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Motor development problems in infancy predict mental disorders in childhood: a longitudinal cohort study

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22 **Abstract**

23

24 *Purpose:* To examine whether motor development problems in infancy predicted mental disorders later in childhood,
25 taking a wide array of potential confounding variables into consideration.

26 *Methods:* This longitudinal study included an unselected study population of 33,238 newborn children from the
27 Copenhagen area, Denmark. Data on the predictor variable: motor development problems at 8-10 months of age, were
28 obtained from the community health nurses' systematic evaluation of the child's motor development during a home
29 visit and stored in the Child Health Database. Data on outcome, diagnosed mental disorders before the age of 8 years,
30 were obtained from the Danish National Patient Register. Potential confounding variables were obtained from the Child
31 Health Database, the National Birth Register, and the Civil Registration System.

32 *Results:* The prevalence of motor development problems at 8-10 months of age was 19.3%; the incidence of any
33 diagnosed mental disorder from 11 months of age to the 8th birthday was 4.0%. Motor development problems were
34 associated with an increased risk of being diagnosed with a mental disorder before the 8th birthday, adjusted odds ratio
35 (AOR) 1.47 (1.29-1.67). Motor development problems were associated with later neurodevelopmental disorders, AOR
36 1.77 (1.52-2.06), in particular autism-spectrum disorders, AOR 1.63 (1.31-2.03), hyperactivity/ attention deficit
37 disorders, AOR 1.29 (1.03-1.61) and disorders of intellectual disability, AOR 3.28 (2.39-4.49).

38 *Conclusion:* Motor development problems as early at 8-10 months of age were predictive of neurodevelopmental
39 disorders before the 8th birthday. The findings call for clinical attention and more research on preventive potentials in
40 the community child health care.

41

42

43 *Keywords:* Children; longitudinal study; community health nurses; infants; mental disorders; motor development
44 problems.

45

46 *List of abbreviations*

47

48 ADHD: Attention deficit hyperactivity disorder

49 AOR: Adjusted odds ratio

50 ASD: Autism spectrum disorders

51 CHN: Community health nurse

52 CI: Confidence Interval

53 ICD-10: International classification of diseases, 10th edition

54 ID Intellectual disability

55 OR: Odds Ratio

56

57

58

59 *What is known*

60

61 • Children with ASD, ADHD, and ID have high prevalence of early motor development problems.

62

63 *What is new*

64

65 • Motor development problems in infancy predicted neuro-developmental disorders before the 8th birthday

66 • This observation could improve early identification and prevention of mental health problems in childhood

67

68 *Statements and declaratios*

69

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71

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73

74 *Availability of data and material:* The data underlying this article will be shared on reasonable request to the Principal
75 Investigator, Dr. Trine Pagh Pedersen (tppe@sdu.dk).

76

77 *Code availability:* Not applicable.

78

79 *Authors' contributions:* All authors contributed substantially to the conception and design of the paper, and to the
80 interpretation of data. TPP and SWP acquired the data. SWP and TPP performed the analyses. SWP and BEH wrote the
81 first draft of the manuscript. All authors contributed to the writing of the manuscript and a critical revision of the
82 intellectual content. All authors have approved the final version of the manuscript and are accountable for all aspects of
83 the work.

84

85 *Ethical approval:* The study was approved by the Danish Data Protection Agency (registration number 10.366,
86 University of Southern Denmark) and complied with national regulations of data protection and consent. Linkage with
87 register data was administered by Statistics Denmark and the involved researchers did not have access to personal
88 identification. According to the Danish legislation, informed consent is not required for register-based studies.

89

90 *Consent to participate:* Not applicable.

91

92 *Consent for publication:* Not applicable.

93

94 **Introduction**

95

96 Available research suggests that motor development problems in infancy may be predictive of childhood
97 neurodevelopmental disorders, such as autism spectrum disorder (ASD) [1-9], disorders of hyperactivity and inattention
98 (ADHD) [4, 5, 10-12], and disorders of intellectual disability (ID) [7]. None of the studies published thus far have
99 explored the predictiveness of systematically assessed motor development regarding the range of mental disorders seen
100 in childhood and considered unmeasured confounding due to child and family variables [1, 6-10]. Athanasiadou et al.
101 (2020) suggested that investigating early motor development in infancy could be important for the study of early
102 biomarkers of common neurodevelopmental disorders [10]. Moreover, there is a need to examine whether the municipal
103 child health system can be used to identify children who are at a developmental risk regarding severe mental disorders
104 [11, 13]. Therefore, the aim of this study was to use a large community-based cohort to examine whether motor
105 development problems in infancy predicted mental disorders later in childhood, taking a wide array of potential
106 confounding variables into consideration.

107

108 **Methods**

109

110 *Setting:* In Denmark, the municipal health care system offers all families with newborn children a series of home visits
111 provided free of charge by a community health nurse (CHN) [13]. CHNs are registered nurses with further education
112 (1½ years) comprising training in the assessment of health and development in children. Approximately 97% of all
113 families participate in these home visits. Most municipalities comply with the recommendations from the National
114 Health Authority and offer at least five home visits at (a) a few days after delivery, (b) 1-2 weeks after delivery, (c) 2-3
115 months after delivery, (d) 4-6 months after delivery and (e) 8-10 months after delivery. CHNs in a range of
116 municipalities have organized a clinical database—the Child Health Database—with standardized data from their
117 records. The CHNs use a manual of definitions to ensure comparability and promote validity of the data in their records.
118 The records include the children’s unique person identification numbers, which makes it possible to link the data with
119 data from national health and sociodemographic registers that cover the total population in Denmark.

120

121 *Study design and study population:* This was a longitudinal study of infants using prospectively collected data from the
122 Child Health Database and register data from the National Birth Register, the Danish National Patient Register, and the
123 Civil Registration System. The inclusion criteria were as follows: 1) all children from 16 municipalities in the
124 Copenhagen region in Denmark born between 1 January 2002 and 31 December 2010 and who had their 8th birthday

125 before 1 January 2019 (n=47,167) and 2) included in the Child Health Database. The exclusion criteria were as follows:
126 1) children with a mental disorder diagnosed at a hospital within the first 10 months of the child's life (n=946) and 2)
127 those with missing data on motor development problems (n=8,634) or any applied control variable (n=4,349), leaving a
128 final sample of 33,238 children. We chose an eight-year follow-up period to include the first years of schooling and still
129 benefit from a large study population.

130

131 *Measures:* The independent variable was motor development problems in infancy. These data stem from the scheduled
132 CHN home visit at 8-10 months of age. The CHN assessed the child's motor development four times in infancy: at 1-2
133 weeks, 2-3 months, 4-6 months, and 8-10 months after delivery. We used the last of these assessments because some
134 infants with slow motor development catch up in their milestones during the first year of life. According to the
135 guidelines and the manual for assessments for children at 8-10 months of age, the CHNs expressed a concern in the
136 record if a child did not meet all of the following specific developmental milestones: able to roll over from their back to
137 their stomach and reverse; able to sit independently; able to move things from hand to hand; able to put things into their
138 mouth; able to crawl forwards and/or backwards; and able to pull to a standing position. We summarized the assessment
139 into a dichotomous variable: +/- motor development problems.

140

141 The dependent variable/outcome variable was any mental disorder diagnosed in a hospital setting from 11 months of
142 age to the 8th birthday. These data were obtained from *the Danish National Patient Register*, which includes all in- and
143 outpatient and emergency hospital contacts with 100% coverage [14]. In these settings, medical doctors conclude, using
144 clinical and paraclinical data, the diagnoses of mental disorders in accordance with the defining criteria of the
145 International Classification of Mental and Behavioral Disorders 10 (ICD-10). Several studies have reported that the
146 Danish National Patient Register is characterized by high validity and reliability [14-16]. We included a range of mental
147 disorders seen in childhood: general developmental disorders or ID (F70-F79); specific developmental disorders (F80-
148 F83); pervasive and other developmental disorders (F84-89); hyperkinetic disorders (F90); attention deficit disorder
149 without hyperactivity (F98.8); mood disorders, emotional and stress-related disorders (F30-F34, F38-F45, F48, F93);
150 disorders of eating and sleeping (F50-F51, F 98.2); disorders of behaviour (F91-F92); and disorders of social
151 functioning (F94.1, F94.2, F94.8). We summarized the data into three dichotomous variables: 1) a diagnosed
152 neurodevelopmental disorder, including disorders of ID, ASD and ADHD (yes, no); 2) a diagnosed behavioural or
153 emotional disorder (yes, no); and 3) at least one diagnosed mental disorder before the age of 8 years (yes, no). We also
154 conducted analyses for some specific diagnoses: ASD (F84), disorders of hyperactivity and inattention (F90, F98.8) and
155 ID (F70).

156

157 The analyses included the following potential confounders: from the *National Birth Register*: sex, parity (first born vs.
158 later), gestational age (continuous variable, days), birth weight (<2500 g, 2500-3999 g, >3999 g), congenital
159 malformation (yes, no), mother's and father's age at childbirth (<25 vs. ≥25 years), pregnancy complications (yes, no),
160 caesarean section (yes, no), and Apgar score (9-10 vs. less than 9); from the *Civil Registration System*: parents'
161 education at childbirth (five levels), parents' employment (2, 1 or 0 employed parents), family composition (child lives
162 with both parents, yes vs. no), and parents' origin (2, 1 or 0 parents of Danish origin); and from *the Child Health*
163 *Database*: concern about the mother's mental health in the first six months after delivery (concern at 0 visits vs. at least
164 one home visit) and concern about the parent-child relationship in the first six months after delivery (concern at 0 visits
165 vs. at least one home visit).

166

167 *Statistical procedures*: We used bivariate contingency tables and chi²-tests to examine the baseline differences between
168 the included and excluded infants. The next step was logistic regression analysis of the association between motor
169 development problems at 8-10 months of age (independent variable) and diagnosed mental disorders from 8-10 months
170 of age to the 8th birthday (dependent variable). We adjusted for the abovementioned potential confounding variables.
171 The assumptions of the regression models were respected: 1) the response variable was binary; 2) the study population
172 was sufficiently large and characterized by independent observations; 3) there were no extreme outliers; and 4) there
173 were no serious problems of collinearity. The main independent variable (motor development problems) was not highly
174 correlated with the other independent variables. The high intercorrelation between the two pairs of confounding
175 variables (mother's and father's age; gestational age and birth weight) hardly affected the examination of the
176 association between motor development problems and mental disorders.

177

178 **Results**

179

180 Table 1 shows the characteristics of the study population compared with the children excluded because of missing data.
181 There was a slight although statistically significant overrepresentation of children with diagnosed mental disorders
182 among the excluded children. Furthermore, more of the excluded children had perinatal risk factors, such as being born
183 before the 37th week, having a low birth weight, having a caesarean section, and having an Apgar score < 9. More of the
184 excluded children had young parents, unemployed parents, parents with low educational attainment, parents who were
185 immigrants or descendants of immigrants, parents who were not living together, mothers for whom the CHN had

186 indicated concern about their mental health in the first six months after delivery, and mothers for whom the CHN had
187 indicated concern about the parent–child relationship in the first six months after delivery.

188

189 Within the study population of 33,238 children, 6,399 (19.3%) had motor development problems at 8-10 months of age.
190 The number of children diagnosed with at least one mental disorder from 11 months of age to the 8th birthday was 1,331
191 (4.0%); 878 (2.6%) were diagnosed with a neurodevelopmental disorder, and 671 (2.0%) were diagnosed with a
192 behavioural or emotional disorder. Among the 6,399 children with motor development problems, 357 (5.6%) were
193 diagnosed with at least one mental disorder, 269 (4.2%) were diagnosed with a neurodevelopmental disorder, and 152
194 (2.4%) were diagnosed with a behavioural or emotional disorder. The numbers of children with ASD, ADHD, and ID
195 were 122 (1.9%), 111 (1.7%) and 79 (1.2%), respectively.

196

197 Children who had motor development problems at 8-10 months of age had an increased risk of being diagnosed with a
198 mental disorder before their 8th birthday, AOR (95% CI) =1.47 (1.29-1.67) (Table 1). The association between motor
199 development problems in infancy and behavioural or emotional disorders was insignificant in the mutually adjusted
200 analysis, AOR 1.13 (0.94-1.36). Children with motor development problems in infancy had an increased risk of any
201 neurodevelopmental disorder, AOR=1.77 (1.52-2.06) and, more specifically, an increased risk of ASD, AOR=1.63
202 (1.31-2.03), disorders of hyperactivity and inattention, AOR=1.29 (1.03-1.61), and ID, AOR=3.28 (2.39-4.49). The
203 estimates were only slightly attenuated when child and family adversities were adjusted for, such as prematurity,
204 pregnancy and birth complications, low parental education, and maternal and relationship problems in infancy. Tables
205 S1-S6 in Online Resource 1 show the full models, i.e., the association between all independent variables and each of the
206 six dichotomous outcome variables.

207

208 **Discussion**

209

210 This longitudinal study showed that motor development problems in infancy were associated with diagnosed
211 neurodevelopmental disorders in childhood but were not associated with behavioural or emotional disorders. Our
212 findings correspond with the current conceptualization of neurodevelopmental disorders [17]: They are characterized by
213 onset in infancy or early childhood; impairments, or delays in the development of functions are strongly related to the
214 biological maturation of the central nervous system; and a steady course that does not involve remissions and relapses
215 that characterize many other mental disorders [18]. Our findings also correspond with the growing recognition that
216 psychosocial and psychomotor problems in infancy are predictive of mental disorders in childhood [3, 4, 6, 10, 11, 19,

217 20]. Due to the comprehensive data from national registries, it was possible to adjust for an array of potential
218 confounding variables of suggested importance in the developmental trajectories of neurodevelopmental disorders,
219 including markers of pre- and perinatal adversities. Notably, the associations between motor development problems at
220 8-10 months of age and mental disorders were only slightly attenuated when adjusted for many potential confounding
221 variables.

222

223 Overall, our findings of an elevated risk for neurodevelopmental disorders correspond with those of recent studies of
224 risk factors for ASD and ADHD [1-4, 6-8, 12]. There are several hypotheses about the link between motor development
225 problems in early childhood and later neurodevelopmental disorders, hypotheses that refer to the neurobiological
226 development of the brain [10, 18]. Delays in brain maturation are associated with delays in motor development and
227 specific motor skills. This is in correspondence with our observations of a significant association between motor
228 development problems and neurodevelopmental disorders and ID but no association between motor development
229 problems and disorders of behaviour and emotions. However, the present study was not suited to further explore the
230 possible neurodevelopmental trajectories.

231

232 The strengths of the study include the large and unselected study population, the use of standardized data on child
233 development from the CHNs' manualized examinations, the use of validated data on child mental disorders, and
234 comprehensive data on child and family variables from population registers, allowing for the extensive control of
235 potential confounding variables.

236

237 One limitation is that the study narrowly focused on motor development problems instead of a wider range of infant
238 development. We chose this narrow focus because the association between motor development problems and mental
239 disorders is an understudied issue, and it would be difficult to maintain focus in a paper that included many aspects of
240 infant development. Furthermore, the study only captured hospital-recorded mental disorders, which misses a large
241 portion of mental disorders in the population. The study may suffer from some selection bias: Participants who were
242 excluded due to missing data about motor development had higher rates of mental disorders and higher prevalences of
243 perinatal and sociodemographic risk factors for mental disorders. Therefore, the study may underestimate the incidence
244 of mental disorders. There were differences between the included and excluded children in many baseline variables.
245 These differences were statistically significant but most of them are not very big. It is highly unlikely that the
246 associations between motor development problems and mental disorders – as they appear in the multivariably adjusted

247 analyses – were affected by the abovementioned differences between included and excluded children. Furthermore, it
248 may be a limitation that the validity of the motor skills examination is unknown, although it follows specific guidelines.

249

250 From a research point of view, there is a need for insight into the neurodevelopmental mechanisms that connect motor
251 development problems and neurodevelopmental disorders. There is also a need to study how motor development
252 interacts with other infant development problems, such as regulatory problems and parent–child problems, which also
253 predict mental disorders [3-5, 9-12, 19, 20]. In the future, the Child Health Database will include children with an 18-
254 year follow-up. At that point in time, it will be interesting to repeat the analyses to study whether motor development
255 problems in infancy are associated with mental disorders in adolescence.

256

257 From a practice point of view, we need more information on how to help parents and professionals deal with motor
258 development problems in infancy. We also need methods for the assessment of motor development problems that are
259 sensitive to problems related to children’s mental health [1]. The early detection of motor development problems would
260 facilitate timely diagnosis and intervention in a critical period of child development. According to Atanasiadou et al.
261 (2020) [10], this would assist clinicians in intervening in a critical period of child development when the brain is rapidly
262 developing, and neuroplasticity is the highest. Furthermore, timely diagnosis and intervention may also contribute to
263 early preventive efforts to help children at risk [10, 18].

264

265 In conclusion, motor development problems that occur as early as 8-10 months of age are predictive of
266 neurodevelopmental disorders before the 8th birthday. The findings call for clinical attention and more research on the
267 preventive potentials in community child health care.

268

269

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271

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344

Table 1 Characteristics of the study population, % (n)

	Included children n=33,238	Excluded children ¹ n=13,929	p
At least one diagnosed mental disorder	4.0 (1,331)	5.4 (754)	<0.01
Diagnosed disorder of behaviour and emotions	2.0 (671)	3.0 (412)	<0.01
Diagnosed neurodevelopmental disorder	2.6 (878)	3.4 (472)	<0.01
Autism-spectrum disorders (F84)	1.3 (423)	1.3 (184)	0.67
Disorders of hyperactivity and inattention (F90, F98.8)	1.4 (453)	1.5 (211)	0.20
Intellectual disability (F70)	0.5 (167)	1.1 (152)	<0.01
Male sex	51.1 (16,998)	51.7 (7,119)	0.31
First born child	41.1 (13,657)	45.6 (5,017)	<0.01
Born before 37 th week	6.2 (2,071)	8.2 (1,020)	<0.01
Birth weight < 2500 g	4.5 (1,500)	6.3 (778)	
2500-3999 g	78.0 (25,938)	78.3 (9,662)	
>3999 g	17.5 (5,800)	15.4 (1,896)	<0.01
Congenital malformation	6.3 (2,078)	6.6 (917)	0.18
Mother's age < 25	12.1 (4,020)	18.6 (2,589)	<0.01
Father's age < 25	6.3 (2,077)	13.6 (1,891)	<0.01
Pregnancy complications	8.4 (2,797)	8.1 (1,126)	0.23
Caesarean section	21.1 (6,999)	20.2 (2,813)	0.04
Apgar score < 9	2.3 (765)	2.9 (356)	<0.01
Parents' education in five levels: 1 (highest)	28.1 (9,340)	26.4 (3,284)	
2	26.0 (8,651)	22.2 (2,755)	
3	11.3 (3,755)	12.1 (1,504)	
4	25.9 (8,596)	24.0 (2,980)	
5	8.7 (2,896)	15.4 (1,910)	<0.01
Number of parents in employment: 2	83.7 (27,807)	77.7 (9,081)	
1	13.0 (4,320)	16.6 (1,960)	
0	3.3 (1,111)	6.3 (743)	<0.01
Number of parents of Danish origin: 2	76.2 (25,328)	66.3 (8,348)	
1	8.8 (2,930)	10.7 (1,347)	
0	15.0 (4,980)	23.0 (2,893)	<0.01
Child living with both parents	89.0 (29,572)	81.5 (9,515)	<0.01
Concern about mother's mental health in the first six months after delivery	27.4 (9,106)	30.7 (3,498)	<0.01
Concerns about the parent-child-relationship in the first six months after delivery	10.7 (3,563)	14.3 (1,631)	<0.01

¹ 13,929 is the maximum number. N varies as the number of missing differs

349 **Table 2** Crude and adjusted ¹ OR (95% CI) for diagnosed mental disorders from 11 months of age to the 8th birthday by
 350 motor development problems in infancy (n=33,238)
 351

Outcome measure	Crude OR (95% CI)	Adjusted OR (95% CI)
At least one diagnosed mental disorder	1.57 (1.39-1.78)	1.47 (1.29-1.67)
Disorders of behaviour and emotions	1.23 (1.03-1.48)	1.11 (0.92-1.34)
Diagnosed neurodevelopmental disorder	1.89 (1.63-2.19)	1.79 (1.54-2.08)
Autism-spectrum disorders (F84)	1.71 (1.39-2.12)	1.66 (1.34-2.07)
Disorders of hyperactivity and inattention (F90, F98.8)	1.37 (1.10-1.70)	1.30 (1.04-1.62)
Intellectual disability (F70)	3.80 (2.80-5.16)	3.39 (2.47-4.65)

352 ¹ Adjusted for sex, parity, gestational age, birth weight, congenital malformation, pregnancy complications, caesarean section, Apgar
 353 score, mother's age, father's age, parents' education, family composition, parents' origin, mother's mental health in the first six
 354 months after delivery, concerns about the parent-child-relationship in the first six months after delivery
 355