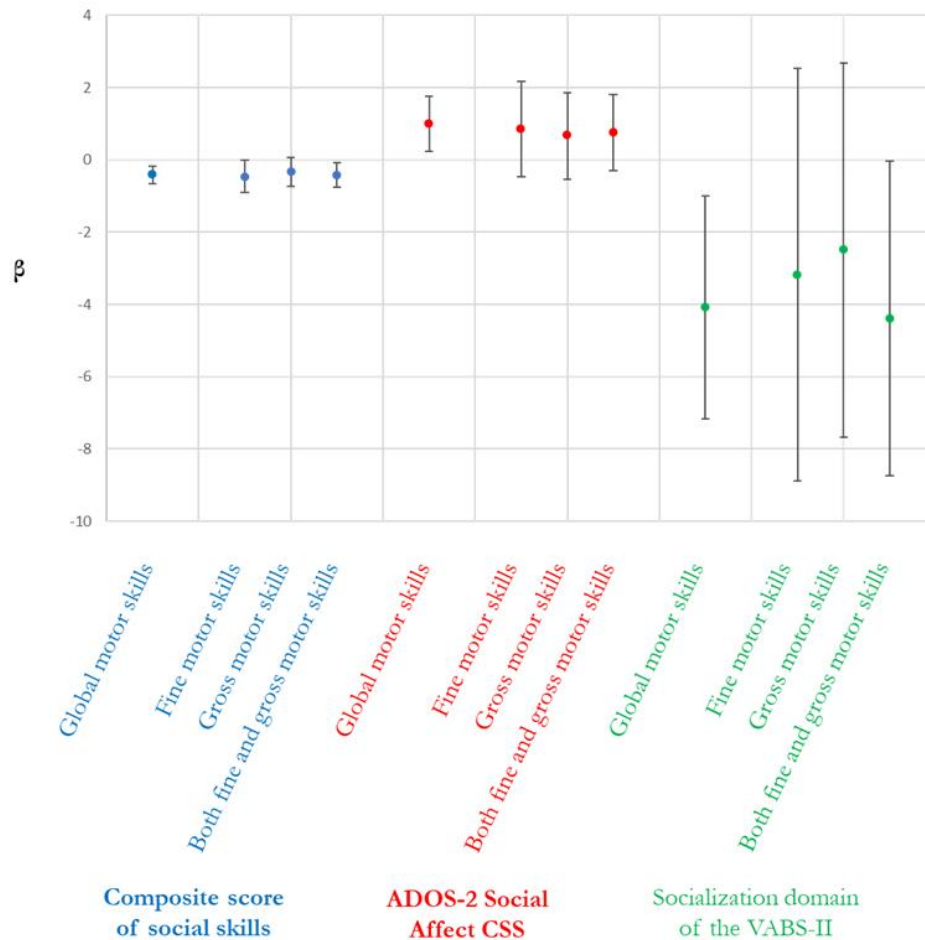
Table 2. Multivariate linear regression examining the effect of difficulties in global motor skills on the longitudinal changes in social skills in the ELENA cohort

	β	IC-95%		p -value
Model 1. Composite score of social skills at follow-up (standardized)				
N = 162				
$R^2 = 0.32$				
Intercept	0.20	-0.35	0.75	0.48
Presence of difficulties in global motor skills	-0.42	-0.66	-0.17	<0.01
Chronological age at baseline (years)
[6-12 years[-0.40	-0.69	-0.11	0.01
≥ 12 years	-0.21	-0.59	0.17	0.28
]5-6 years[(ref.)				
Gender: girls (boys as ref.)	-0.01	-0.30	0.27	0.94
Composite score of social skills at baseline (standardized)	0.37	0.20	0.51	<0.01
Intellectual Quotient (IQ)	0.00	0.00	0.01	0.07
Model 1a. ADOS-2-CSS-SA at the follow-up evaluation (unstandardized).				
N = 135				
$R^2 = 0.12$				
Intercept	6.91	5.02	8.81	<0.01
Presence of difficulties in global motor skills	0.99	0.23	1.75	0.01

Chronological age at baseline (years)
[6-12 years[0.94	0.14	1.75	0.02
≥12 years	0.84	-0.64	2.31	0.26
]5-6 years[(ref.)				
Gender: girls (boys as ref.)	-0.89	-1.80	0.02	0.06
ADOS-2-CSS-SA at baseline (unstandardized)	0.00	-0.17	0.16	0.97
Intellectual Quotient (IQ)	-0.01	-0.02	0.01	0.40
<hr/>				
Model 1b. VABS-II Socialization domain at follow-up.				
N = 161				
R ² = 0.36				
Intercept	42.68	31.26	54.11	<0.01
Presence of difficulties in global motor skills	-4.09	-7.17	-1.01	0.01
Chronological age at baseline (years)				
[6-12 years[-4.57	-8.28	-0.85	0.02
≥12 years	-1.27	-6.23	3.70	0.62
]5-6 years[(ref.)				
Gender: girls (boys as ref.)	-2.09	-5.76	1.59	0.26
VABS-II Socialization domain at baseline (unstandardized)	0.44	0.30	0.57	<0.01
Intellectual Quotient (IQ)	0.05	-0.02	0.12	0.13

The variance explained (R²) by the model 1a was inferior to the one of the model 1b because the ADOS-2 Social Affect CSS was less stable than the socialization domain of the VABS-II, indeed the Spearman correlation between the scores at baseline and follow-up were 0.07 for ADOS-2 SA CSS and 0.53 for VABS-II. In these three models (1, 1a and 1b), children aged 5 years showed a more favorable trajectory in their socialization outcome trajectory compared to those aged 6 to 12 years. This may be at least partially explained by the fact that children aged 5 years that were included had significantly better social skills at baseline (0.37 (SD = 0.60), p-value = 0.01) than those excluded (-0.11 (SD = 1.00)), whereas it was not the case for children aged 6 to 12 years (included: 0.12 (SD = 0.82), excluded: 0.01 (SD = 0.94), p-value = 0.4). Taking children without motor difficulties as the reference group, the estimates of the parameters of changes in social skills were in the same range for difficulties in fine motor skills ($\beta = -0.46$ (95%-CI = [-0.90; -0.02], Figure 3), difficulties in gross motor skills ($\beta = -0.33$ (95%-CI = [-0.74; 0.07]) and difficulties in both gross and motor skills ($\beta = -0.41$ (95%-CI = [-0.76; -0.07])).

Fig 3 Beta coefficients associated with the presence of motor difficulties from multivariate regression models (standardized β for the composite score of social skills and unstandardized β for the ADOS-2 Social Affect CSS and socialization domain of the VABS-II)



We did not find clear evidence that the types of motor difficulties at baseline were differentially associated with poorer changes in social skills (global test p-value of the composite score of social skills = 0.74, model 2; p-value = 0.50 for the ADOS-2 Social Affect CSS, model 2a; p-value = 0.63 for the socialization domain of the VABS-II, model 2b).

In supplementary analyses, we re-ran these analyses separately in the subsample of 134 children who completed both the ADOS-2 Social Affect CSS and the socialization domain of the VABS-II at baseline and follow-up and found generally comparable results except a smaller standardized β than model 1 ($\beta = -0.33$ (95%-CI = [-0.58; -0.08]) (Online Resource 2).

DISCUSSION

This study is, to our knowledge, one of the few using standardized measures of both motor and socialization skills, to examine prospectively the predictive value of early motor skills difficulties in childhood for long term socialization outcome trajectories in ASD. In a subsample of children

recruited from the ELENA cohort, our findings indicate a clear negative impact of the presence of motor skill problems on the socialization trajectories. This result was consistently found in models adjusted for IQ (and other socio-demographic characteristics), regardless of the measure of social skills used (whether direct measurement (ADOS-2 Social Affect CSS) or indirect measurements (socialization domain of the VABS-II)), and regardless of the type of difficulties in motor skills (difficulties in fine, gross or both motor domains). Although the standardized β were small in magnitude (-0.33 in the complete cases analysis and -0.42 in the full sample of analysis, 0.51 when examining separately changes in the ADOS-2 Social Affect CSS and -0.38 when examining separately changes in the socialization domain of the VABS-II), these findings confirm that children with a diagnosis of ASD who have difficulties in motor skills have less favorable social outcomes when compared to those with an ASD and without motor difficulties [10, 11, 17, 19, 20].

According to the activity difficulties hypothesis, children with motor difficulties show additionally low physical activity, limiting their opportunities to practice and improve their social skills [19]. However, this compelling hypothesis is only supported by the results of two pilot studies of interventions targeting primarily gross motor skills. [19, 20] and has never been verified in large samples from cohorts, in particular. In addition, if this hypothesis is true, it would not be restricted to activities involving gross motor skills (e.g. running, jumping or riding a bicycle) but also fine motor skills (e.g. drawing, cutting with scissors or playing with building blocks). Indeed, our study showed that the different types of difficulties in motor skills were similarly associated with changes in social skills. Other alternative hypotheses need to be considered, in particular the possibility that a common neuropsychological deficit, likely involving an aspect of executive functions, could explain both the difficulties in motor skills and the less favorable course of social skills. This hypothesis deserves serious consideration because it implies that interventions targeting the difficulties in motor skills would not necessarily have an influence on the trajectory of social development (unlike the activity difficulties hypothesis).

Our findings are consistent with those reported in cross-sectional studies using the ADOS CSS [10, 11] but not with the study by Green et al using the VABS [8]. Green et al found that the association of motor skills difficulties with adaptive behaviors wasn't maintained after adjustment for IQ,

challenging the view that motor impairment makes an independent contribution to the adaptive behaviors of children with ASD and pointing to a discrepancy between the results of studies conducted using the ADOS CSS [10, 11] and those using the VABS [8]. Instead, we found a high level of agreement between our longitudinal analyses conducted using the ADOS CSS and the VABS and supporting the idea of an independent contribution of difficulties in motor skills (beyond IQ) to social outcomes in children with ASD.

The present study has many strengths, its large sample of children with a confirmed diagnosis of ASD, its longitudinal and prospective design, the standardized assessment of motor skills using the well-established and validated M-ABC, and the multidimensional assessment of social skills with both direct examination (ADOS-2 Social Affect CSS) and indirect and ecological measurements (socialization domain of the VABS-II) both at baseline and at follow-up. However, some limitations should be raised. First, our sample of analysis is not representative of the whole population of children with ASD as they were recruited from specialized units. Moreover, there was a selection bias in our analysis sample from the ELENA cohort; children included in the present study were older, had a higher IQ and better adaptive skills than those that were excluded. This limitation could explain the lower percentage of children with motor difficulties in our sample compared to previous studies (70% against 80%-85% [6–9]). Secondly, due to missing data, parental occupational class was excluded from the multivariate models. However, there was a trend towards a difference (p -value = 0.15) in its distribution according to whether or not the children with ASD had motor difficulties. Additional analyses including this variable again were carried out on a smaller sample ($N = 140$) without significantly modifying the results (Online Resource 3).

Conclusion

Given that motor difficulties, both fine and gross, are frequently reported in children with ASD (about $\frac{3}{4}$ of our sample), and are associated with poorer trajectories of social skills, our data further reinforce the need of their early identification and assessment in children with ASD. In addition, interventions aimed at improving motor skills in children and adolescents with ASD could have a positive impact not only in the motor domain but also in the social domain. Well-designed clinical trials are still needed to confirm this last hypothesis.

Ethical Approval: The ELENA cohort has been approved by the Ethics Committee on the Research of Human Subjects at Marseille Mediterranean and the National Commission for Computing and Liberties (CNIL, number DR-2015-393).

Consent to participate: Signed informed consent is obtained from all participating families included in the ELENA cohort.

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