Development of fine motor skills in preterm infants

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ABBREVIATIONS

ASQ	Ages and Stage Questionnaire
BOTMP	Bruininks–Oseretsky Test of Motor Proficiency
MABC	Movement Assessment Battery for Children

Fine motor skills are related to functioning in daily life and at school. We reviewed the status of knowledge, in preterm children, on the development of fine motor skills, the relation with gross motor skills, and risk factors for impaired fine motor skills.
We searched the past 15 years in PubMed, using ['motor skills' or 'fine motor function' and 'preterm infant'] as the search string. Impaired gross and fine motor skills are among the most frequently occurring problems encountered by preterm children who do not develop cerebral palsy.
The prevalence is around 40% for mild to moderate impairment and 20% for moderate impairment. Fine motor skill scores on the Movement Assessment Battery for Children are about 0.62 of a standard deviation lower compared with term children. Risk factors for fine motor impairments include moderately preterm birth (odds ratio [OR] 2.0) and, among very preterm children (<32wk gestation), intra-uterine growth restriction (ORs 2–3), inflammatory conditions (late-onset sepsis and necrotizing enterocolitis, ORs 3–5), and dexamethasone therapy for bronchopulmonary dysplasia (OR 2.7).
A better understanding of factors that play a role in the development of and recovery from brain injury could guide future intervention attempts aimed at improving fine motor skills of preterm children.

Survival rates of preterm infants have improved during recent decades, and this tendency is continuing. During the same period, the prevalence of major impairments has remained relatively constant or even decreased,[1] but the prevalence of milder dysfunctions is high,[2,3] with a tendency to increase.[4,5] This mainly appears to be the result of the increased survival of very preterm infants (gestational age <32wk), although more sensitive testing may also play a role.[5]

Cognitive, behavioural, and mild motor problems without major motor deficits are by now the most dominant neurodevelopmental sequelae in children born preterm, with prevalences reported up to 50 to 70%.[5] These 'high prevalence, low severity' impairments often do not occur in isolation and may considerably hamper the children's functional abilities in daily life.[6,7]

Among the most frequently occurring problems encountered by preterm children who do not develop cerebral palsy (CP), are impaired gross and fine motor skills.[2,4] Because particularly fine motor skills are related to adequate functioning in daily life and at school, our aim was to review the current status of knowledge, in preterm children, on the development of fine motor skills, the relation with gross motor skills, and risk factors for impaired fine motor skills. To this end, we searched PubMed for relevant articles.

Impairments in fine motor skills may hamper various aspects of daily functioning such as getting dressed, lacing shoes, eating, and writing. In preterm children without CP, it has been shown that poor fine motor skills affect the learning of writing skills.[8] During school time, children spend 30 to 60% of the day performing fine motor tasks.[9] Not surprisingly, impaired fine motor skills have a negative influence on school performance and academic achievement.[10]

METHOD

Selection of articles

We searched PubMed for all articles from the past 15 years, using the combination ['motor skill' or 'fine motor function' and 'preterm infant'] as search string. We limited our search to articles in English, with age ranges of the children between 1 month and 12 years. This revealed 231 articles. Based on title and abstract, we selected 52 articles fitting our aim. We selected an additional 21 articles by checking the references of these articles. As far as possible we tried to select those studies excluding children with CP, to limit our discussion on the findings on fine motor skills in children without CP. In some articles, however, it was not clear whether children with CP were included or not. Even so, if children with CP were included in these studies, they would only have changed the prevalences slightly. Children with CP make up 5 to 10% of preterm cohorts;[1] those with severe CP are often excluded from testing or were not able to perform the tests. Thus, if our prevalences are overestimations, then they are only slightly so.

Tests to assess fine motor skills at school age

Here, we review the way in which most clinically and epidemiologically oriented studies assess fine motor function. Assessing fine motor skills accurately is a challenge, because many fine motor tasks require not only manual abilities but also appropriate perceptual skills, motor planning, as well as intact and rapid tactile, kinaesthetic, and visual feedback information processing for bilateral visual–motor coordination.[10] These skills are often not measured separately and therefore cannot be accounted for when interpreting fine motor skill test results.

Currently, the Movement Assessment Battery for Children (MABC)[11] is the most widely used test to investigate fine motor skills at school age in preterm children.[4] The MABC is a test battery assessing fine motor skills (manual dexterity), balance, and ball skills. For each of these domains, there are multiple subtests. Fine motor skills are assessed using two subtests of speed and accuracy of finger movements, for example inserting pegs in a pegboard or screwing a screw on a bolt, and one subtest of accuracy, for example drawing a line between two closely positioned lines forming a flower. Another frequently used test is the Bruininks–Oseretsky Test of Motor Proficiency (BOTMP),[12] which assesses a broad array of skills involving fine manual control, for example cutting out a circle and connecting dots, and manual coordination, for example transferring pennies and stringing blocks. Finally, the Jebsen Hand Function Test[13] is widely used in rehabilitation research. This test consists of seven timed subtests such as writing, turning over cards, and picking up light and heavy objects.

RESULTS

Prevalence of fine motor impairments

The prevalence of motor skill impairment (i.e. both gross and fine motor skills) in very preterm children without CP is estimated around 40% for mild and moderate impairment (defined as <15th centile [<P15] on standardized tests, e.g. the MABC) and 20% for moderate impairment (defined as <5th centile [<P5]).[4] This is several times more than in typically developing children, because P15 and P5 represent at least 15% and 5% of the population of typically developing children having a mild and moderate motor impairment respectively. Mild impairments may affect a wide array of activities of daily functioning, and a close relation exists between motor skill impairment (<P15 on the MABC) and developmental coordination disorder.[14] A recent meta-analysis of 41 studies on motor development in very preterm children, born with a gestational age younger than 32 weeks, reported that effect sizes of impairment of motor skills are approximately 0.57 to 0.88 of a standard deviation for the MABC and 0.51 to 0.94 for the BOTMP.[2]

Gross motor and fine motor skills are more or less equally affected, with scores on the MABC being 0.62 of a standard deviation lower for fine motor skills, 0.77 lower for balance skills, and 0.34 lower for ball skills.[2] For the subscales of the BOTMP, fine motor skills were slightly more affected than gross motor skills, with 0.86 of a standard deviation lower for fine motor skills, and 0.53 for gross motor skills.[2]

Specific risk factors for impaired fine motor skills at school age in very preterm infants

Most studies have reported on outcomes of very preterm children. Among these children, several studies have reported on risk factors being associated with an increased prevalence of in particular fine motor skill impairments at school age. These risk factors include intra-uterine growth restriction,[15,16] severe infections,[17–19] and bronchopulmonary dysplasia.[20–22]

Intra-uterine growth restriction

Intra-uterine growth restriction has long been identified as a risk factor for a wide variety of developmental problems in term and preterm children.[23] In particular, children born very preterm with intra-uterine growth restriction are at increased risk, not only for motor problems but also for behavioural and cognitive impairments.[15,16] Recently, it has been reported that the prevalence of fine motor impairments (using the MABC <P15 as a cut-off point) is increased in very preterm children with growth restriction compared with non-growth-restricted preterm children (68% vs 43%; Fig. 1a).[16] Of the motor domains, only fine motor skills were affected.[17] Intra-uterine growth restriction increases the risk of fine motor skill impairments, with raw and adjusted ORs around 2 to 3. The prevalence of motor skill impairments, however, is high in both groups, as very preterm birth in itself is associated with poor motor skills. Apart from fine motor skills, attention appeared to be the only other neuropsychological domain that is affected more in very preterm children with intra-uterine growth restriction.[16]

What this paper adds

- Preterm infants, even those born moderately preterm, are at risk of impaired fine motor development.
- In very preterm infants, the prevalence of fine motor skill impairments is between 40% and 60% for mild to moderate impairment.
- Risk factors include intra-uterine growth restriction, inflammatory conditions, and bronchopulmonary dysplasia.
- Future studies should focus on intervention strategies, through understanding of factors involved in the pathogenesis of and recovery from brain injury.

Infections and necrotizing enterocolitis

Inflammatory conditions during the preterm period, such as those present during severe infections and necrotizing enterocolitis, have recently been identified as risk factors for impaired motor, cognitive, and developmental outcomes in very preterm infants.[17,24] Again, fine motor skills in particular seem to be more affected in these children. In a recent case–control study of late-onset sepsis in very preterm infants, van der Ree et al.[19] reported an increased prevalence of impaired outcomes on several domains compared with gestational age-matched comparison infants, including intelligence, attention, motor skills, and verbal memory. Motor skills, particularly fine motor skills, are impaired, with the prevalence being 68% compared with 28% in comparison infants (Fig. 1b). Similar findings were reported by Roze et al.[18] in a case–control study of preterm children with necrotizing enterocolitis or intestinal perforation. Domains that showed an increased prevalence of impairments in these children included intelligence, attention, visual perception, and motor skills. The prevalence of impaired fine motor skills is 60% in children with necrotizing enterocolitis or intestinal perforation, and 33% in preterm comparison children (Fig. 1c). These inflammatory conditions thus lead to a considerable increased risk of impairment of fine motor skills, with ORs between 3 and more than 5.[18,19] These studies suggest a relation between abnormal outcomes and white matter injury due to an inflammatory response.[17]

Bronchopulmonary dysplasia and dexamethasone treatment

Bronchopulmonary dysplasia is a well-known risk factor for impaired cognitive and motor development in very preterm children.[20] It has been reported that impaired fine motor skills are related to the severity of bronchopulmonary dysplasia, reflected in the duration of oxygen treatment.[21] Treatment with systemic corticosteroids of children with bronchopulmonary dysplasia, in particular dexamethasone, is another risk factor for development of severe motor disorders such as CP.[25] Recently, data have been presented on a case–control study of preterm children with bronchopulmonary dysplasia who had been treated with dexamethasone.[22] Domains affected in these children included intelligence and motor skills. The prevalence of fine motor skill impairments was 72% in children treated with dexa-

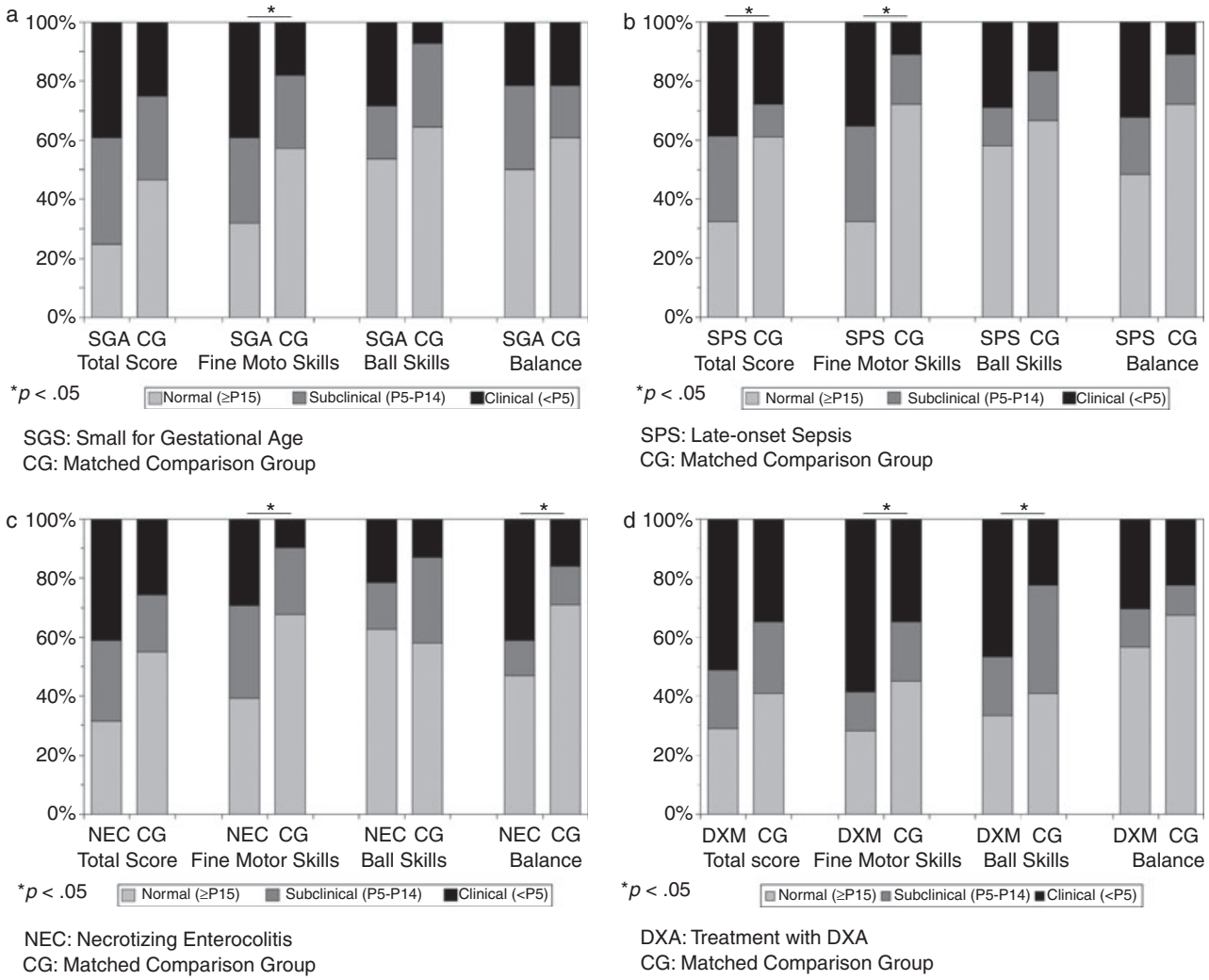

Figure 1: Distribution of motor outcomes according to the Movement Assessment Battery for Children of very preterm children with various complications versus a matched comparison group (CG); *p<0.05, unadjusted for confounders. Groups were as follows: (a) very preterm children born small for gestational age (SGA, n=28) versus a very preterm comparison group (CG, n=28); (b) very preterm children with late-onset sepsis (SPS, n=31) versus very preterm children without sepsis (CG, n=18); (c) preterm children with necrotizing enterocolitis or intestinal perforation (NEC, n=51) versus a preterm comparison group (CG, n=31); (d) very preterm children at risk of bronchopulmonary dysplasia, treated with dexamethasone (DXA, n=45) versus a very preterm comparison group (CG, n=49). P, centile.

methasone, and 55% in matched comparison children (Fig. 1d).[22] Compared with the control group, treatment with dexamethasone increased the risk of fine motor impairment (OR 2.7), but the significance was lost after adjustment for bronchopulmonary dysplasia. These data, therefore, suggest that illness severity, including bronchopulmonary dysplasia, may pose an additional risk for impaired fine motor outcomes, beyond that of dexamethasone treatment.

Moderately preterm birth as risk factor for impaired fine motor skills

For moderately preterm birth (32–36wk gestation), evidence is emerging that the risk of developmental problems is increased.[26] Using the Ages and Stage Questionnaire (ASQ), filled out by parents at the age of 4 years, Kerstjens et al.[26] demonstrated a twofold increased risk for an abnormal total score on the ASQ (adjusted OR 2.1). For the motor domains of the ASQ, both moderately and very preterm children had increased risks of fine motor problems compared with term children (ORs 2.0 and 3.6, respectively). Moderately preterm children, however, did not have a greater risk of problems with gross motor functioning (OR 1.3), whereas very preterm children did (OR 3.5).[26] Apparently, fine motor skills are more vulnerable than gross motor skills, at least for birth within the moderately preterm gestational age range. It has to be noted that lower scores on the ASQ suggest motor impairment, but do not necessarily ascertain that it is actually present. Thus, more observational studies are needed to confirm these findings. In fact, a follow-up study of this cohort was unable to find differences anymore, testing the children at 7 years using the MABC.[27]

Pathogenesis

The pathogenesis of fine motor impairments in preterm infants is gradually being elucidated. Global, diffuse white matter injury is the most common type of brain injury in the preterm infant.[24] Pre-oligodendrocytes are the principal cellular target in cerebral white matter injury leading to this type of brain injury and subsequently to impairment in motor functioning in pre-

term infants. This accounts for both gross and fine motor skills. Primary injury to pre-oligodendrocytes relates to a confluence of maturation-dependent characteristics that render these cells vulnerable to two principal upstream mechanisms: hypoxia–ischemia and systemic infection or inflammation.[17] These upstream mechanisms converge on three interacting downstream mechanisms: microglial activation, excitotoxicity, and, ultimately, free radical attack, which contribute to neuronal damage. As every preterm infant is subjected to various degrees of hypoxia–ischemia and inflammation, and because particularly fine motor behaviour requires an integrated, highly efficient brain network to feed online sensory information from multiple sensory cortices to the motor cortex rapidly, the preterm child's increased susceptibility to white matter damage may easily affect the development of such networks. This may explain why the rate of these 'low severity' impairments in fine motor skills is so high. Specific types of brain injury, such as haemorrhages and ischemic lesions, which affect the motor cortex and corticospinal tract, may further contribute to impairments in fine motor networks.[24]

Finally, preterm children often exhibit impairments in multiple developmental domains such as executive functions, visual perception, and visual–spatial information processing.[7] This complex neurocognitive profile of comorbidities in multiple domains may further worsen performance of fine motor tasks in daily life.

CONCLUSIONS AND IMPLICATIONS FOR PRACTICE

The prevalence of fine motor skill impairments in very preterm infants lies between 40 and 60%, with scores on standardized tests approximately two-thirds of a standard deviation lower than the norm population. Preterm infants (even those who are born after 32wk gestation) are at risk for impaired motor development. Additional risk factors for impaired fine motor skills in these children include intra-uterine growth restriction, inflammatory conditions, and bronchopulmonary dysplasia. A better understanding of factors that play a role in the development and recovery from brain injury could guide future prevention and intervention attempts aimed at improving motor skills of preterm children. Prevention of moderately preterm birth, intra-uterine growth restriction, inflammatory conditions, and bronchopulmonary dysplasia is pivotal. Potential therapeutic interventions to improve outcome include strategies providing neuroprotection, neural recovery, or neurogenesis by means of cerebral plasticity. They can be deployed at a neurobiological level such as administrating anti-inflammatory and anti-apoptotic drugs, growth factors, and hypothermia in the early neonatal period after perinatal brain injury. Additionally, numerous studies have developed a variety of intervention strategies at a functional level. Examples are interventions on handwriting skills in children with fine motor impairments that show encouraging results.[10] Future research should investigate which newborn infants at risk for adverse outcome will benefit most from these intervention strategies, which aspects of the different programs are most effective, and how these programmes can be implemented cost-effectively.

CONFLICTS OF INTEREST

None of the authors has any potential conflicts of interest.

REFERENCES

1. Himmelmann K, Hagberg G, Uvebrant P. The changing panorama of cerebral palsy in Sweden. X. Prevalence and origin in the birth-year period 1999–2002. *Acta Paediatr* 2010; **99**: 1337–43.
2. de Kieviet JF, Piek JP, Aarnoudse-Moens CS, Oosterlaan J. Motor development in very preterm and very low-birth-weight children from birth to adolescence: a meta-analysis. *JAMA* 2009; **302**: 2235–42.
3. Aarnoudse-Moens CS, Weisglas-Kuperus N, van Goudoever JB, Oosterlaan J. Meta-analysis of neurobehavioral outcomes in very preterm and/or very low birth weight children. *Pediatrics* 2009; **124**: 717–28.
4. Williams J, Lee KJ, Anderson PJ. Prevalence of motor-skill impairment in preterm children who do not develop cerebral palsy: a systematic review. *Dev Med Child Neurol* 2010; **52**: 232–7.
5. zAylward GP. Neurodevelopmental outcomes of infants born prematurely. *J Dev Behav Pediatr* 2005; **26**: 427–40.
6. Bos AF, Roze E. Neurodevelopmental outcome in preterm infants. *Dev Med Child Neurol* 2011; **53**(Suppl. 4): 35–9.
7. Potharst ES, van Wassenaer AG, Houtzager BA, van Hus JW, Last BF, Kok JH. High incidence of multi-domain disabilities in very preterm children at five years of age. *J Pediatr* 2011; **159**: 79–85.
8. Feder KP, Majnemer A, Bourbonnais D, Platt R, Blayney M, Synnes A. Handwriting performance in preterm children compared with term peers at age 6 to 7 years. *Dev Med Child Neurol* 2005; **47**: 163–70.
9. McHale K, Cermak SA. Fine motor activities in elementary school: preliminary findings and provisional implications for children with fine motor problems. *Am J Occup Ther* 1992; **46**: 898–903.
10. Feder KP, Majnemer A. Handwriting development, competency, and intervention. *Dev Med Child Neurol* 2007; **49**: 312–7.
11. Henderson SE, Sugden DA. Movement Assessment Battery for Children. Kent, UK: The Psychological Corporation, 1992.
12. Bruininks-Oseretsky R. Test of Motor Proficiency: Examiner's Manual. Circle Pines, MN: American Guidance Service, 1978.
13. Jebsen RH, Taylor N, Trieschmann RB, Trotter MJ, Howard LA. An objective and standardised test of hand function. *Arch Phys Med Rehabil* 1969; **50**: 311–9.
14. Goyen TA, Lui K. Developmental coordination disorder in "apparently normal" schoolchildren born extremely preterm. *Arch Dis Child* 2009; **94**: 298–302.
15. Raz S, Debastos AK, Newman JB, Batton D. Intrauterine growth and neuropsychological performance in very low birth weight preschoolers. *J Int Neuropsychol Soc* 2012; **18**: 200–11.
16. Tanis JC, van der Ree MH, Roze E, et al. Functional outcome of very preterm-born and small for gestational age children at school age. *Pediatr Res* 2012; **72**: 641–8.
17. Shah DK, Doyle LW, Anderson PJ, et al. Adverse neurodevelopment in preterm infants with postnatal sepsis or necrotizing enterocolitis is mediated by white matter abnormalities on magnetic resonance imaging at term. *J Pediatr* 2008; **153**: 170–5 e1.
18. Roze E, Ta BD, van der Ree MH, et al. Functional impairments at school age of children with necrotizing enterocolitis or spontaneous intestinal perforation. *Pediatr Res* 2011; **70**: 619–25.
19. van der Ree M, Tanis JC, Van Braeckel KN, Bos AF, Roze E. Functional impairments at school age of preterm born children with late-onset sepsis. *Early Hum Dev* 2011; **87**: 821–6.
20. Majnemer A, Riley P, Shevell M, Birnbaum R, Greenstone H, Coates AL. Severe bronchopulmonary dysplasia increases risk for later neurological and motor sequelae in preterm survivors. *Dev Med Child Neurol* 2000; **42**: 53–60.
21. Newman JB, Debastos AG, Batton D, Raz S. Neonatal respiratory dysfunction and neuropsychological performance at the preschool age: a study of very preterm infants with bronchopulmonary dysplasia. *Neuropsychology* 2011; **25**: 666–78.
22. Hitzert MM, Van Braeckel KNJA, Roze E, Bos AF. Functional outcome at school age of preterm born children treated with dexamethasone after the first week of life. [Abstract.] *Pediatr Acad Soc* 2012; 1531. 518.
23. Bos AF, Einspieler C, Prechtl HFR. Intrauterine growth retardation, general movements and neurodevelopmental outcome – a review. *Dev Med Child Neurol* 2001; **43**: 61–8.
24. Volpe JJ. Brain injury in premature infants: a complex amalgam of destructive and developmental disturbances. *Lancet Neurol* 2009; **8**: 110–24.
25. Shinwell ES, Eventov-Friedman S. Impact of perinatal corticosteroids on neuromotor development and outcome: review of the literature and new meta-analysis. *Semin Fetal Neonatal Med* 2009; **14**: 164–70.
26. Kerstjens JM, de Winter AF, Bocca-Tjeertes IF, ten Vergert EM, Reijneveld SA, Bos AF. Developmental delay in moderately preterm-born children at school entry. *J Pediatr* 2011; **159**: 92–8.
27. Cserjesi R, van Braeckel KNJA, Butcher PR, et al. Functioning of 7-year-old children born at 32 to 35 weeks gestational age. *Pediatrics* 2012; **130**: e838–46.