Effects of infant motor problems and treatment with physiotherapy on child outcomes at school-age

Abstract

Background. Early motor coordination problems have previously been associated with various developmental outcomes at school-age.

Aims. Investigate whether and how treatment with physiotherapy may alter associations between early motor problems and subsequent developmental outcomes.

Study design. A prospective whole-population study.

Subjects. 1,374 children were followed from birth to 8 years.

Outcome measures. Early motor functioning was determined with standard neurological examinations at birth and at 5 months. Information on receipt of physiotherapy was collected through parent interviews at 5, 20 and 56 months. Developmental outcomes at 6 and 8 years included motor skills, mental health, cognitive function, and attention regulation and were determined through standard tests, parent reports and observed behavior ratings.

Results. Early motor problems were associated with lower motor skills, cognitive function, and attention regulation at school-age, but not with mental health. In addition to early motor problems, receipt of physiotherapy was independently and negatively related to outcomes at school-age. Accounting for imbalances in covariates, including initial motor scores, via propensity score matching attenuated the adverse effects of receipt of physiotherapy on school-aged outcomes.

Conclusions. Infant motor problems are associated with motor and cognitive outcomes at school-age. Early motor problems may represent a starting point of a trajectory of difficulties that may lead to a higher risk of problems in multiple developmental domains. No evidence for a beneficial effect of treatment with physiotherapy was found.

Keywords: motor function; cognitive function; attention regulation; school-age; neonatal at-risk children; cohort study

Motor impairments, including cerebral palsy (CP) and developmental coordination disorder (DCD), have been found to be associated with adverse developmental outcomes [1]. Motor functioning assessed in infancy or toddlerhood has been found to be associated with subsequent developmental outcomes, including motor, cognitive and behavioral function, in both healthy and at-risk children, such as those born preterm [2-5].

Many children with early motor problems are referred for intervention [6]. In particular, physiotherapy is a widely used treatment for children with neurological motor dysfunctions [7, 8]. It is thus important to consider the effect of treatment with physiotherapy when testing associations between early motor problems and later developmental outcomes in observational, longitudinal studies [9].

The present observational study assessed a large sample of children born across the whole range of gestational age from birth to school-age. Early motor problems were assessed prospectively with extensive and age-appropriate physical and neurological examinations at birth and at 5 months [10]. Developmental outcomes including motor skills, mental health, cognitive function and attention regulation were assessed at 6 and 8 years. Information on physiotherapeutic treatment was extracted from standard parent interviews at 5, 20 and 56 months. Physiotherapy programs given to the children in this longitudinal study were primarily based on concepts developed by Bobath and Vojta in the 1960s [8]. Physiotherapeutic intervention or treatment based on these concepts are still being prescribed, albeit in modified forms that reflect the current understanding of motor control and neuroplasticity [7, 8].

The aims of this study were, first, to assess whether motor problems assessed in infancy are specifically associated with motor skills, and/or also with other developmental outcomes, such as mental health, cognitive function, and attention regulation at school-age. Second, it was investigated whether receipt of physiotherapy between birth and age 56 months altered the association between infant motor problems and developmental outcomes at school-age. In observational studies the allocation of receipt of physiotherapy is rarely random. We thus applied propensity score matching for evaluating the effect of physiotherapy on developmental outcome.

Methods

Design and participants

Data were collected as part of the prospective Bavarian Longitudinal Study (BLS). The BLS is a geographically defined, whole population sample of neonatal at-risk children born in 1985 and 1986 in Southern Bavaria, Germany, who required admission to a children's hospital within the first 10 days after birth (N=7,505; 10.6% of all live births). Additionally, healthy infants born at term in the same hospitals were recruited as controls (N=916). Parents were approached within 48 hours of the infant's hospital admission and asked to give written informed consent to participate. The present study utilizes data collected from birth to 8 years. Of the initial 8,421 participants, 1,513 children were selected for intensive follow-up at 6 and 8 years according to the following criteria: (1) born either very preterm (<32 weeks gestation) or at very low birth weight (<1500g); (2) a subsample of children born at >=32 weeks gestation randomly selected within stratification factors sex, socioeconomic status and degree of neonatal risk; (3) control children. Sampling criteria and dropout rates are provided elsewhere [11]. Longitudinal data were available for 1,374 children.

Children and their parents were assessed at birth and followed up at age 5 and 20 months corrected for prematurity, and at 56 months, 6 and 8 years chronological age, by an interdisciplinary team for an entire day including neurological and motor assessments, parent interviews, cognitive assessments, and observations of behavior.

Ethical permissions were granted by the ethics committee of the University of Munich Children's Hospital and the Bavarian Health Council (Landesärztekammer Bayern).

Measures

Infant motor problems

At birth and at age 5 months an extensive and detailed neurological and physical examination based on Prechtl's neurological examination method [12] was carried out by specially trained pediatricians. Items on neurological and motor functioning were dichotomized into 'within' and 'outside the normal range' of motor function (for more detail on items and numbers see Tables S1 and S2) and computed into a motor problem score based on the sum of motor functioning 'outside the normal range' (i.e. a higher score indicates more motor problems). To allow for comparability across ages the motor problem score was computed and subsequently converted into z-scores using the total sample at birth and 5 months, respectively [10]. Guided by current recommendations to differentiate children at risk or with probable motor problems [13], the 15th percentile was chosen as a cut-off point to recode both motor scores into binary variables: 0=no or low motor problems and 1= motor problems.

Physiotherapy from birth to 56 months

At 5, 20 or 56 months parents were asked whether and for how long their child had received or was receiving physiotherapy, based on Bobath, Vojta, or another physiotherapeutic approach. Detailed frequencies and duration of physiotherapeutic approach for each age are presented in Table S3. Overall, 372 children (27.1%) received physiotherapy between birth and 56 months. Of those children, more than half (N=211, 56.7%) were treated before age 5 months. While 283 children were treated at age 20 months, 114 children received physiotherapy at age 56 months.

Childhood outcomes at 6 and 8 years

Developmental outcomes obtained at 6 and 8 years are described in detail in Tables S4a/S4b. An overview is given here: *Motor impairment* was evaluated using the Test of Motor Impairment (TOMI) [14]. *Mental health problems* were assessed via parent reports with the

Child Behavior Checklist (CBCL) [15]. *Cognitive function* was measured with the simultaneous processing scale of the German version of the Kaufman Assessment Battery for Children (K-ABC) [16]. The K-ABC simultaneous processing scale is based on subtests that do not include motor skill components. *Attention regulation* was evaluated using the Tester's Rating of Child Behavior (TRCB) [17] task orientation scale, a team consensus rating (TEAM) of attention span, and the attention problem subscale of the Child Behavior Checklist (CBCL) [15].

Motor impairment, mental health problem and cognitive function scores at 6 and 8 years were combined into composite scores by calculating the mean score across both time points. Composite scores for motor impairment and mental health problems were subsequently recoded so that higher scores indicated better mental health and motor skills. To obtain overall scores from various measures of attention regulation assessed at 6 and 8 years, confirmatory factor analysis was performed using Mplus (Muthen and Muthen, Los Angeles, California, USA). Measures were used as factor indicators and a standardized factor score was retrieved. Factor loadings are reported in Table S5.

Covariates

The following variables were considered as potential confounders: gestational age, small for gestational age (SGA), sex, and family socioeconomic status (SES).

Statistical analyses

All analyses were performed using SPSS Version 22 (IBM SPSS Statistics, IBM Corporation). Differences between children with early motor problems and those without or low motor problems, were tested using t-tests for interval scaled variables or chi-square tests for dichotomous variables.

To test associations between motor problems at birth or at 5 months and motor skills, mental health, cognitive function and attention regulation at 6 to 8 years, univariate and multivariate linear regression analyses were applied. Analyses were adjusted for potential neonatal confounders: gestational age, SGA, sex, and family SES.

A second set of univariate and multivariate linear regression analyses tested the effect of motor problems at birth or at 5 months and receipt of physiotherapy on outcomes at 6 and 8 years. To test whether treatment with physiotherapy would affect the association between early motor problems and school-aged outcome, we included an interaction term 'motor problems * physiotherapy'.

Lastly, given that the referral to and treatment with physiotherapy may not be random in our observation study, and therefore related to initial motor problems, peri- and neonatal risk factors, and neurological impairments, we applied propensity score matching (PSM) using Stata statistical software (StataCorp, College Station, TX, USA). Propensity scores were estimated with a logistic regression of physiotherapy when compared with no physiotherapy on baseline characteristics (i.e., motor problem scores at birth and at 5 months, child biological characteristics, peri- and neonatal health and medical factors, early socio-environmental risk factors, and diagnosed neurological impairments in early childhood [e.g., cerebral palsy]; for details on baseline characteristics see Table S6). PSM allowed an unbiased estimate of receipt of physiotherapy/no receipt of physiotherapy with motor skills at 6 and 8 years. As a result, baseline characteristics were comparable between treatment groups (i.e., children who received physiotherapy and those who did not) (see Table 4). A radius algorithm was used to match each child who received physiotherapy with one or more children who did not receive physiotherapy with a similar propensity score. Children were excluded if a matching was not possible. The same PSM algorithm was subsequently applied to the other tested outcomes, i.e. cognitive function and attention regulation (Tables S7 and S8).

Results

Sample characteristics

Children with infant motor problems had a lower gestational age and birth weight than the comparison group (Table 1). They were also more often male, born SGA and more frequently born into a family with lower SES. Compared to children without or low motor problems, children with motor problems were more likely to have received physiotherapy between birth and age 56 months. However, while more than half of the children with motor problems received physiotherapy, the majority of children who received physiotherapy had no or low motor problems in infancy.

Effects of infant motor problems on childhood outcomes

Except for mental health, unadjusted and adjusted models showed that early motor problems at both time points (birth and 5 months, respectively) were negatively associated with childhood outcomes (Table 2). However, the association between early motor problems and later motor skill was not significant after adjusting for gestational age, SGA, sex, and SES.

Effects of infant motor problems and treatment with physiotherapy on childhood outcomes

Unadjusted models showed that the delivery of physiotherapy was negatively associated with all childhood outcomes (Table 3). In most adjusted models, i.e., considering infant motor problems and treatment with physiotherapy, the negative effects of both factors diminished but remained significant and independent of each other. However, the effect of motor problems measured at birth on motor skills at school-age was not significant in adjusted models. An interaction effect between motor problems at birth and receipt of physiotherapy was observed for attention regulation at school-age while the main effect of motor problems at birth was rendered not significant. This shows that children who received physiotherapy and those who had motor problems at birth *and* were treated with physiotherapy had poorer attention regulation, but not children who had motor problems only. No interaction effect was found between motor problems at 5 month and receipt of physiotherapy for motor skills and cognitive function at age 6 and 8 years.

Effects of treatment with physiotherapy on childhood outcomes after PSM

After accounting for imbalances in baseline characteristics (see Table 4) through PSM, the average treatment effect (ATE) of physiotherapy on motor skills and cognitive function at school-age was reduced and no longer significant (ATE on motor skill: -0.11, standard error: 0.10, t-statistic: -1.82, p=0.07; ATE on cognitive function: -0.19, standard error: 0.09, t-statistic: -1.80, p=0.07). However, the adverse effect on attention regulation remained significant (ATE: -0.07, standard error: 0.03, t-statistic: -2.12, p=0.03), but was small in magnitude.

Discussion

We found that children with motor problems in infancy were more likely to have lower motor and cognitive function, and lower attention regulation abilities at school-age, even after controlling for gestational age, SGA, sex, and family SES. Mental health was not associated with early motor problems. Physiotherapy neither improved nor reduced scores in school-aged motor and cognitive function after adjusting for imbalance in early motor scores and other baseline characteristics associated with receipt of physiotherapy. However, there remained a small adverse effect of receipt of physiotherapy on attention regulation.

Motor problems assessed in early infancy were associated with outcomes across multiple developmental domains at school-age. Compared with motor problems assessed at birth, motor problems measured at 5 months were more strongly associated with developmental outcomes at school-age. This has been previously observed [4] and may be attributed to a more detailed motor assessment enabled by the infant’s more frequent and versatile motor function at 5 months compared to motor function at birth.

The association between infant motor problems and school-aged motor skills were of a medium to large effect size. This finding is in line with previous at-risk, preterm population studies [4, 18], but in contrast to studies that included healthy low-risk children [2, 3]. It has been suggested that this discrepancy can be explained by a stronger effect of underlying medical or neurological problems on motor development in at-risk children, whereas the development of healthy low-risk children is instead influenced and shaped by experience and other environmental factors [19]. This may result in more catch-up development in low-risk children and a lower stability and poorer predictive value of early motor problems [19]. However, it has been argued that even if children with early motor problems eventually catch up with their peers, these early difficulties should still be considered as a 'marker' for other developmental outcomes outside the motor domain [20]. Indeed, a previous longitudinal study showed that early motor performance can initiate a developmental cascade that affects subsequent intellectual outcomes which in turn influences academic achievement in adolescence [21].

In this study, infant motor problems predicted later cognitive function and attention regulation. This is consistent with previous findings of an association between early motor problems and cognitive outcomes in childhood [2, 3, 5, 18]. Motor and cognitive development are also related in terms of brain functions as both domains use and rely on the same cortical and subcortical neural structures, in particular in early sensorimotor development [22].

Regarding mental health, previous findings are inconsistent, with some studies having provided evidence for an association between early motor function and later mental health [3] and others not [5]. Children with motor impairments, such as DCD, are more likely to have mental health problems, in particular anxiety, depression and ADHD [23]. However, this association may not be directly (or only) driven by the child's early motor problems but by other social-environmental difficulties, such as social exclusion or bullying, that mediate the effects of motor problems on later mental health [24]. Therefore, it may be possible that although mental health at school-age was not directly predicted by infant motor problems in our study, they may represent a starting point of a cascade of developmental and social difficulties that can affect mental health at a later age, and even into adulthood [25].

The unique aspect of this study is that it considered whether associations between early motor problems and multiple developmental outcomes at school-age were altered by treatment with physiotherapy. Children who received physiotherapy (N=372) had higher initial motor problem scores and poorer scores across neonatal child health and medical risk factors. Adjusting for imbalances in these baseline characteristics through PSM showed that receipt of physiotherapy neither negatively nor positively affected motor skills and cognitive function. Despite a small adverse effect on attention regulation that was below the level that is considered clinically relevant these results should be interpreted cautiously, particularly as observational studies that use PSM may still underestimate beneficial effects of treatment on outcomes (in contrast to a randomized controlled trial (RCT)) [26].

Overall, early treatment with physiotherapy was not found to improve motor skills into school-age – nor did it have a positive effect on other, related, developmental outcomes; at least not physiotherapy alone. As to the reason for this we can only speculate. Firstly, in this study physiotherapy may have been overprescribed or used as a preventative measure, as most children who received physiotherapy had no early motor problems. Secondly, the complexity of developmental and health problems in at-risk children who receive early intervention, including physiotherapeutic treatment, may impede the child’s ability and capacity to process information and profit from treatment adequately [27].

Despite its widespread use, previous research (including RCTs) has so far not been able to provide convincing support for physiotherapy as a treatment for sustained and long-term improvement of motor functioning for infants with a high biological risk or disability [6, 7, 28]. However, there is some evidence that intervention programs or activities that focus on supporting parents-infant relationships, target specific motor functions or promote infants' exploration and active motor behavior can have positive effects on motor development [28]. Future research should examine whether and how physiotherapeutic or other environmental factors that can influence children's everyday activity and learning, such as social relationships and parental support [29], may play an important role in the association between early motor development and subsequent outcomes.

The strengths of this study are its prospective longitudinal design, large sample size, the inclusion of children born across the whole gestation spectrum, and the evaluation of motor functioning via detailed physical and neurological examinations at birth and at 5 months. To test the potential moderating effect of treatment with physiotherapy on associations between early motor problems and later developmental outcomes, PSM was used to control for treatment bias. However, an RCT is needed to test the effectiveness of physiotherapy. There are also limitations. Referral for physiotherapy was reported by parents. Although parent reports are often used in general population samples, they may be biased. Further, some positive effects that result from treatment with physiotherapy (for example, compensations of atypical motor functioning) cannot be measured with standard motor functioning tests and may therefore be additionally assessed with participation or activity measures [23]. However, RCTs are the only known method to fully assess the effects of treatment with physiotherapy. Overall, whether the results of this study generalize beyond our at-risk sample requires testing. Due to medical advances and improvements in neonatal care, more at-risk children survive. However, findings from recent cohorts indicate that reduced mortality rates have not resulted in reduced prevalence rates of neurodevelopmental sequelae, including motor impairment [30].

To conclude, our findings show that infant motor problems are associated with developmental problems across motor, cognitive and attention domains into school-age, but not with mental health. No evidence for a beneficial effect of receipt of physiotherapy on developmental outcomes at school-age in children at risk for motor problems was found. This requires further investigation in a RCT.

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Conflicts of Interest Statement

None declared.

References

[1] A.J. Spittle, J. Orton, Cerebral palsy and developmental coordination disorder in children born preterm, Semin. Fetal Neonatal Med., 19 (2) (2014) 84-89. https://doi.org/10.1016/j.siny.2013.11.005.

[2] J.P. Piek, L. Dawson, L.M. Smith, N. Gasson, The role of early fine and gross motor development on later motor and cognitive ability, Hum. Mov. Sci., 27(5) (2008) 668-681. https://doi.org/10.1016/j.humov.2007.11.002.

[3] M.M. Hitzert, E. Roze, K.N. Van Braeckel, A.F. Bos, Motor development in 3-month-old healthy term-born infants is associated with cognitive and behavioural outcomes at early school age, Dev. Med. Child Neurol., 56(9) (2014) 869-76. https://doi.org/10.1111/dmcn.12468.

[4] A.J. Spittle, M.M. Spencer-Smith, J.L. Cheong, A.L. Eeles, K.J. Lee, P.J. Anderson, L.W. Doyle, General movements in very preterm children and neurodevelopment at 2 and 4 years, Pediatrics, 132(2) (2013) e452-8. https://doi.org/10.1542/peds.2013-0177.

[5] P.R. Butcher, K. van Braeckel, A. Bouma, C. Einspieler, E.F. Stremmelaar, A.F. Bos, The quality of preterm infants' spontaneous movements: an early indicator of intelligence and behaviour at school age, J. Child Psychol. Psychiatry, 50(8) (2009) 920-30. https://doi.org/10.1111/j.1469-7610.2009.02066.x.

[6] A. Herskind, G. Greisen, J.B. Nielsen, Early identification and intervention in cerebral palsy, Dev. Med. Child Neurol., 57(1) (2015) 29-36. https://doi.org/10.1111/dmcn.12531.

[7] G.T. Brown, S.A. Burns, The Efficacy of Neurodevelopmental Treatment in Paediatrics: a Systematic Review, Br. J. Occup. Ther., 64(5) (2001) 235-244. https://doi.org/10.1177/030802260106400505.

[8] Spittle, A. and C. Morgan, Early Intervention for Children with Cerebral Palsy, in: C.P. Panteliadis (Eds.), Cerebral Palsy: A Multidisciplinary Approach, Springer International Publishing, Cham, 2018, pp. 193-200.

[9] G.P. Aylward, Developmental screening and assessment: what are we thinking? J. Dev. Behav. Pediatr., 30(2) (2009) 169-73. https://doi.org/10.1097/DBP.0b013e31819f1c3e.

[10] N. Baumann, J. Tresilian, K. Heinonen, K. Raikkonen, D. Wolke, Predictors of early motor trajectories from birth to 5 years in neonatal at-risk and control children, Acta Paediatr., 109(4) (2020) 728-37. https://doi.org/10.1111/apa.14985.

[11] J. Jaekel, N. Baumann, D. Wolke, Effects of Gestational Age at Birth on Cognitive Performance: A Function of Cognitive Workload Demands, Plos One, 8(5) (2013) e65219. https://doi.org/10.1371/journal.pone.0065219.

[12] H. Prechtl, The neurological examination of the full term newborn infant (Second Edition), Clinics in Developmental Medicine No. 63, Spastics International Medical Publications, London, 1977.

[13] R. Blank, B. Smits-Engelsman, H. Polatajko, P. Wilson, European Academy for Childhood Disability (EACD): Recommendations on the definition, diagnosis and intervention of developmental coordination disorder (long version), Dev. Med. Child Neurol., 54(1) (2012) 54-93. https://doi.org/10.1111/j.1469-8749.2011.04171.x.

[14] D. Stott, F. Moyes, S. Henderson, Henderson revision of the Stott-Moyes-Henderson Test of Motor Impairment, Brook Educational Publishing Ltd., Ontario,1984.

[15] T.M. Achenbach, The Manual for the Child Behavior Checklist/ 4-18 and 1991 Profile, University of Vermont, Department of Psychiatry, Burlington, VT, 1991.

[16] P. Melchers, U. Preuss, K-ABC: Kaufman Battery for Children: Deutschsprachige Fassung, Swets & Zeitlinger, Frankfurt am Main, 1991.
[17] J. Jaekel, D. Wolke, P. Bartmann, Poor attention rather than hyperactivity/impulsivity predicts academic achievement in very preterm and fullterm adolescents, Psychol. Med., 43(1) (2013) 183-196. https://doi.org/10.1017/S0033291712001031.
[18] Y.-H, Su, S.-F. Jeng, W.-S. Hsieh, Y.-K. Tu, Y.-T. Wu, L.-C. Chen, Gross Motor Trajectories During the First Year of Life for Preterm Infants With Very Low Birth Weight, Phys. Ther., 97(3) (2017) 365-373. https://doi.org/10.1093/ptj/pzx007.
[19] O.G. Jenni, A. Chaouch, J. Caflisch, V. Rousson, Infant motor milestones: poor predictive value for outcome of healthy children, Acta Paediatr.,102(4) (2013) e181-4. https://doi.org/10.1111/apa.12129.
[20] M.B. Denckla, Why assess motor functions "early and often?", Ment. Retard. Dev. Disabil. Res. Rev., 11(1) (2005) 3. https://doi.org/10.1002/mrdd.20054.
[21] M.H. Bornstein, C.S. Hahn, J.T. Suwalsky, Physically developed and exploratory young infants contribute to their own long-term academic achievement, Psychol. Sci., 24(10) (2013) 1906-17. https://doi.org/10.1177/0956797613479974.
[22] M.M. Pangelinan, G. Zhang, J.W. VanMeter, J.E. Clark, B.D. Hatfield, A.J. Haufler, Beyond age and gender: relationships between cortical and subcortical brain volume and cognitive-motor abilities in school-age children, Neuroimage, 54(4) (2011) 3093-100. https://doi.org/10.1016/j.neuroimage.2010.11.021.
[23] R. Blank, A. L. Barnett, J. Cairney, D. Green, A. Kirby, H. Polatajko, S. Rosenblum, B. Smits-Engelsman, D. Sugden, P. Wilson, S. Vincon, International clinical practice recommendations on the definition, diagnosis, assessment, intervention, and psychosocial aspects of developmental coordination disorder, Dev. Med. Child Neurol., 61(3) (2019) 242-285. https://doi.org/10.1111/dmcn.14132.
[24] R. Lingam, M.J. Jongmans, M. Ellis, L.P. Hunt, J. Golding, A. Emond. Mental Health Difficulties in Children With Developmental Coordination Disorder, Pediatrics, 129(4) (2012) E882-E891. https://doi.org/10.1542/peds.2011-1556.
[25] A.M.W. Laerum, S.K. Reitan, K.A. I. Evensen, S. Lydersen, A.M. Brubakk, J. Skranes, M.S. Indredavik, Psychiatric symptoms and risk factors in adults born preterm with very low birthweight or born small for gestational age at term, BMC Psychiatry, 19(1) (2019) 223. https://doi.org/10.1186/s12888-019-2202-8.
[26] Z. Zhang, H. Ni, X. Xu, Observational studies using propensity score analysis underestimated the effect sizes in critical care medicine, J. Clin. Epidemiol., 67(8) (2014) 932-9. https://doi.org/10.1016/j.jclinepi.2014.02.018.
[27] H. Als, NIDCAP: testing the effectiveness of a relationship-based comprehensive intervention, Pediatrics, 124(4) (2009) 1208-10. https://doi.org/10.1542/peds.2009-1646.
[28] A.J. Hughes, S.A. Redsell, C. Glazebrook, Motor Development Interventions for Preterm Infants: A Systematic Review and Meta-analysis, Pediatrics, 138(4) (2016) e20160147. https://doi.org/10.1542/peds.2016-0147.
[29] A. Spittle, K. Treyvaud, The role of early developmental intervention to influence neurobehavioral outcomes of children born preterm, Semin. Perinatol., 40(8) (2016) 542-48. https://doi.org/10.1053/j.semperi.2016.09.006.
[30] A.J. Spittle, K. Cameron, L.W. Doyle, J.L. Cheong, Motor Impairment Trends in Extremely Preterm Children: 1991-2005, Pediatrics, 141(4) (2018) e20173410. https://doi.org/10.1542/peds.2017-3410.

Table 1. Sample characteristics according to status of motor problems at birth and at 5 months

	Motor problems at birth			Motor problems at 5 months		
	No/low motor problems	Motor problems	p-value	No/low motor problems	Motor problems	p-value
	N=1171 (85.2%)	N=203 (14.8%)		N=1175 (85.5%)	N=199 (14.5%)	
Gestational age (GA)	37.25 (3.73)	33.81 (4.26)	**<0.001**	37.14 (3.80)	34.34 (4.33)	**<0.001**
Birth weight (grams)	2797 (902)	2001 (886)	**<0.001**	2774 (906)	2121 (966)	**<0.001**
Small for GA	266 (22.7%)	76 (37.4%)	**<0.001**	271 (23.1%)	71 (35.7%)	**<0.001**
Male sex	572 (48.8%)	119 (58.6%)	**0.010**	579 (49.3%)	112 (56.3%)	0.068
SES at birth			0.119			**<0.001**
High	355 (30.3%)	55 (27.1%)		374 (31.8%)	36 (18.1%)	
Middle	441 (37.7%)	68 (33.5%)		434 (36.9%)	75 (37.7%)	
Low	375 (32.0%)	80 (39.4%)		367 (31.2%)	88 (44.2%)	
Physiotherapy						
At 5, 20 or 56 months	259 (22.1%)	113 (55.7%)	**<0.001**	257 (21.9%)	115 (57.8%)	**<0.001**

Note. Mean (SD) or N (%)

Table 2. Unadjusted and adjusted associations between motor problems (MP) at birth (Model 1) and 5 months (Model 2), and childhood outcomes at 6 and 8 years

	Unadjusted effect				Adjusted effect[a]			
	B	95% CI	β	p-value	B	95% CI	β	p-value
Motor skills at 6 & 8 years								
Model 1: MP at birth	-0.35	(-0.51, -0.18)	-0.12	**<0.001**	-0.06	(-0.23, 0.10)	-0.02	0.459
Model 2: MP at 5 months	-0.81	(-0.98, -0.65)	-0.27	**<0.001**	-0.58	(-0.74, -0.41)	-0.20	**<0.001**
Mental health at 6 & 8 years								
Model 1: MP at birth	-0.01	(-0.16, 0.15)	-0.00	0.926	-	-	-	-
Model 2: MP at 5 months	-0.07	(-0.23, 0.09)	-0.03	0.377	-	-	-	-
Cognitive function at 6 & 8 years								
Model 1: MP at birth	-0.48	(-0.63, -0.32)	-0.17	**<0.001**	-0.16	(-0.31, -0.00)	-0.06	**0.044**
Model 2: MP at 5 months	-0.59	(-0.75, -0.44)	-0.21	**<0.001**	-0.30	(-0.45, -0.15)	-0.10	**<0.001**
Attention regulation at 6 & 8 years								
Model 1: MP at birth	-0.18	(-0.24, -0.12)	-0.16	**<0.001**	-0.08	(-0.14, -0.02)	-0.07	**0.005**
Model 2: MP at 5 months	-0.20	(-0.26, -0.14)	-0.18	**<0.001**	-0.10	(-0.16, -0.04)	-0.09	**0.001**

[a] Adjusted for gestational age, small for gestational age, male sex, and socioeconomic status.

Table 3. Unadjusted and adjusted associations between motor problems (MP) at birth (Model 1) and 5 months (Model 2), receipt of physiotherapy (PT) and childhood outcomes at 6 and 8 years

	Unadjusted effect				Adjusted effect[a]				Adjusted effect + interaction[b]			
	B	95% CI	β	p-value	B	95% CI	β	p-value	B	95% CI	β	p-value
Motor skills at 6 & 8 years												
Model 1:												
MP	-0.35	(-0.51, -0.18)	-0.12	**<0.001**	-0.16	(-0.33, 0.06)	-0.06	0.059	-0.08	(-0.31, 0.15)	-0.03	0.478
PT	-0.62	(-0.74, -0.49)	-0.27	**<0.001**	-0.58	(-0.72, -0.45)	-0.25	**<0.001**	-0.55	(-0.70, -0.40)	-0.24	**<0.001**
Interaction: MP*PT	-	-	-	-	-	-	-	-	-0.17	(-0.50, 0.17)	-0.04	0.325
Model 2:												
MP	-0.81	(-0.98, -0.65)	-0.27	**<0.001**	-0.64	(-0.81, -0.47)	-0.22	**<0.001**	-0.52	(-0.76, -0.28)	-0.18	**<0.001**
PT	-0.62	(-0.74, -0.49)	-0.27	**<0.001**	-0.48	(-0.61, -0.35)	-0.21	**<0.001**	-0.43	(-0.58, -0.29)	-0.19	**<0.001**
Interaction: MP*PT	-	-	-	-	-	-	-	-	-0.25	(-0.59, 0.09)	-0.07	0.146
Cognitive function at 6 & 8 years												
Model 1:												
MP	-0.48	(-0.63, -0.32)	-0.17	**<0.001**	-0.29	(-0.45, -0.13)	-0.10	**<0.001**	-0.18	(-0.19, -0.04)	-0.06	0.109
PT	-0.61	(-0.73, -0.49)	-0.27	**<0.001**	-0.55	(-0.67, -0.42)	-0.24	**<0.001**	-0.50	(-0.63, -0.38)	-0.22	**<0.001**
Interaction: MP*PT	-	-	-	-	-	-	-	-	-0.22	(-0.20, 0.03)	-0.06	0.178
Model 2:												
MP	-0.59	(-0.75, -0.44)	-0.21	**<0.001**	-0.40	(-0.56, -0.24)	-0.14	**<0.001**	-0.46	(-0.69, -0.23)	-0.16	**<0.001**
PT	-0.61	(-0.73, -0.49)	-0.27	**<0.001**	-0.52	(-0.64, -0.39)	-0.23	**<0.001**	-0.54	(-0.68, -0.40)	-0.24	**<0.001**
Interaction: MP*PT	-	-	-	-	-	-	-	-	0.11	(-0.21, 0.43)	0.03	0.494
Attention regulation at 6 & 8 years												
Model 1:												

	Unadjusted effect				Adjusted effect[a]				Adjusted effect + interaction[b]			
	B	95% CI	β	p-value	B	95% CI	β	p-value	B	95% CI	β	p-value
MP	-0.18	(-0.24, -0.12)	-0.16	<**0.001**	-0.12	(-0.18, -0.06)	-0.11	<**0.001**	-0.04	(-0.12, 0.04)	-0.04	0.354
PT	-0.20	(-0.25, -0.16)	-0.23	<**0.001**	-0.18	(-0.22, -0.13)	-0.20	<**0.001**	-0.14	(-0.20, -0.09)	-0.16	<**0.001**
Interaction: MP*PT	-	-	-	-	-	-	-	-	-0.17	(-0.29, -0.05)	-0.12	**0.005**
Model 2:												
MP	-0.20	(-0.26, -0.14)	-0.18	<**0.001**	-0.14	(-0.20, -0.08)	-0.12	<**0.001**	-0.12	(-0.20, -0.03)	-0.11	**0.006**
PT	-0.20	(-0.25, -0.16)	-0.23	<**0.001**	-0.17	(-0.22, -0.12)	-0.19	<**0.001**	-0.17	(-0.22, -0.11)	-0.19	<**0.001**
Interaction: MP*PT	-	-	-	-	-	-	-	-	-0.04	(-0.16, 0.08)	-0.03	0.541

[a] Adjusted for both predictors.

[b] Adjusted for both predictors and interaction term 'MP * PT'.

Table 4. Means and prevalence of baseline covariates of children who received physiotherapy versus those who received no physiotherapy before and after propensity score matching (PSM) for childhood outcome 'Motor skill at 6 and 8 years'

	Physiotherapy unmatched: n=271 matched: n=245	No Physiotherapy unmatched: n=800 matched: n=768	Standardized bias (%)
Initial motor problem scores			
Motor problems at birth (z-score), mean			
Unmatched	0.39	-0.22	63.5
Matched	0.24	0.17	7.3
Motor problems at 5 months (z-score), mean			
Unmatched	0.49	-0.22	75.8
Matched	0.27	0.28	0.0
Child biological characteristics			
Gestational age (weeks), mean			
Unmatched	34.34	37.73	-84.6
Matched	34.82	35.23	-10.4
Birthweight (g), mean			
Unmatched	2182	2895	-77.9
Matched	2263	2289	-2.9
Small for gestational age, %			
Unmatched	32.8	20.8	27.5
Matched	32.7	34.3	-3.5
Head circumference (cm), mean			
Unmatched	30.82	33.34	-75.0
Matched	31.19	31.31	-3.5
Male sex, %			
Unmatched	57.2	48.4	17.7
Matched	56.7	58.1	-2.8
Multiples, %			
Unmatched	12.5	5.4	25.3
Matched	12.7	10.8	6.6
Peri- and neonatal health and medical factors			
Pre-pregnancy complications			
Unmatched	1.23	1.20	4.1
Matched	1.22	1.24	-1.6
Complications during pregnancy			
Unmatched	1.60	1.24	29.3
Matched	1.59	1.58	0.4

	Physiotherapy unmatched: n=271 matched: n=245	No Physiotherapy unmatched: n=800 matched: n=768	Standardized bias (%)
Complications during birth			
Unmatched	3.81	2.93	50.9
Matched	3.76	3.73	1.7
Neonatal complications			
Unmatched	6.57	3.42	86.6
Matched	6.08	5.73	9.7
Neonatal neurological problems, mean			
Unmatched	8.12	3.91	84.4
Matched	7.48	6.98	10.0
Duration in hospital (days), mean			
Unmatched	49.14	20.72	68.9
Matched	43.94	47.55	-8.8
Early socio-environmental factors			
Socioeconomic status, %			
Middle			
Unmatched	32.5	37.1	-9.8
Matched	32.2	29.6	5.6
Low			
Unmatched	36.5	29.5	15.0
Matched	36.7	38.1	-2.8
No breastfeeding, %			
Unmatched	52.8	39.0	27.9
Matched	51.0	53.0	-3.9
Neurological impairments diagnosed in early childhood[a]			
Severe neurological impairments at 56 months, %			
Unmatched	5.5	0.6	28.7
Matched	2.8	2.7	1.2

Note. Mean bias (%): unmatched=47.4, matched=4.6; For a detailed description of covariates (i.e., child biological characteristics, peri-and neonatal health and medical factors, early socio-environmental factors, and neurological impairments diagnosed in early childhood) see Table S6 (supporting information).

[a] Severe neurological impairments were diagnosed by pediatricians at 56 months and include cerebral palsy (CP), epilepsy, hydrocephalus, blindness, or deafness (not corrected or insufficiently corrected).