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Motor Impairment and Clumsiness in Childhood,

Predictors and Long-Term Consequences

By

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List of Abbreviations

ADHD	-	Attention Deficit Hyperactivity Disorder
ASD	-	Autism Spectrum Disorder
ATE	-	Average Treatment Effect
AYLS	-	Arvo Ylppö Longitudinal Study
BFLS	-	Bavarian-Finnish Longitudinal Study
BIC	-	Bayesian Information Criterion
BLRT	-	Bootstrapped Likelihood Ratio Test
BLS	-	Bavarian Longitudinal Study
BOTMP	-	Bruininks-Oseretsky Test of Motor Proficiency
CBCL	-	Child Behavior Checklist
CFI	-	Comparative Fit Index
CI	-	Confidence Interval
CP	-	Cerebral Palsy
GA	-	Gestational Age
GMFCS	-	Gross Motor Function Classification System
DCD	-	Developmental Coordination Disorder
DSM	-	Diagnostic and Statistical Manual of Mental Disorders
ELBW	-	Extremely Low Birth Weight
EP	-	Extremely Preterm
FAI	-	Family Adversity Index
GAD	-	Generalised Anxiety Disorder
IQ	-	Intelligence Quotient
ICD-10	-	10^{th} Revision of the International Classification of Diseases

INTI	-	Intensity of Neonatal Treatment Index
IVH	-	Intraventricular Haemorrhage
K-ABC	-	Kaufman Assessment Battery for Children
LCGA	-	Latent Class Growth Analysis
LMR	-	Lo-Mendel-Rubin Likelihood Ratio Test
M-ABC	-	Movement Assessment Battery for Children
MDD	-	Major Depressive Disorder
MRI	-	Magnetic Resonance Imaging
MP	-	Motor Problems
NBW	-	Normal Birth Weight
NDT	-	Neurodevelopmental Treatment
NIDCAP	-	Newborn Individualised Developmental Care and Assessment Program
NICU	-	Neonatal Intensive Care Unit
OR	-	Odds Ratio
PIRI	-	Parent-Infant Relationship Index
PSI	-	Psychosocial Stress Index
PSM	-	Propensity Score Matching
PVL	-	Periventricular Leukomalacia
PT	-	Physiotherapy
RCT	-	Randomised Controlled Trial
RMSEA	-	Root Mean Squared Error of Approximation
RR	-	Relative Risk
SD	-	Standard Deviations
SEM	-	Structural Equation Modelling

SES	-	Socioeconomic Status
SGA	-	Small for gestational age
TEAM	-	Team consensus rating
TIMP	-	Test of Infant Motor Performance
TOMI	-	Test of Motor Impairment
TRCB	-	Tester's Rating of Child Behaviour
VLBW	-	Very Low Birth Weight
VLMR	-	Vuong-Lo-Mendell-Rubin Likelihood Ratio Test
VP	-	Very Preterm
WAIS	-	Wechsler Adult Intelligence Scale
WLSMV	-	Weight Least Square Estimation

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Declaration

I hereby confirm that I completed this thesis independently, that I have not heretofore presented this thesis to another department or university, and that I have listed all references used, and have given credit to all additional sources of assistance.

The work presented was carried out by me except in the cases outlined below:

Data collection

The data presented in this thesis have been collected and made available by the Bavarian Longitudinal Study (BLS) and the Arvo Ylppö Longitudinal Study (AYLS).

Study 1 – Chapter 3: Published in Acta Paediatrica

Contributions:

- James Tresilian: planning, revisions
- Dieter Wolke: planning, revisions
- Kati Heinonen: revisions
- Katri Räikkönen: revisions

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- James Tresilian: planning, revisions
- Dieter Wolke: planning, revisions

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Note of Inclusion of Published Work

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Baumann, N., Tresilian, J., Wolke, D. (2020). Effects of infant motor problems and treatment with physiotherapy on child outcomes at school-age. *Early Human Development.* 149:105140. doi: 10.1016/j.earlhumdev.2020.105140.

Baumann, N., Tresilian, J., Bartmann, P., Wolke, D. (2020). Early motor trajectories predict motor but not cognitive function in preterm- and term-born adults without pre-existing neurological conditions. *International Journal of Environmental Research and Public Health, 17*(9). 3258. doi: 10.3390/ijerph17093258.

Abstract

The acquisition of motor coordination and motor control is dependent upon and shaped by the child's growing and maturing body, as well as by the physical and social environment. Within this framework, motor development is linked with other functional and psychological domains, such as cognitive, behavioural and social development. Although motor impairments have been associated with adverse developmental and functional outcomes, even into adolescence and adulthood, investigations of lifespan psychological development often seem to underestimate and sometimes even neglect the contribution of motor factors and their development.

Using data from two prospective longitudinal cohorts of neonatal at-risk and healthy term born children in Germany and Finland, this thesis focusses on the course of motor functioning from birth to 5 years of age. It investigates perinatal, neonatal and early social environmental risk factors of early motor difficulties, as well as associations between early motor difficulties and subsequent child and adult outcomes. Study 1 used data from both cohorts, and Study 2 and 3 used data from the German cohort only.

Study 1 found that early motor development is influenced by neonatal complications, abnormal neonatal neurological status, length of initial hospitalisation and poor early parent-infant relationships. Study 2 showed that motor problems in infancy are likely to affect motor and cognitive outcomes at school-age, but not mental health, while receipt of physiotherapy had no beneficial effect. Study 3 demonstrated that early motor difficulties during the first 5 years of life have long-term implications for adult motor competence, but not for adult IQ.

In summary, the thesis highlights the importance of early parent-infant relationships alongside the monitoring of neonatal health for early motor development. Further, evidence of early motor development as an important precursor of long-term outcomes across multiple psychological domains in both healthy term and neonatal at-risk born individuals is provided.

Chapter 1: General Introduction

The overall aim of this thesis is to track early motor performance over the first 5 years of life in children born at-risk (e.g., children born prematurely <37 weeks of gestation) and to determine how later psychological outcomes depend upon early motor performance. More specifically, this thesis aims to track early motor development by identifying trajectories of early motor performance over the first 5 years of life. Further, this thesis explores precursors and peri- and neonatal risk factors of poor early motor development, including known biological, medical and child health factors, such as preterm birth and neonatal complications (e.g., intraventricular haemorrhage), but also early social-environmental risk factors, such as family adversity or parent-infant relationships. It will further be assessed whether motor difficulties that occur in infancy are associated with adverse developmental outcomes at school-age, and whether these associations are affected by early treatment with physiotherapy. Lastly, it will be examined whether early motor difficulties have long-term consequences for behaviour and wellbeing in adult life.

The purpose of this chapter is to provide a general introduction and description of early motor development and its role and importance in facilitating children's overall learning and development across a range of psychological domains. The prognosis and long-term consequences of motor problems or motor impairments are described, and perinatal and neonatal risk factors of poor motor development are identified. Further, interventions and treatment prescribed for children who are at risk or who have received a diagnosis of motor impairment, and possible effects of these interventions on subsequent developmental outcomes are

explored. The aim is to provide a foundation for the following chapters which investigate specific research questions that have emerged from the literature overview in this introduction.

The Importance of Early Motor Development

Origins of Motor Development

Prior to birth, core systems of the brain, including the motor and sensory systems, are set up as a foundation for infants' developmental and functional abilities (Spittle & Morgan, 2018; Thomason et al., 2018). Motor skill development (broadly) happens in a sequential manner. This is because it is dependent on the myelination of the sensory and motor systems of the brain which begins before birth and continues into adulthood, with the most rapid period during the first two years after birth (Cech & Martin, 2012; Kinney & Volpe, 2018; Piek, 2006; Thomason et al., 2018). The first movements are involuntary, reflexive movements that are cued by stimulation (i.e., response elicited by stimuli) (Tresilian, 2012). Some reflexes emerge prenatally while others appear and mature at or after birth. For example, reflexes that are important for survival outside the womb (such as sucking, swallowing, and rooting) occur before birth while other reflexes, such as pull-up, neck righting, and stepping emerge at or after birth (Piek, 2006). While the infant's body grows and matures, postural control and muscle power improves and motor functions change from reflexive to volitional. This increases the infant's ability to move, interact and receive input from the physical and social environment (Adolph & Berger, 2015; Piek, 2006). During the first years of life the most fundamental physical and motor functions are acquired. These include postural control (i.e., head

and trunk control), manual control (e.g., grasping), locomotion (i.e., crawling and walking), oculomotor control (i.e., eye movements), oromotor functions (e.g., chewing), and motor functions that are necessary for facial movements and vocalisation/speech sound (Adolph & Berger, 2015; Piek, 2006).

Motor Functioning and Motor Learning

A child's everyday activities are shaped either entirely or to a significant extent by motor functions and skills that are often taken for granted. These activities include play, sports, and school and leisure activities (for example, walking up and down stairs, jumping, running, catching a ball, riding a bike, dressing, tying shoelaces, writing, drawing and using scissors). Motor functions are generally categorised into gross and fine motor functions or skills (Keenan, Evans, & Crowley, 2016; Payne & Isaacs, 2012). The acquisition of gross motor functions or skills involves the control and coordination of the large muscles, muscle groups and joints which include movements of the head, trunk and limbs, and facilitate sitting, standing, locomotion, and reaching. Fine motor function and skills are generally described as movements of the small muscles or muscle groups (Payne & Isaacs, 2012). These functions include prehension and grasping, eye movement within the oculomotor system, and movements of the small muscle groups responsible to produce speech (i.e., larynx, throat, tongue, and mouth). Some fine motor functions, such as eye movements, improve in their accuracy and effectiveness and become more volitional, while other fine motor function and skills, including buttoning and handwriting, are acquired or refined at a later developmental stage, i.e., during preschool or school years (Payne & Isaacs, 2012). However, not all motor functions and skills fit into broad definitions of gross and fine motor functioning or skills, as

many motor functions are governed by both large and small muscles or muscle groups (Payne & Isaacs, 2012). For example, although drawing or handwriting is usually considered a fine motor skill, both small (i.e., small muscles and tendons of the fingers) and large muscles (i.e., shoulder and arm muscles) may be utilised to carry out the movements.

Learning to move and the acquisition and refinement of motor skills is not an isolated phenomenon but is a result of an interplay between the child's body, the physical environment, and the social and cultural context (Adolph & Franchak, 2017; Malina, 2004). As the child's body grows and matures continuously, the child is required to learn to adapt to the developmental status and changes of the body (i.e., growth, changes in muscle strength etc.) as well as to temporary changes that may impede movement, for example, clothes or holding a toy (Adolph & Hoch, 2018). The age of appearance and form of motor skills also depends on interactions with parents or caregivers, parents' expectations and childrearing practices (Adolph, Rachwani, & Hoch, 2018; Thelen, 1995). Parents or caregivers play an important role in their child's motor development and motor skill learning. They interact with the child using speech and gestures to direct or regulate infants' actions, for example through hands-on interventions, explaining consequences of unsafe actions, using stern voices, pointing, or positively encourage the child. This can happen through positioning the child physically, or through demonstrating a motor action for the child to imitate (Karasik, Tamis-LeMonda, Adolph, & Dimitropoulou, 2008; Tamis-LeMonda et al., 2008). In other words, parents provide the social and physical environment for active motor experience, learning and practice.

Motor Development and Other Psychological Functions

Motor development is linked and interdependent with other psychological functions allowing for the child to learn and develop new skills across various psychological domains (Adolph & Berger, 2015). Through movement children collect perceptual information and learn from their physical environment and social interactions with parents or caregivers which in turn give rise to adaptations and the mastery of new skills, not only regarding motor development but also for the development of other psychological skills, such as cognitive, emotional, and social skills (Adolph & Joh, 2007). Through social interaction with the parent or caregiver and exploration of surroundings, the child is able to experience, adapt, integrate and learn new skills. For example, locomotion skills, such as crawling and walking changes the child's perspective and brings into view and gives more and independent access to a wider range and opportunities of different stimuli and interaction that allow for strengthening and advances in cognitive, social or language skill development (Adolph & Robinson, 2015; Franchak, Kretch, & Adolph, 2018; Karasik, Tamis-LeMonda, & Adolph, 2011). Motor skills are also necessary to engage in play with parents, caregivers or other children, which provides opportunities to enhance and refine social skills and to develop peer relationships. Later, particularly in the school setting, fine motor skills, such as handwriting, represent an essential prerequisite for cognitive and academic skill development and functioning (Lingam et al., 2010; Martzog, Stoeger, & Suggate, 2019). In other words, the importance of motor development is not confined to the learning or adaption of motor skills.

How Motor Development Affects and Is Affected by Other Psychological Functions

The attainment and continuous development of new motor skills provide the child with opportunities for exploring and learning more about the physical and social environment (Adolph & Joh, 2007; Von Hofsten, 2009) which consequentially influence other developmental domains and functions. Such associations have been demonstrated empirically for a range of functions, skills or problems, including cognition, language, attention, mental health (i.e., anxiety and depressive symptoms), and social and affective functioning (Chen & Cohn, 2003; Houwen, Visser, van der Putten, & Vlaskamp, 2016; Iverson, 2010; Kanioglou, Tsorbatzoudis, & Barkoukis, 2005; Kovaniemi et al., 2018; Oudgenoeg-Paz, Leseman, & Volman, 2015; Schoemaker & Kalverboer, 1994; Scola, Bourjade, & Jover, 2015; Sylvestre, Nadeau, Charron, Larose, & Lepage, 2013; A. Wilson, Piek, & Kane, 2013) in children aged 3 months to 10 years.

However, motor development is also affected by functions of other developmental domains that share similar or the same underlying mechanisms and processes, such as cognition and perception (Barsalou, 2008; Hesslow, 2012; D. A. Rosenbaum, Carlson, & Gilmore, 2001). For example, cognitive and perceptual skills are used by infants to guide their motor planning and action (Von Hofsten, 2009) and for active problem solving (Thelen, 2005). Similarly, social interactions with a parent or caregiver can influence and promote motor development (Adolph & Berger, 2015; Adolph & Hoch, 2018). For example, playing with a toy, can animate the child to imitate a movement or motor action, or to move to or try and grasp a toy. Further, parents can actively promote their child's postural control and motor

proficiency by holding their child upright by the hands and walk them around, for example (Adolph & Hoch, 2018).

The link between sensorimotor development and other psychological functions through interaction with the physical and social environment is not new and at least partly reflected in Piaget's description of the sensorimotor stage (Lloyd, 2018; Piaget & Cook, 1952; Thelen, 1995) but also by more recent theories, such as the embodiment approach (Guell, Gabrieli, & Schmahmann, 2018; Kiefer & Trumpp, 2012), which posits that the body and the physical, social and cultural environment influence cognitive and emotional functions, such as thinking and feeling. Cognition or cognitive functions encompass or are traditionally defined by a range of cognitive processes, including intellectual skills, which are often measured with standardized intelligence test scores (i.e., intelligence quotient (IQ) scores), but also attention, learning, memory, reasoning, language and perception. The embodiment approach suggests that cognitive processes and cognitive development cannot happen without sensorimotor experience and action through the body and its movements (McGann, 2018; Ritterband-Rosenbaum, Justiniano, Nielsen, & Christensen, 2019). These processes form mental simulations of sensorimotor experience (Kiefer & Trumpp, 2012; D. A. Rosenbaum et al., 2001). In other words, only through physical interaction, cognition and other psychological processes can happen, and all cognitive functions are based on, and use, motor or physical function. Thus, cognitive functions are motor function internalised. In a play situation, for example, when a parent hands a toy to the child and names the toy while doing so, the child can learn about language as well as about paying attention. These sensorimotor experiences are memorised and used by the child to learn and

recall from these experiences (Kiefer & Trumpp, 2012; McGann, 2018). In school-aged children, writing and reading skills are essentially sensorimotor and perceptual skills (Kiefer & Trumpp, 2012). This means that motor action or behaviour is not an outcome of cognitive processes but rather a part of it (McGann, 2018). Cognitive or intellectual skills are thus grounded and supported, but also dependent on motor and sensorimotor behaviour (Barsalou, 2008; D. A. Rosenbaum et al., 2001; Thelen, 2000). As a result, the boundaries of cognitive and motor functions, and their definition, can sometimes overlap. Examples of overlapping cognitive and motor functions are perception or language (in particular language production).

Because motor control and motor coordination are essential to effective functioning in the world they represent an important part in children's overall development and learning. Motor problems or motor impairments can therefore have significant implications for sensorimotor learning, cognition and social functioning. Therefore, it is crucial to identify children at risk for motor problems to enable early referral to intervention or treatment. Given that infants are not able to understand questions, follow instructions or respond and express themselves verbally, parents and health professionals rely on observations of young children's movement and motor behaviour to deduce developmental problems or delay. Due to an 'overlap' of motor functions with other psychological or developmental domains that are not considered 'motor' (e.g., cognitive and social skill development), delayed or atypical development of motor functioning and skills, such as crawling and walking, can also signify delays or problems within other developmental domains particularly in infancy and toddlerhood (Adolph & Berger, 2015; Aylward, 2009; Denckla, 2005; Harris, 2016). Therefore, although early motor delays or problems can be transient

and part of the normal variation of development, observations of atypical or delayed motor functioning can be important for early identification of neurodevelopmental disorders that manifest over time and are associated with motor difficulties, for example, cerebral palsy (CP) or developmental coordination disorder (DCD), autism spectrum disorder (ASD) or attention deficit hyperactivity disorder (ADHD) (Arabameri & Sotoodeh, 2015; Ferrari et al., 2012; Harris, 2016).

Definition and Prevalence of Motor Impairment

The spectrum of motor impairment in young children can range in severity and form. Mild motor problems include delays in the acquisition of crawling and walking that result in not reaching motor developmental milestones but are not accompanied by any cognitive or functional problems (American Psychiatric Association, 2013; Spittle & Orton, 2014). These delays are part of the natural variability in motor skill acquisition and are often transient in nature, with children growing out of these problems or catching up with their peers at a later time point. In contrast to these transient motor problems, neurodevelopmental conditions that primarily affect children's motor development, such as CP and DCD, often have different causal factors and can range in their presentation and severity (Acharya, Pellerite, Lagatta, Andrews, & Msall, 2016; Spittle & Orton, 2014). However, even without a clinical diagnosis motor impairment can adversely impact children's development and functioning. These motor impairments can include difficulties with motor coordination (i.e., the ability to coordinate movement or motor action), motor control (i.e., the ability to control motor functions and voluntary movements) and visual-motor integration (i.e., the ability to process visual information to carry out fine motor tasks, such as writing or drawing). For example, a child's difficulty to

perform or coordinate specific gross or fine movements in everyday activities or tasks such as buttoning, tying shoelaces, or climbing stairs (Mancini, Rigoli, Cairney, Roberts, & Piek, 2016; Marlow, Roberts, & Cooke, 1989; Spittle & Orton, 2014). This makes it important to assess or test children's motor development early, particularly in children who are at-risk for neurodevelopmental or motor impairments (e.g., preterm children). Depending on the child's age, different measures are used to identify, assess and diagnose children with motor delays or disorders. For younger children, i.e., from infancy to preschool age, assessment tools range from general and motor development diagnostic tools (e.g., the Bayley Scales of Infant Development, the Griffiths Mental Developmental Scales, the Peabody Developmental Motor Scales, the Alberta Infant Motor Scale) to developmental screening tools (e.g., the Ages and Stages Questionnaire), and to classic neurological examinations or neurobehavioural assessments (e.g., Prechtl's Neurological Examination of the Full Term Newborn Infant, or the Test of Motor Performance (TIMP)) (Piek, 2006). For older children, that is, children beyond infancy or toddler age, standardized motor tests, such as the Movement Assessment Battery for Children (M-ABC) or the Bruininks-Oseretsky Test of Motor Proficiency (BOTMP), are often utilised (Griffiths, Toovey, Morgan, & Spittle, 2018; Tieman, Palisano, & Sutlive, 2005).

Cerebral palsy

CP is a neurodevelopmental condition that primarily affects the development of movement and posture, leading to abnormal gross and fine motor functioning and motor control, and limitations in activity (Acharya et al., 2016; McIntyre, Morgan, Walker, & Novak, 2011; Spittle, Orton, Anderson, Boyd, & Doyle, 2012), that are

due to interference with or an insult to the developing foetal or infant brain (Acharya et al., 2016; P. Rosenbaum et al., 2007). The motor problems that are associated with CP include difficulties with crawling, walking, swallowing, and poor coordination of eye movement and oromotor skills (Aisen et al., 2011; P. Rosenbaum et al., 2007). Despite an early onset of symptoms, motor impairments of children with CP usually manifest around age 2 years and persists across the life span (P. Rosenbaum et al., 2007). CP is the most common cause for motor impairment in childhood and is often associated with other impairments, such as chronic pain, learning disabilities, epilepsy, musculoskeletal problems (e.g., muscle contractures and abnormal bone growth), behavioural and sleep disorders, and visual and hearing impairments (Surveillance of Cerebral Palsy in Europe (SCPE), 2000; Gormley, 2001; Himmelmann, Beckung, Hagberg, & Uvebrant, 2006; Novak et al., 2017). Special needs and costs that may result from CP and related impairments can place great demands on families, health, educational and social services (Surman et al., 2006; Tonmukayakul et al., 2018) with parents being particularly concerned about their child's prognosis in regards to motor function and mobility (P. Rosenbaum, 2006; P. Rosenbaum, Walter, Hanna, & et al., 2002).

The definition of CP has been agreed upon and described during an International Workshop on Definition and Classification of Cerebral Palsy (Richards & Malouin, 2013; P. Rosenbaum et al., 2007):

> "Cerebral palsy (CP) describes a group of permanent disorders of the development of movement and posture, causing activity limitation that are attributed to non-progressive disturbances that occurred in the developing foetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems."

While severe CP can be predicted early by using cranial ultrasonography, magnetic resonance imaging (MRI) or other imaging techniques, mild or moderate forms of CP are often identified when children fail, or show a delay, in the acquisition of motor milestones. The severity or grade of CP varies from mild forms (e.g., more pronounced in rapid movements (either with or without impairments of fine motor functions), the impairment has a hardly noticeable negative impact) to severe forms (e.g., no active movement is possible). A systematic review has shown that 56% of children with CP are able to walk independently, 16% could walk with assistance, and 28% could not walk at all (Novak, Hines, Goldsmith, & Barclay, 2012). Although most studies use the Gross Motor Function Classification System (GMFCS) to define severity levels, categories of severity still vary between studies (Himpens, Van den Broeck, Oostra, Calders, & Vanhaesebrouck, 2008). Among all CP subtypes that include spastic, dyskinetic and ataxic CP, the most frequent CP subtypes are spastic hemiplegia and diplegia (Himmelmann & Uvebrant, 2014). However, as the severity and form of early motor difficulties or abnormalities that constitute a diagnosis of CP or suspected CP may change over time (Nelson & Ellenberg, 1982), particularly for mild forms of CP, a diagnosis is often not made

before the age of 2 years (Herskind, Greisen, & Nielsen, 2015; McIntyre et al., 2011; Novak et al., 2012).

In the general population the prevalence rate for CP is reported to be about 0.1 to 0.2% of live births (McIntyre et al., 2011; Novak et al., 2017; Platt et al., 2007; Surman et al., 2006). Due to the strong association between CP and gestational age, prevalence rates increase markedly for children born very preterm (28-31 weeks of gestation) and extremely preterm (22 to 27 weeks of gestation) to 6.2% and 14.6%, respectively (Himpens et al., 2008). However, a recent meta-analysis that included children born after 2006 showed decreased prevalence rates of 4% for very low birth weight (<1,500g; VLBW) and very preterm (VP) infants, and 8 to 10 % for extremely low birth weight (<1,000g; ELBW) and extremely preterm (EP) infants (Pascal et al., 2018).

Motor impairments without CP

Children who have motor coordination or motor skill problems without developing CP often meet the criteria for DCD. Despite being described as a mild or moderate impairment, DCD has a substantial adverse effect on different aspects of a child's development and function (Lingam et al., 2010; Spittle & Orton, 2014). DCD is a neurodevelopmental condition and often also referred to as developmental dyspraxia, minor neurological dysfunction, minimal brain damage or clumsiness (Geuze, Jongmans, Schoemaker, & Smits-Engelsman, 2001; Hyde, Rigoli, & Piek, 2017; Zwicker, Missiuna, Harris, & Boyd, 2012). DCD is characterised by a developmental delay and deficits in motor coordination, motor control and visuomotor integration that are not due to a diagnosed medical condition (such as major motor, sensory or intellectual disability) and affect child's academic

achievement and activities of everyday living at home and in school (e.g., dressing, personal hygiene and eating) (Hyde et al., 2017; Wang, Tseng, Wilson, & Hu, 2009; Zwicker et al., 2012). Children with DCD have been found to have problems in postural control and fine motor skills (Visser, 2003). For instance, children with DCD have problems to carry out gross and fine motor tasks, difficulties with handwriting and drawing, and they avoid participating in physical or sports activities (John Cairney, Hay, Veldhuizen, Missiuna, & Faught, 2010; Hyde et al., 2017; Izadi-Najafabadi, Ryan, Ghafooripoor, Gill, & Zwicker, 2019; Zwicker et al., 2012). Parents are particularly concerned about their children's ability to perform motor tasks, such as riding a bike, catching a ball, or tying shoelaces, and their emotional and social function and participation (Mandich, Polatajko, & Rodger, 2003; Missiuna, Moll, King, King, & Law, 2007; Stephenson & Chesson, 2008; Summers, Larkin, & Dewey, 2008).

Although DCD is often not diagnosed before school-age, symptoms may emerge in early childhood and can persist into adolescence and adulthood (Cantell, Smyth, & Ahonen, 2003; Cousins & Smyth, 2003; Husby, Skranes, Olsen, Brubakk, & Evensen, 2013; Losse et al., 1991; Poole et al., 2015a; Tal-Saban, Zarka, Grotto, Ornoy, & Parush, 2012). The diagnostic criteria for motor functioning problems in children and adolescents have been described in two widely used classification systems, the Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 2013) and the 10th revision of the International Classification of Diseases (ICD-10) (World Health Organization, 1992). Recently updated recommendations of an international consensus group (Blank et al., 2019), defined DCD according to diagnostic criteria of the current version of the DSM

(DSM, Version 5). The DSM-5 describes the four diagnostic criteria for DCD as follows:

Diagnostic Criteria for ‘Developmental Coordination Disorder’
A. The acquisition and execution of coordinated motor skills is substantially below that expected given the individual’s chronological age and opportunity for skill learning and use. Difficulties are manifested as clumsiness (e.g., dropping or bumping into objects) as well as slowness and inaccuracy of performance of motor skills (e.g., catching an object, using scissors or cutlery, handwriting, riding a bike, or participating in sports). B. The motor skills deficit in Criterion A significantly and persistently interferes with activities of daily living appropriate to chronological age (e.g., self-care and self-maintenance) and impacts academic/school productivity, prevocational and vocational activities, leisure, and play. C. Onset of symptoms is in the early developmental period. D. The motor skills deficits are not better explained by intellectual disability (intellectual developmental disorder) or visual impairment and are not attributable to a neurological condition affecting movement (e.g., cerebral palsy, muscular dystrophy, degenerative disorder).

While the criteria for DCD require the onset of symptoms in early childhood, a diagnosis is often not made before the age of 5 years. A definitive diagnosis before that age is difficult to make. This has been attributed to two reasons: first, the lack of age-appropriate assessment tools (Blank et al., 2019), and second, the high

variability and change in motor performance in infancy and toddlerhood (Darrah, Hodge, Magill-Evans, & Kembhavi, 2003) which can lead to a possible catch-up in motor development in young children (Bartlett, 2000). That means that despite the achievement of early motor milestones, some motor difficulties, for example, running, jumping, handwriting and drawing, only become apparent during the preschool- and school-years when greater intellectual, social and physical demands are placed on the child (Ream & Lehwald, 2018; Spittle & Orton, 2014).

While many studies have largely followed the DSM-criteria to describe and diagnose DCD, there is a wide variety in instruments and quantitative cut-offs used (Geuze et al., 2001). The 5th percentile is regarded as the standard cut-off for motor coordination problems (i.e., below 2 standard deviations [SD]) on a given motor skill or motor coordination test (e.g., the M-ABC). In contrast, children with motor test scores between the 5th and 15th percentile (i.e., below 1 SD) are considered to be at risk for motor coordination problems or to have probable motor problems (Geuze et al., 2001; D. A. Sugden, Chambers, & Utley, 2006). A consistent description and diagnosis of DCD is often further impeded by the lack of studies that have used standardized measures for, or have reported on, the impact of motor impairments on school performance or activities of daily living (Magalhaes, Cardoso, & Missiuna, 2011; Visser, 2003).

Depending on the definition and applied cut-off, prevalence rates for non-CP motor impairments or DCD vary widely and can range between 2% to 20%, but is most frequently and consistently reported to affect about 5% to 6 % of children in the general population (Blank et al., 2019; Spittle & Orton, 2014). In at-risk populations, i.e., preterm born children, the prevalence rate for DCD or non-CP

motor outcomes rises markedly and can reach rates of about 40% (Bolk, Farooqi, Hafström, Åden, & Serenius, 2018; Evensen, Ustad, Tikanmäki, Haaramo, & Kajantie, 2020; Spittle & Orton, 2014; Williams, Lee, & Anderson, 2010). In contrast to CP, prevalence rates of non-CP motor impairments in preterm children have risen between 1991 and 2005 (Spittle, Cameron, Doyle, & Cheong, 2018).

Discussion and Conclusions

Motor coordination and motor skills are important in children's everyday life and activities. Motor skills enable children to move about and communicate with their physical and social environment. In this manner, other psychological functions and skills are influenced by motor skills which in turn are affected by other psychological functions. Therefore, it can be difficult, or even impossible, to ascertain the direction of association between motor and other psychological function, and/or to clearly discriminate between motor and other psychological functions because of an overlap between those functions (for example, perception or language). Nevertheless, delayed or atypical motor development can adversely affect subsequent development and functions across motor and other psychological domains, including cognitive abilities, mental health, social functioning.

Motor impairments often involve marked problems or deficits in motor coordination, motor control, and visual-motor integration, and can occur across a wide spectrum of severity and form. CP and DCD are the most common cause of motor impairments in children. The prevalence for CP worldwide is 0.1 to 0.2%, whilst the prevalence for DCD is relatively high with 5 to 6% in school-aged children. However, the prevalence rates of both movement conditions increases significantly in at-risk children, i.e., preterm born children.

Definitions for motor impairment are varied in the literature and range from the use of clinical diagnoses, such as CP or DCD, to the application of cut-offs on a given standardized motor test score (e.g., M-ABC or BOTMP) to describe non-CP motor impairments. However, there are certain caveats to this. First, motor tests may measure or assess different areas and aspects of motor development or motor skill. For example, the BOTMP assesses fine manual control, manual coordination, body coordination, and strength and agility, whereas the M-ABC measures manual dexterity, ball skills, and static and dynamic balance. And second, although these cut-offs are well-established and recognised as a useful tool in defining motor impairment, they are arbitrary and not consistently used to define motor impairment, or disorders such as DCD (Evensen et al., 2020; Spittle & Orton, 2014). That is, a diagnosis of DCD is often made, or assumed, regardless of whether additional criteria for a DCD diagnosis are met (for example, whether the motor impairment impacts school performance or activities of daily living). This suggests that there remains disagreement or uncertainty about the definition for motor impairment.

Another important caveat for defining motor impairment is the age of a child. Although CP can be diagnosed early (in particular, if the motor impairment is considered severe), a diagnosis for DCD is often not made before school age, i.e., when a child fails a standardized motor test. However, these tests are not designed for infants and toddlers. Assessment tools for neonates, infants and toddlers vary widely, and often go beyond an assessment of motor functioning and ability. These assessment tools include: age of reaching developmental or motor milestones (e.g., reaching, crawling), quality of early movements or motor repertoire, general

developmental or neuromotor tests (e.g., Bayley Scales of Infant Development, Griffiths Mental Developmental Scales, TIMP), and neurological examinations.

Taken together, this makes comparing and interpreting findings from different studies and across ages difficult.

Comorbidities and Consequences of Motor Impairment

Given that motor behaviour is the sole means by which a child interacts with the physical and social environment, it is not surprising that motor impairments often co-occur with other developmental or functional difficulties. And these difficulties can have a profound impact on children's psychological and functional development, health, and quality of life (Karras, Morin, Gill, Izadi-Najafabadi, & Zwicker, 2019; Spittle & Orton, 2014; Zwicker et al., 2012).

Despite some indication that children may grow out of mild early motor problems (Bartlett, 2000; Nelson & Ellenberg, 1982), increasing evidence suggests that motor problems persist beyond school-age and into adolescence (de Kieviet, Piek, Aarnoudse-Moens, & Oosterlaan, 2009; Losse et al., 1991; Powls, Botting, Cooke, & Marlow, 1995) and adulthood (Cousins & Smyth, 2003; Husby et al., 2013; Kirby, Williams, Thomas, & Hill, 2013; Poole et al., 2015b) in both typically developing and at-risk children.

Motor Problems in Early Childhood

Longitudinal studies in preterm populations without major disabilities have shown that early motor performance, even as early as at term age (Olsen et al., 2018), are associated and predictive of later motor development in infancy, toddlerhood, and at preschool and school-age (Danks et al., 2012; Olsen et al., 2018;

Spittle et al., 2013). However, such associations were not found in term born or low-risk populations (Ghassabian et al., 2016; Hitzert, Roze, Van Braeckel, & Bos, 2014; Jenni, Chaouch, Caflisch, & Rousson, 2013; Piek, Dawson, Smith, & Gasson, 2008; Roze et al., 2010).

Multiple studies have shown that early motor functioning is associated with subsequent cognitive function, measured by general developmental or intelligence scales, in preterm or low birth weight populations (Burns, O'Callaghan, McDonell, & Rogers, 2004; Butcher et al., 2009; Oudgenoeg-Paz, Mulder, Jongmans, van der Ham, & Van der Stigchel, 2017) but not with behavioural outcomes, such as internalising, externalising and attention (Butcher et al., 2009) into preschool- or school-age. In children who are at risk for ASD it was found that early motor skills were associated with subsequent ASD status and expressive language scores at age 2 to 3 years (LeBarton & Landa, 2019).

General population studies found that children's early motor skills or functioning was associated with general intelligence (Peyre, Charkaluk, Forhan, Heude, & Ramus, 2017) and overall developmental skills, in particular with cognitive and adaptive skills, but not with social or communication skills (Ghassabian et al., 2016) at preschool and school-age. However, contrasting results from another population-based study showed infants' poorer neuromotor development was associated with a higher risk for language and nonverbal cognitive delay at age 1.5 to 2.5 years (van Batenburg-Eddes et al., 2013). In term born children, it was found that quality of early motor repertoire was associated with general intelligence, attention and visual-spatial perception, as well as with total behavioural and internalising outcomes at age 5 to 7 years (Hitzert et al., 2014).

Moreover, there is evidence that motor explorative function in infancy can instigate a developmental cascade influencing academic achievement in adolescence through intelligence and academic achievement in toddlerhood and at school-age (Bornstein, Hahn, & Suwalsky, 2013). There is even evidence of long-term associations between early motor performance (i.e., age at acquisition of motor milestones) and adult language, cognitive and executive function, educational achievement, and neuroticism (Flensborg-Madsen & Mortensen, 2015, 2018; Flensborg-Madsen, Sorensen, Revsbech, & Mortensen, 2013; Murray, Jones, Kuh, & Richards, 2007; Murray et al., 2006; Poranen-Clark et al., 2015; Taanila, Murray, Jokelainen, Isohanni, & Rantakallio, 2005).

Overall, studies used a wide variety of measures to assess early motor functioning or skills, including motor milestones, quality of early movements or motor repertoire, and general developmental or neuromotor tests. Therefore, it is not surprising that results across studies were not always consistent. Notably, most of these studies examined associations with subsequent motor and cognitive functioning into preschool-age. Only very few studies investigated associations between motor performance in infancy and other developmental outcomes and functioning at school-age, or into adolescence and adulthood.

Trajectories of Early Motor Problems

Cross-sectional and follow-up studies often examine children at certain specified ages or test differences between groups that are defined by child age, or degree of prematurity. As a result, these studies may be unable to distinguish between delayed versus non-typical motor development, resulting in flawed conclusions about underlying developmental trajectories (Adolph & Berger, 2006;

Adolph & Berger, 2015). Due to the large inter-individual variability (Forssberg, 1999; Kakebeeke et al., 2013; L. B. Smith & Thelen, 2003) associated with early motor development and brought about by neurological changes, experience and other environmental factors (Touwen, 1993), changes in function and new skills appear at different ages. In order to identify children who are at risk of motor coordination problems it is important to assess development of motor functioning across time and ages (Geuze et al., 2001).

Longitudinal studies allow multiple motor functioning assessments over longer periods of time and ages and can thus determine children who develop or 'grow' at a similar rate. Researchers in social and psychological science, such as developmental or paediatric psychologists, are often interested in developmental trajectories, trajectories of growth, or in finding patterns of change in heterogeneous longitudinal data (Berlin, Parra, & Williams, 2014; Jung & Wickrama, 2008; Sterba & Bauer, 2010). However, few longitudinal studies have investigated trajectories of motor performance. Instead, motor trajectories are frequently described by using motor milestones and thereby not taking changes, individual differences or quality of motor performance into account (Adolph & Franchak, 2017; S. L. Edwards & Sarwark, 2005; Kakebeeke, Caflisch, Locatelli, Rousson, & Jenni, 2012; Van Haastert, De Vries, Headers, & Jongmans, 2006). Further, many studies have simply described and compared the progress of motor performance scores of pre-defined groups of children (for example, preterm and term born children) by using mean group differences across multiple time points (Pin, Darrer, Eldridge, & Galea, 2009; Pin, Eldridge, & Galea, 2010; Van Haastert et al., 2006; Yaari et al., 2017).

Instead of using developmental milestones or mean group comparisons to describe young children's motor development, a small number of longitudinal studies (Hameed et al., 2017; Heineman, Schendelaar, Van den Heuvel, & Hadders-Algra, 2018; Su et al., 2017) investigated motor trajectories by adapting a person-centred statistical approach (for example, Latent Class Growth Analysis (LCGA), (Jung & Wickrama, 2008)) to investigate whether different groups with similar patterns of motor development can be identified in a given sample across time.

A longitudinal study in the United Kingdom that used data from a general population cohort (Hameed et al., 2017) examined associations between early childhood development skills and psychotic experience in adolescence. Fine and gross motor skills were assessed at four time points (at 6, 18, 30 and 42 months), and developmental growth modelling yielded six fine motor skill trajectories (i.e., stable: high average, average, improvement; declining: low, moderate, high) and five gross motor skill trajectories (i.e., stable: high average, average; and declining: low, moderate, high). Another study in Taiwan (Su et al., 2017) focussed on investigating motor trajectories during the first year of life in a cohort of preterm infants and associations with perinatal factors and developmental outcomes at 24 months. Gross motor functioning was examined across four time points (at 4, 6, 9, and 12 month) and identified three groups of distinct motor trajectories: "stably normal", "deteriorating" and "persistently delayed". A prospective cohort study in the Netherlands of children born after assisted reproductive techniques examined associations between motor behaviour in infancy and cognitive function at age 4 years. Motor behaviour was assessed across three time points, at 4, 10 and 18 months. Three distinct groups of children with similar motor trajectories emerged

from a total motor behaviour score and were described as follows: a rapid onset group, a typically developing group, and a slow group. All three studies thus identified more than one group of children with a distinct pattern of motor functioning over time.

To summarise, the identification of meaningful groups of children, i.e. children with a similar pattern of motor functioning over time, through a person-centred statistical approach allows for a better understanding of developmental trajectories and patterns of change within a given sample (Berlin et al., 2014; Jung & Wickrama, 2008). Trajectories can be superior to single assessment of motor functioning, particularly in early childhood. This is because observed motor delays at a single time point often are within normal variation of motor development, whereas trajectories of motor problem that are based on repeated measures across multiple time points and ages strongly suggest that motor problems are not transient. Using early motor trajectories instead of a single motor measure can therefore be a powerful tool for prognosis of motor development and for testing associations between motor development and other developmental domains or functions. For example, the aforementioned studies that have investigated and identified distinct trajectories of motor functioning have subsequently used these early motor trajectories to test and confirm associations with subsequent outcomes, such as cognitive and motor outcomes at preschool-age (Heineman et al., 2018; Su et al., 2017), and psychotic experience in early adolescence (Hameed et al., 2017), or examined peri- and neonatal predictors of motor trajectories (Su et al., 2017).

Motor Impairment in Childhood

Most research on comorbidities and consequences of motor impairment involves school-aged children. This is because motor impairments, such as DCD, are often not diagnosed before school-age, while CP is not typically diagnosed before age 2 (Acharya et al., 2016; Spittle & Orton, 2014). Children with CP can exhibit multiple comorbidities, including intellectual, speech and communication disability, epilepsy, pain, seizures, and sleep and behavioural problems (Acharya et al., 2016; McIntyre et al., 2011; Novak et al., 2012; Odding, Roebroeck, & Stam, 2006), and further are likely to have lower educational and employment prospects (Michelsen, Uldall, Kejs, & Madsen, 2005).

Non-CP motor impairments can have a considerable impact on children and their families (Spittle & Orton, 2014). DCD is often associated with other neurodevelopmental disorders, such as ADHD, learning and language difficulties (Dewey, Kaplan, Crawford, & Wilson, 2002; Kadesjo & Gillberg, 1998; Lingam et al., 2010; Visser, 2003), and ASD (Gillberg, 2003; Provost, Lopez, & Heimerl, 2007; Reiersen, Constantino, & Todd, 2008). ADHD is the most frequently co-occurring disorder with an overlap of about 50% (Blank et al., 2019), while it has been suggested that these neurodevelopmental disorders may be linked through a common genetic factor (Pettersson, Anckarsater, Gillberg, & Lichtenstein, 2013).

Several studies of general and preterm populations have shown that children with DCD or probable DCD are more likely to display difficulties in activities of daily living (i.e., self-care, play, mobility and handwriting) and social skills (Bolk et al., 2018; Dewey et al., 2002; Lingam et al., 2010; Schoemaker, Lingam, Jongmans, van Heuvelen, & Emond, 2013). Children with DCD have also demonstrated a

higher risk for mental health problems, including inattention, hyperactivity, anxiety and depression (Bolk et al., 2018; King-Dowling, Missiuna, Rodriguez, Greenway, & Cairney, 2015; Lingam et al., 2012; Schoemaker et al., 2013), up until adolescence (Sigurdsson, Van Os, & Fombonne, 2002; Skinner & Piek, 2001). Further, children with DCD are more likely to display difficulties in learning or academic abilities (i.e., reading, writing, and spelling) (Dewey et al., 2002; Lingam et al., 2010; Schoemaker et al., 2013), and to have special educational needs and diminished educational achievement (Harrowell, Hollen, Lingam, & Emond, 2018; Marlow, Hennessy, Bracewell, Wolke, 2007).

Other developmental and functional issues that have been linked to motor impairment in children and adolescents include lower self-esteem (Losse et al., 1991; Piek, Baynam, & Barrett, 2006), bullying victimisation (Campbell, Missiuna, & Vaillancourt, 2012), lower physical health and fitness (Burns et al., 2009; King-Dowling, Rodriguez, Missiuna, Timmons, & Cairney, 2018; Schott, Alof, Hultsch, & Meermann, 2007), overweight and obesity (Hendrix, Prins, & Dekkers, 2014). Moreover, children with motor impairments are less likely to participate in social activities (Chen & Cohn, 2003; Izadi-Najafabadi et al., 2019; Magalhaes et al., 2011; Tan et al., 2014), particularly in areas of education and communication (Sylvestre et al., 2013), as well as in physical activities, such as organised activity and free play (J. Cairney et al., 2005).

Further, there is evidence that motor impairments in older adolescents and young adults are associated with physical and mental health issues, and lower quality of life and educational attainment (Harrowell, Hollen, Lingam, & Emond, 2017; Husby et al., 2016; Kirby et al., 2013; Laerum et al., 2019; Poole et al., 2017; Poole

et al., 2015a, 2016; Tal-Saban et al., 2012). And in a recent study it has even been demonstrated that childhood motor impairments may lead to a higher mortality risk (Batty, Deary, Hamer, Frank, & Bann, 2020).

Overall, it has been shown that motor impairments in childhood affect a wide range of developmental and functional outcomes that seem to last into adolescence and adulthood. However, it is important to note that definitions of motor impairment varied as studies often used different motor test score cut-offs. Further, most studies had a cross-sectional design and included a general population sample, while only few studies have focussed on preterm children (Bolk et al., 2018; Burns et al., 2009; Marlow et al., 2007) or adults (Husby et al., 2016; Laerum et al., 2019; Poole et al., 2017; Poole et al., 2015a, 2016).

Parents, Family and Society

Motor impairments not only affect the child's development and functioning. Having a child with motor impairments can impact parents' and family's quality of life, including the work and social life of parents and well-being of siblings (Cleaton, Lorgelly, & Kirby, 2019; Stephenson & Chesson, 2008). Due to the high prevalence rate of motor impairment and its adverse and long-term effect on everyday activities, academic achievement, psychosocial functioning, and physical and mental health, the burden and costs for the child's family and society is significant (Blank et al., 2019; Cleaton et al., 2019; Kruse et al., 2009; Richards & Malouin, 2013; Tonmukayakul et al., 2018).

Summary and Conclusions

Motor development, that is, the acquisition and refinement of motor functions and skills, happens across the life span. Motor problems that occur early in infancy and during childhood can have far-reaching consequences, not only within the motor domain but also across other developmental domains and functions. If motor problems persist, they can have long-lasting effects on everyday activities and functions (Cousins & Smyth, 2003) which in turn can have an even higher impact on children's scholastic and academic achievement, social relationships, and everyday functioning and quality of life (Zwicker, Harris, & Klassen, 2013). Therefore, it is important to identify children with poor motor development early and provide appropriate treatment and support.

Although motor problems or delays that occur in infancy have been associated with subsequent problems across different developmental domains into childhood, and even into adolescence and adulthood, results are often inconsistent. These inconsistencies are likely due to different inclusion criteria (i.e., developmental risk status of the sample) and the use of a wide range of motor functioning measures, but also, and importantly, due to the transient nature of early motor problems or delay. Measuring motor performance across different time points and ages in infancy and toddlerhood and determining groups of children that develop similarly over time may offer a more stable measure of motor performance and thereby improve the predictive value.

In contrast to motor problems in infancy, a large body of studies has investigated co-morbidities and consequences of motor impairments assessed and diagnosed in childhood, i.e., at school-age. Studies that examined co-morbidities of

motor impairment in childhood are particularly lacking in at-risk samples. Further, while these associations seem to last into adolescence and adulthood, investigations into long-term consequences of child motor impairments remain rare.

Precursors and Risk Factors of Motor Impairment

One of the main precursors of motor impairment is prematurity (Acharya et al., 2016; S. L. Edwards & Sarwark, 2005). Every year about 15 million babies are born premature, defined as birth < 37 completed weeks of gestation (March of Dimes, 2012). This equates to approximately 11% of all live births worldwide and about 9% in Europe (Chawanpaiboon et al., 2019). Due to advances in perinatal medicine and neonatal care over the past decades, survival rates of preterm born babies and increasingly those that are born at even earlier gestational ages have improved. Despite these improvements preterm born children remain at a higher risk for mortality, morbidity, and developmental and behavioural impairments, including impaired motor development (Spittle et al., 2018). However, in the majority of cases the mechanisms and causal paths that lead to motor impairment are unclear. As a possible cause, the interplay of perinatal and neonatal risk factors for motor impairments, including biological, medical, child health, socio-environmental and genetic factors are discussed in the literature (Novak et al., 2017; Odding et al., 2006; Spittle & Orton, 2014).

Perinatal and Neonatal Risk Factors

Only a small number of studies investigated perinatal and neonatal risk factors for motor problems in preterm or low birth weight children during infancy and toddlerhood. These studies measured gross motor performance using age of

achievement of motor milestones, motor test scores, or motor trajectories across multiple time points (Erikson, Allert, Carlberg, & Katz-Salamon, 2003; Janssen et al., 2011; Pin et al., 2010; Su et al., 2017). Birth weight, brain injury (e.g., periventricular leukomalacia [PVL], intraventricular haemorrhage [IVH], white matter abnomalities), postnatal steroid use, bronchopulmonary dysplasia, retinopathy of prematurity, and male sex were found to influenced motor performance.

As risk and prognostic factors for CP and motor impairment in preterm and term born children low gestational age, brain injury (i.e., IVH and PVL), intrauterine growth restriction, encephalopathy, seizures, infection, multiple births, male sex, and postnatal corticosteroids have been identified (Linsell, Malouf, Morris, Kurinczuk, & Marlow, 2016; McIntyre et al., 2011; Novak et al., 2017; Odding et al., 2006; Spittle & Orton, 2014; Stavsky et al., 2017).

Studies that investigated risk and prognostic factors of motor impairments without CP (i.e., DCD and probable DCD) in VP or VLBW children vary largely in terms of number and type of potential risk factors investigated, as well as in sample size and methodological criteria, including definitions for inclusion (e.g., birth year, degree of prematurity), child age at motor assessment, measure of motor function or impairment, and definition of motor impairment (i.e., usage of different cut-offs of motor tests scores) (Cooke, 2005; Davis, Ford, Anderson, & Doyle, 2007; Goyen & Lui, 2009; Holsti, Grunau, & Whitfield, 2002; Whitaker et al., 2006; Zwicker, Yoon, et al., 2013). While one study only reported unadjusted results (Cooke, 2005) and another one did not find any difference in neonatal risk factors between DCD and non-DCD groups (Holsti et al., 2002), risk factors that were found to be independently associated with DCD in preterm children and adolescents aged 4 to 16

years include low birthweight, male sex, postnatal steroids, prolonged rupture of membranes, and retinopathy of prematurity (Davis et al., 2007; Goyen & Lui, 2009; Whitaker et al., 2006; Zwicker, Yoon, et al., 2013).

Studies that have investigated the association between perinatal and neonatal risk factors with motor difficulties in general or term born populations are rare. One such study, a large Danish birth cohort study (*N*=33,354), reported that in addition to gestational age, intrauterine growth restrictions and delayed walking was independently associated with DCD in children aged 7 years (Faebo Larsen, Hvas Mortensen, Martinussen, & Nybo Andersen, 2013). Another large population-based study in Denmark (*N*=5,765) found that gestational age, birth weight, parity, and growth over the first year of life, breastfeeding and having lived in a full-time institution, predicted gross motor milestone attainment in infants aged 12 months (Flensborg-Madsen & Mortensen, 2017).

Early Social Environmental Factors

Previous research suggests that psychosocial and social environmental risk factors, such as family adversity, socioeconomic status, maternal stress or anxiety, and parent-infant interaction, significantly influence child motor, cognitive and social-emotional function in addition to biological and medical risks (e.g., preterm birth, medical complications, and neonatal morbidities) (Burnett, Cheong, & Doyle, 2018; Greene, Rossman, Meier, & Patra, 2017; Laucht, Esser, & Schmidt, 1997; Levy-Shiff, Einat, Mogilner, Lerman, & Krikler, 1994; Treyvaud et al., 2009). Few studies, however, have investigated effects of social environmental and biological risk factors on motor outcome simultaneously, and those that did often only included maternal education or occupation, with mixed results (Benavente-Fernandez et al.,

2019; Goyen & Lui, 2009; Janssen et al., 2011; Marin Gabriel et al., 2009; Whitaker et al., 2006). In contrast to studies that included infants or toddlers (Janssen et al., 2011; Marin Gabriel et al., 2009), studies in older children and adolescents showed that biological and medical factors (such as male sex, small for gestational age, brain injury (i.e., PVL and IVH), chronic lung disease, and duration of ventilation) instead of maternal education or social risk influenced motor outcomes (Benavente-Fernandez et al., 2019; Goyen & Lui, 2009; Whitaker et al., 2006).

Summary and Conclusions

Several studies have investigated perinatal and neonatal risk factors for motor impairments in children. Despite attempts to formally summarise or systematically examine perinatal and neonatal risk factors for motor impairment (e.g., Linsell et al., 2016; Zwicker, Yoon, et al., 2013), heterogeneity between previous studies regarding sample size, measures of motor functioning, definition for motor impairment, and number of risk factors tested make interpretation of findings difficult. However, peri- and neonatal factors that were repeatedly reported to increase the risk for motor impairment were prematurity, male sex, and brain injury during the pre- and perinatal period such as IVH and PVL, emphasising the multifactorial nature of risk factors.

Given that prematurity is one of the main predictors or precursors for motor impairment, it is not surprising that most studies focussed on children born VP or with VLBW. In contrast, studies in general population samples or samples that include children born across the whole range of gestational age are rare. However, the majority of children with motor impairments are term born (Faebo Larsen et al., 2013; Moster, Lie, & Markestad, 2008; Moster, Wilcox, Vollset, Markestad, & Lie,

2010). Therefore, it is important that studies include children across the whole range of gestational age.

Further, studies mostly investigated biological and medical factors, despite evidence that social environmental factors can additionally affect children's motor, cognitive and social-emotional functioning. That is, except for maternal socioeconomic factors, such as maternal education and occupation, social environmental factors rarely have been included when perinatal and neonatal risk factors of motor impairment were investigated. While most child health and medical factors cannot be changed, social environmental factors may be malleable and should therefore be included in studies that investigate risk factors of motor impairment.

Interventions and Treatment for Motor Impairment

Motor impairment can severely limit children's daily and leisure activities, physical play and participation (Izadi-Najafabadi et al., 2019). Parents are particularly concerned that their child's motor impairment is affecting development and functioning throughout childhood in terms of self-care, academic achievement, participation in activities and play, peer relationships, self-esteem, and emotional health (Missiuna et al., 2007; Segal, Mandich, Polatajko, & Cook, 2002). Given the evidence for persistent motor impairment beyond childhood, along with or increasing prevalence rates for non-CP motor impairment (Cousins & Smyth, 2003; Husby et al., 2013; Poole et al., 2015b; Spittle et al., 2018), it is critical for young children with, or at risk of, motor impairment to receive effective interventions and treatment to support motor development and to prevent or ameliorate motor problems as well as associated psychological and functional problems (Bejerot,

2011; Blank et al., 2019; Blauw-Hospers, de Graaf-Peters, Dirks, Bos, & Hadders-Algra, 2007; Novak et al., 2017; Riethmuller, Jones, & Okely, 2009; Spittle & Morgan, 2018; Spittle, Orton, Anderson, Boyd, & Doyle, 2015; Veldman, Jones, & Okely, 2016).

Early Intervention

The period from conceptions to two years after birth is crucially important for brain development (T. T. Brown & Jernigan, 2012; Hadders-Algra, 2005). These early years are a period during which the brain is shaped through sensory, motor and language experience, but is also vulnerable to adverse environmental events and psychosocial factors, including preterm birth and associated brain injuries and insults (e.g., IVH and PVL, and white matter injuries), early experience and stress associated with care and medical interventions in the neonatal intensive care unit (NICU), as well as parental stress and anxiety that can affect developmental outcome (Chaudhari, 2011; DeMaster et al., 2019; Kolb, Harker, & Gibb, 2017; Rogers, 2018; Volpe, 2009). This period of 'brain plasticity' can provide an opportunity for intervention (Volpe, 2019), in particular interventions that feature stimulating and high quality home environment and parenting (Anderson, Treyvaud, & Spittle, 2020; DeMaster et al., 2019; Morgan, Novak, & Badawi, 2013). The importance of parent involvement in early intervention programmes for neonatal at-risk children in the NICU and beyond has been noted in a number of studies and review articles (Anderson et al., 2020; Milgrom et al., 2010; Spittle & Morgan, 2018; Spittle & Treyvaud, 2016; Vanderveen, Bassler, Robertson, & Kirpalani, 2009).

Early intervention typically encompasses a time period from birth to about 5 years of age, and often commences before long-term problems are apparent or a

diagnosis of motor impairment has been made (Spittle & Morgan, 2018). They are designed to predominantly target children with a general risk for a developmental delay or deficit in multiple domains (including cognitive, behavioural, and motor functions) (e.g., Koldewijn et al., 2010), in particular children born preterm. But they can also be targeted towards a specific developmental problem or outcome (e.g., Ustad et al., 2016). Because the aim of early interventions is primarily preventative, they use strategies that are designed to promote optimal development of the infant and limit or ameliorate negative effects and long-term impairment of biological (e.g., prematurity) or medical (e.g., brain injury, respiratory disease) risks (Anderson et al., 2020; Blauw-Hospers et al., 2007; Johnson & Marlow, 2011).

Due to multifaceted and complex developmental problems in at-risk or high-risk infants, early intervention programmes are often multidisciplinary and vary widely in their theoretical construct (e.g., physiotherapy, occupational therapy, teaching parents about infant development and milestones, enhancement of parent-infant relationship, or enrichment of the home environment) and make-up, i.e., how they are set up and composed in terms of intervention elements, setting, duration and intensity of treatment (Anderson et al., 2020; Orton, Spittle, Doyle, Anderson, & Boyd, 2009). The wide variety between early intervention programmes across studies makes it therefore difficult to identify effective intervention features or activities (Hughes, Redsell, & Glazebrook, 2016; Orton et al., 2009).

Infants who are at risk for developmental delay or problems are frequently enrolled into intervention programmes while they are still in the NICU (Spittle & Morgan, 2018). Although early intervention delivered to high-risk infants in the NICU, such as the Newborn Individualised Developmental Care and Assessment

Program (NIDCAP), have shown to have a temporary positive effect on motor development (Blauw-Hospers et al., 2007), evidence of improved long-term neurodevelopmental or short-term medical outcomes is lacking (Ohlsson & Jacobs, 2013).

A number of review articles, including meta-analyses, have demonstrated that early interventions that continue or start once the infant has been discharged from the neonatal unit can have a beneficial, if only a small and short-term (i.e., up to 36 months), effect on motor development (Blauw-Hospers & Hadders-Algra, 2005; Hughes et al., 2016; Orton et al., 2009; Spittle et al., 2015). However, there is no evidence for a positive effect into preschool or school-age, which was attributed to a small number of studies conducted at that age range (Orton et al., 2009; Spittle et al., 2015). When meta-analysing studies according to age groups in infancy, it was found that positive and initially large effects of early intervention for motor outcomes diminished over time, from 3 months to 24 months (Hughes et al., 2016). While no clear beneficial effect for physiotherapeutic approaches based on neurodevelopmental treatment (NDT) were found (Blauw-Hospers et al., 2007; G. T. Brown & Burns, 2001), intervention programmes that target specific motor functions and promote child's exploration and active motor behaviour (e.g., treadmill or conductive training), or strategies for an enriched environment and parent support and training, proved to be effective (Blauw-Hospers & Hadders-Algra, 2005; Hughes et al., 2016; Morgan et al., 2016; Morgan et al., 2013). Accordingly, a recent RCT in Norway reported improved motor performance scores with a small to medium effect size in infants born very preterm after a 3-week intervention that consisted of parent-

administered physiotherapy that aimed to promote head and postural control, and midline orientation (Ustad et al., 2016).

Physiotherapy as an early intervention for children at-risk or with motor impairment

Children or infants that are identified to have or to be at risk for abnormal motor developmental or motor delay are usually referred to therapeutic intervention within the health service. Among other therapeutic interventions, such as occupational therapy, physiotherapy (often also called physical therapy) specifically aims to ameliorate or improve motor outcome, including activity and participation in daily life (Imms & Gibson, 2018). Physiotherapy can be based on diverse theoretical and practical approaches and settings. Traditional physiotherapy focusses on the improvement or normalisation of movement and movement patterns (for example, through positioning), while modern or newer physiotherapeutic interventions often take social and environmental surroundings into account, with a focus on improving participation and motor activities at home, in school and leisure (Spittle & Morgan, 2018).

Despite reports of positive effects of physiotherapy on motor skills in children with motor coordination problems, these studies were often flawed in their methodological design, lack of a control group, did not use a randomised design, and/or were underpowered (i.e., small samples), and thus could not provide sufficient evidence to prove the effectiveness of physiotherapy (e.g., Schoemaker, Hijlkema, & Kalverboer, 1994; Niemeijer, Smits-Engelsman, & Schoemaker, 2007). To test whether physiotherapy is effective or has an effect on motor outcomes, randomised controlled trials (RCTs) or controlled trials are needed. However, reports

of RCTs that included infants with or at risk for motor impairment show no differences or only short term effects on motor outcomes compared with a control group that either received no treatment, or conventional treatment, or other forms of early intervention (Blauw-Hospers, Dirks, Hulshof, Bos, & Hadders-Algra, 2011; E. C. Cameron, Maehle, & Reid, 2005; M. Goodman et al., 1985; Palmer et al., 1988; Piper et al., 1986; Ustad et al., 2016; Weindling et al., 1996). Despite the lack of proven efficacy, it is a frequently prescribed therapy for infants at risk of motor problems such as those born preterm or with neonatal complications.

Although the effectiveness of physiotherapy cannot be tested in observational or longitudinal cohort studies, participants of these cohorts often receive therapeutic interventions, including physiotherapy. It is therefore important to account for these interventions, when studying motor related outcomes, in particular when longitudinal associations are investigated.

Intervention for Children with Motor Impairment

Motor impairment is one of the major reasons that children are referred to or receive interventions and support, such as physiotherapy, occupational therapy, or within school and educational services (Blauw-Hospers et al., 2007). Based on different theoretical frameworks of motor development and motor learning (e.g., the neuromaturational and hierarchical theories, and the dynamic systems theory), a variety of approaches to intervention for children with motor impairment (e.g., CP and DCD), including process-oriented, task-oriented (or activity- or participation-oriented) and traditional physiotherapy (e.g., Bobath, Vojta, and motor learning approaches) or occupational therapy exist (Blank et al., 2019; Blank, Smits-Engelsman, Polatajko, & Wilson, 2012; D. Sugden, 2007).

Both process-oriented and task-oriented interventions use activity-based approaches. In contrast to the process-oriented approach that aims to improve motor deficiencies, the task-oriented approach is designed to promote motor functioning (Smits-Engelsman et al., 2018). In other words, process-oriented interventions target specific motor control functions that are subservient to motor performance (P. H. Wilson, 2005), while task-oriented interventions aim to improve motor skills or functions that the child needs for a specific task or activity of daily living to promote participation at home, school, and sports and leisure (Hyde et al., 2017). Physiotherapy and occupational therapy make use of both by encompassing process-oriented approaches and focusing on movement through motor skills training for the child to learn fundamental gross and fine motor skills, such as hopping, jumping, throwing catching, cutting, drawing and writing (Smits-Engelsman et al., 2013).

A number of systematic reviews and meta-analysis that mostly but not exclusively included randomised controlled trials (RCTs) have shown that task- or activity-based interventions and conventional or movement-based interventions, including physiotherapy or occupational therapy can have positive and moderate to large effects on gross or overall motor outcomes in children with CP or DCD (K. L. Cameron et al., 2020; Lucas et al., 2016; Offor, Williamson, & Caçola, 2016; Preston et al., 2017; Smits-Engelsman et al., 2013; Smits-Engelsman et al., 2018; Yu, Burnett, & Sit, 2018). However, authors have been cautious in their interpretation of observed effect sizes as there was only a small number of studies available with inconsistencies that hampered comparability, for example regarding intervention design and duration. Further, most of these studies had a small sample size (i.e., below N=100) and were considered to be limited in methodological

quality, such as inadequate blinding of outcome assessors, follow-up, and between group differences, as well as high risk of bias for randomisation and allocation concealment.

Summary and Conclusions

The first two to three years of life mark an important period of brain and musculoskeletal development and represent an opportune widow for early intervention with the aim to improve children's motor development and thus prevent motor difficulties (DeMaster et al., 2019; Volpe, 2019; Zeanah, Boris, & Larrieu, 1997). Early intervention programmes are predominately directed at children who are at risk for general developmental problems, including cognitive, behavioural and motor difficulties. Accordingly, these programmes are often multidisciplinary and vary widely in their make-up and target population. Motor-specific and task- or activity-based interventions that involve and support parents have shown positive effects on early motor development in children with, or at risk for, motor impairment (Hughes et al., 2016; Morgan et al., 2013; Smits-Engelsman et al., 2018; Spittle et al., 2015; Spittle & Treyvaud, 2016; Yu et al., 2018). However, lack of long-term effectiveness, small sample sizes, low methodological quality, and risk of bias, limit the interpretation of results.

Given that environmental factors, such as familial socioeconomic position and intervention or treatment, are important determinants of child development (Anderson et al., 2020; Benavente-Fernandez et al., 2019; Burnett et al., 2018; McCormick et al., 2006), it is essential to account for the potential effects of these factors in observational longitudinal studies.

Key Objectives and Research Questions

This section describes the three empirical studies that were planned and carried out for this thesis. Following from the literature overview in the preceding sections that highlighted gaps in current knowledge and research, the rationale for each empirical study as well as their main objectives and research questions are briefly outlined here. More detailed information about the three studies is given in Chapters 3, 4 and 5.

Study 1: Predictors of Early Motor Trajectories from Birth to 5 Years in Neonatal At-Risk and Control Children

Emerging evidence suggests that mild or moderate motor impairments without a diagnosis of CP or DCD can profoundly affect children's development and everyday activities. It is therefore important to identify children with or at-risk for motor problems early to enable invention and treatment.

With some consistency, prior research has identified prognostic factors for motor impairments that occur with CP or DCD, including biological and medical factors, such as preterm birth, males sex and peri- or neonatal complications, for example IVH. However, despite evidence that early environmental factors, such as socioeconomic status, family adversity, and parent-infant relationships, may additionally affect, motor, cognitive and social-emotional development, these factors have seldom been included in investigations for prognostic or risk factors of motor impairment.

The aims of this study were: first, to identify groups of children with a similar pattern of motor functioning across multiple time points and ages (i.e.,

trajectories of motor functioning from birth to age 56 months), and second, to investigate biological and social-environment factors that influence early motor development (i.e., motor trajectories). In addition, it was tested whether findings would be replicated in a second cohort.

Study 2: Effects of Infant Motor Problems and Treatment with Physiotherapy on Child Outcomes at School-Age

Evidence has shown that motor problems in infancy can influence subsequent developmental problems, including motor skills, cognitive function (including, intelligence and attention), and mental health. However, results have not always been consistent across studies, and there are not many studies that have conducted longitudinal analyses from infancy to school-age.

Early intervention and treatment can influence development and improve motor performance. Indeed, most children who show abnormal functioning or who are at-risk for developmental delay are referred to intervention or treatment. However, observational studies often do not take into account or test whether early intervention and treatment changes longitudinal associations between motor functioning in infancy and later developmental outcomes.

The objective of Study 2 was to investigate whether there is a longitudinal association between early motor functioning and developmental outcomes at school-age, including motor skill, intelligence, attention regulation and mental health. Further, it was tested whether physiotherapy may affect the association between early motor problems and subsequent developmental outcomes.

Study 3: Early Motor Trajectories Predict Motor but not Cognitive Function in Preterm and Term-Born Adults

Early motor and cognitive impairments have been associated with subsequent and long-term adverse outcomes across diverse developmental domains and functions, such as scholastic and educational achievement, physical and mental health, and quality of life. Motor and cognitive function are linked through sensorimotor experience and skills, particularly during infancy and the preschool years. The association between motor and cognitive function has been evidenced by multiple cross-sectional studies. However, by lack of longitudinal studies, particularly in preterm populations, it is not clear, whether this association holds into adulthood.

Following from this, Study 3 sought to answer the following questions: Are preterm birth and early motor development (from birth to 56 months) associated with cognitive function in adulthood? Or can long-term associations only be ascertained within the same developmental domain?

Chapter 2: Methodology

This chapter provides an overview of the Bavarian-Finnish Longitudinal Study which includes two cohort samples: The German Bavarian Longitudinal Study (BLS) and the Finnish Arvo Ylppö Longitudinal Study (AYLS). Both cohorts served as data sources for the studies and analyses outlined in the previous section: The BLS cohort data were used as the main data source for Study 1, 2 and 3, while the AYLS cohort data were used as an additional data source for Study 1.

The general design and cohort samples, recruitment of participants, and methods and instruments of data collections will be described. Specific methods and instruments that were used to answer the outlined research questions through secondary data analyses will be introduced and described, with a focus on the description and computation of early motor functioning. Other variables of interest that include prenatal and neonatal predictors and risk factors, receipt of physiotherapy in early childhood, and developmental outcomes in childhood and adulthood are only briefly mentioned with more detailed information provided in the respective methods sections of the three empirical studies (Chapters 3, 4 and 5).

Study Design and Participants of the Bavarian-Finnish Longitudinal Study

The Bavarian-Finnish Longitudinal Study (BFLS) includes two geographically defined, whole population samples of neonatal at-risk children born between January 1985 and March 1986 in Southern Bavaria, Germany (Bavarian Longitudinal Study, BLS) and in the county of Uusimaa, Finland (Arvo Ylppö Longitudinal Study, AYLS). The initial study aims of the BFLS were: (a) to document the prevalence of somatic and psychosocial outcomes of neonatal

problems and early delivery in an unselected population of children; and (b) to evaluate the impact of a regionalised neonatal service to the locally organised service provisions in Germany and Finland.

The target sample for both cohorts comprised all children who were born in in an obstetric unit (153 obstetric units in Bavaria and 7 obstetric units in Finland) and required admission to a neonatal unit in a children's hospital (16 hospitals in Bavaria and 5 hospitals in Finland) within the first 10 days after birth (BLS: *N*=7,505 [10.6% of all births]; AYLS: *N*=1,536 [9.8% of all births]). This group of children, defined as the at-risk group, included very ill preterm infants (born from 20 weeks of gestation) to term born infants who required only brief inpatient observation for diagnostic purposes. During the same time, healthy infants who were not transferred and cared for on normal postnatal wards in the same obstetric units/hospitals were recruited as controls (BLS: *N*=916; AYLS: *N*=658). Notably, at the time (i.e., in the mid-80s) most special or neonatal care units in Bavaria were situated in children's hospitals and not part of an obstetric hospital. In contrast, almost all special care units and children's hospitals in Finland were associated with an obstetric hospital (i.e., perinatal centres).

Phase I: Infancy and Early Childhood (Birth to age 56 months)

Phase I of the BFLS includes the full geographical population in Southern Finland and Southern Bavaria (Figure 1).

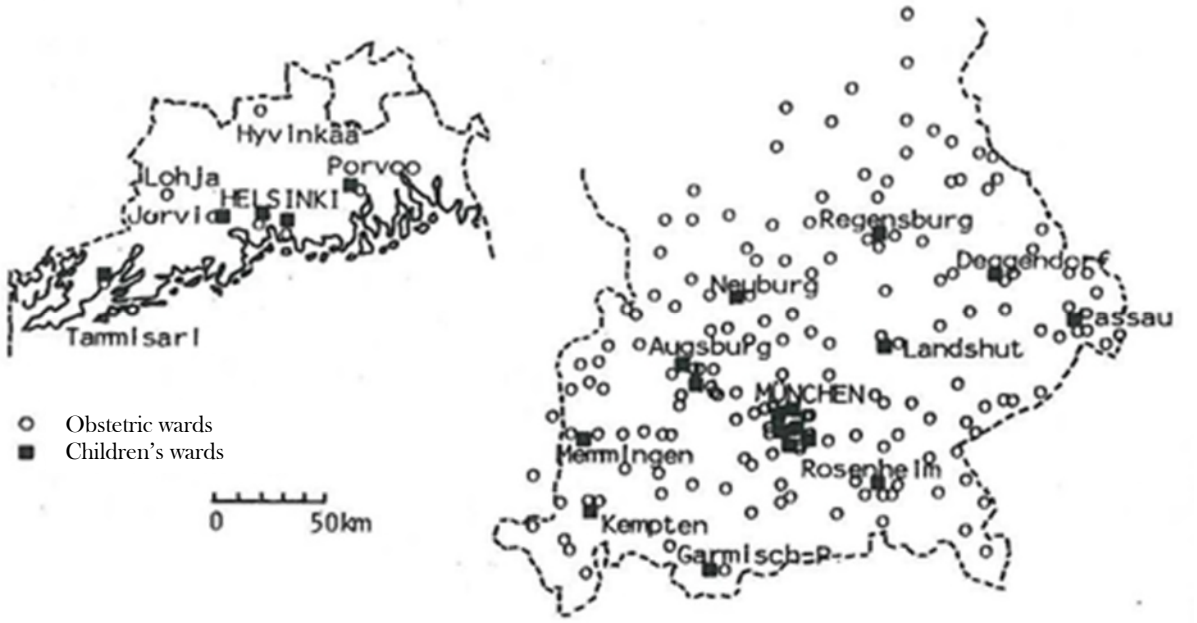

Figure 1. AYLS and BLS cohorts.

Overall, four assessments were carried out at birth (i.e., daily during the neonatal period and at discharge from hospital), at 5 and 20 months (corrected for prematurity) and at 56 months (chronological age). Identical measures and instruments were used in both cohorts. Children and their parents were assessed by an interdisciplinary team for an entire day including neurological assessments, parent interviews, cognitive assessments and observations of behaviour.

The baseline characteristics, including indicators of perinatal and neonatal health, and family socioeconomic status, for the BLS and AYLS cohorts are presented in Table 1.

Table 1. *Baseline characteristics of the BLS and AYLS cohorts, stratified by groups of at-risk and control children recruited during the first 10 days after birth (survivors and those who died before discharge).*

	BLS			*AYLS*		
	Total	At-risk group	Control group	Total	At-risk group	Control group
	N=8,421	*N*=7,505	*N*=916	*N*=2,194	*N*=1,536	*N*=658
Gestational age (weeks), mean (SD)	37.46 (3.35)	37.12 (3.43)	39.35 (1.46)	38.16 (3.05	37.58 (3.37)	39.52 (1.36)
Birth weight (grams), mean (SD)	2,796 (819)	2,733 (828)	3,315 (502)	3,251 (815)	3,111 (888)	3,576 (476)
Small for Gestational Age, N (%)	2,150 (25.5)	2,047 (27.3)	103 (11.2)	312 (14.2)	263 (17.1)	49 (7.4)
Multiple, N (%)	860 (10.2)	791 (10.5)	69 (7.5)	115 (5.2)	99 (6.4)	16 (2.4)
Child sex, N (%)						
Male	4,497 (53.4)	4,043 (53.9)	454 (49.6)	1,194 (54.4)	868 (56.5)	326 (49.5)
Female	3,924 (46.6)	3,462 (46.1)	462 (50.4)	1,000 (45.6)	668 (43.5)	332 (50.5)
Length of stay in hospital[b] (days), mean (SD)	22.17 (26.09)	23.95 (27.07)	7.58 (3.69)	9.52 (20.55)	11.06 (23.52)	5.94 (9.94)
Family Socioeconomic Status[c], N (%)						
High	1,518 (20.6)	1221 (18.9)	297 (32.7)	657 (31.4)	417 (29.0)	240 (36.6)
Medium	2,748 (37.3)	2380 (36.8)	368 (40.5)	944 (45.1)	654 (45.5)	290 (44.2)
Low	3,110 (42.2)	2867 (44.3)	243 (26.8)	493 (23.5)	367 (25.5)	126 (19.2)

[a] BLS: N=24 missing data (for the at-risk group); [b] BLS: N=11 and AYLS N=2 missing data; [c] BLS: N=1,045 and AYLS: N=100 missing data.

Follow-up Assessments of the Bavarian Longitudinal Study

Phase II: Early Childhood – School-Age (6 and 8 years)

After the first phase of the BFLS study (birth to 56 months), the BLS sample in Germany was followed up around school-age (6 and 8 years). To allow for more intensive psychological and neurological assessments, the sample was reduced while preserving sufficient statistical power. From the initial BLS sample, 1,543 children were examined at 6 and 8 years. This sample included all very preterm (<32 weeks of gestation, VP) and/or very low birth weight (<1500g, VLBW) children and a sub-sample of children born ≥32 weeks of gestation (randomly drawn within the stratification factors child sex, family socioeconomic status and degree of neonatal risk) of the initial target or at-risk group, and 344 healthy term control children. At both time points, participants and their parents were assessed for one whole day including neurological assessments, parent interviews, cognitive assessments, and observations of behaviour.

Phase III: Young Adulthood (26 years)

A further follow-up assessment of the BLS cohort was carried out in young adulthood (26 years). The assessments at 26 years comprised a further reduced sample (*N*=489) that focused on VP/VLBW and term born control individuals. The main aims of this assessment included the identification of protective and resiliency factors in the development of children exposed to biological or environmental adversity. Participants were assessed for one whole day. The assessments focused on neuronal, neuro-cognitive and behavioural development, health utility, and quality of life.

Measures

All predictors, outcome and control variables used across all three empirical studies are shown in Table 2.

Table 2. *Summary of cohorts, time frame, and predictors, outcome and control variables across studies.*

	Study 1	*Study 2*	*Study 3*
Cohort	BLS and AYLS	BLS	BLS
Study Phase	Phase I	Phase II	Phase III
Time Frame	Birth to 56 months	Birth to 6 and 8 years	Birth to 26 years
Predictor Variables	- Pre-pregnancy, Pregnancy and Perinatal Complications - Neonatal Characteristics and Health - Neonatal Course - Early Social Environment (birth/5 months)	- Risk of Motor Impairment (at birth and at 5 months, respectively) - Receipt of Physiotherapy (between birth and 56 months)	- Trajectories of Motor Difficulties (birth to 56 months) - Cognitive function (at 56 months)
Outcome Variables	Trajectories of Motor Difficulties (birth to 56 months)	- Motor Skills - Mental Health - Cognitive Function (IQ) - Attention Regulation (all four at 6 and 8 years)	- Motor Competence - Cognitive Function (IQ) (both at 26 years)
Control Variables	All predictor variables	Gestational Age (GA), Small for GA, Sex, Socioeconomic Status at Birth	Gestational Age (GA), Small for GA, Sex, Socioeconomic Status at Birth

Note. A detailed description of all measures and variables used in the three studies can be found in Chapters 3, 4 and 5.

Motor Functioning

In order to determine appropriate intervention or treatment it is essential to assess motor functioning. A variety of diagnostic and assessment tools are available to assess and identify motor problems in children (Cools, De Martelaer, Samaey, & Andries, 2009; S. L. Edwards & Sarwark, 2005; Griffiths et al., 2018). Young infants and toddlers at risk of a developmental delay (e.g., preterm born children), including cognitive and motor functioning, are often assessed with general assessment and screening tools (e.g., the Bayley Scales of Infant Development, the Griffiths Scales, the Ages and Stages Questionnaire, the Peabody Developmental Motor Scales, the Alberta Infant Motor Scale, and the Ages and Stages Questionnaire) or classic neurological examinations that are able to measure early motor activities and motor capabilities, and to identify delayed or abnormal development (S. L. Edwards & Sarwark, 2005; Piek, 2006).

For both cohorts of the BFLS study (i.e., BLS and AYLS) an extensive and detailed standardized physical and neurological examination based on Prechtl's method (Prechtl, 1977) was carried out by specially trained developmental paediatricians at birth, at 5 and 20 months (corrected for prematurity) and 56 months (chronological age). For the purpose of the analyses planned for this thesis, a *motor problem score* was computed for each time point from the data obtained through the standardized physical and neurological examination at each age. Both motor and neurological items that involve motor functions (for example, items on fine and gross motor skills, oculomotor function, muscle tone, and reflexes) were extracted and categorised into 'within' and 'outside the normal range' of motor functioning (see Tables 4 to 7; for an overview of the extracted items with information on their

original categorisation/scaling see Appendix A to D). For an overview of main motor functioning areas of extracted items see Table 3.

Table 3. *Main areas of assessed motor functioning from birth to 56 months*.*

	Birth	*5 months*	*20 months*	*56 months*
Fine motor	- Oculomotor/ orofacial	- Oculomotor/ orofacial - Prehension (quality: movement pattern/sequence, co-movements)	- Oculomotor/ orofacial - Prehension (quantity & quality: movement pattern/sequence, co-movements)	- Oculomotor/ orofacial - Fine motor skills testing (e.g., drawing, pinboard)
Gross motor/ sensorimotor/patterns of movement, postural development	- Supine posture - Spontaneous motor activity - Movement pattern/sequence - Involuntary movements - Muscle tone - Head control - Arm position/posture	- Supine and prone posture - Quantity/ quality of motor function - Muscle tone and strength - Pulling up to sit - Vertical, tilted and horizontal suspension	- Sitting - Standing - Walking - (Crawling) - Muscle tone and strength	- Sitting - Standing - Walking - Climbing stairs - Balance testing (e.g., walking on toes, one leg balance)

	Birth	*5 months*	*20 months*	*56 months*
Responses/ Reflexes	- Grasping (hands/feet) - Knee jerk - Achilles tendon - Biceps tendon - Moro response	- Knee jerk - Achilles tendon - Biceps tendon - Foot clonus - Tactile-kinaesthetic responses	- Knee jerk - Achilles tendon - Biceps tendon - Tactile-kinaesthetic responses	- Knee jerk - Achilles tendon - Biceps tendon - Tactile sensitivity

* For a more detail on of motor and neurological items at each assessment see Tables 4 to 7 and Appendices A to D.

Table 4. *Raw Motor and Neurological Items at Birth for the BLS and AYLS: Frequencies, %*

	BLS (*N*=8,094)			AYLS (*N*=2,071)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
Fine motor: oculomotor, orofacial						
1. Pupils (shape)	97.0	0.6	2.4	97.6	0.3	2.0
2. Pupil reaction to light	92.6	2.6	4.8	94.9	1.3	3.8
3. Eye position	89.7	6.5	3.8	91.7	5.4	2.8
4. Fixate & follow eye movement	62.3	28.6	9.1	78.2	15.8	6.0
5. Ears (reaction to a loud acoustic noise)	81.7	17.7	0.6	92.5	6.0	1.5
6. Facial expression	95.9	3.7	0.4	97.4	1.7	0.8
7. Glabella reflex	94.7	5.1	0.2	95.2	4.0	0.8
8. Sucking	94.0	5.8	0.2	97.3	2.6	0.0
9. Swallowing	96.4	0.9	2.7	98.7	0.4	0.8
Gross motor: sensorimotor						
10. Posture in supine position	71.1	28.2	0.7	92.1	6.9	1.0
11. Quantity of spontaneous motor activity	78.6	21.2	0.2	87.9	11.9	0.1
12. Movement pattern	88.4	10.4	1.2	96.3	2.9	0.8
13. Movement sequence	75.4	23.8	0.8	94.8	4.5	0.7

Items	BLS (*N*=8,094) Within normal range	Outside normal range	Missing data	AYLS (*N*=2,071) Within normal range	Outside normal range	Missing data
14. Involuntary movements	80.9	18.4	0.7	90.1	9.7	0.3
15. Muscle tone at rest, posture	75.8	23.6	0.6	93.0	6.6	0.4
16. Muscle tone at rest, resistance against passive movement	68.0	31.2	0.9	73.2	25.7	1.2
17. Head control	62.2	35.6	2.2	62.7	36.1	1.2
18. Arm position/posture	80.0	17.8	2.1	85.4	13.3	1.3
Reaction/Reflexes/Responses						
19. Grasping reaction hands	88.8	10.8	0.4	96.7	3.1	0.2
20. Grasping reaction feet	89.4	9.7	0.8	98.1	1.7	0.1
21. Knee jerk/Patellar reflex	77.8	20.8	1.4	86.8	12.7	0.5
22. Achilles tendon reflex	53.3	38.4	8.3	86.6	12.8	0.6
23. Biceps reflex	70.2	25.5	4.3	92.0	7.6	0.4
24. Moro response, phase I (adduction, extension of arms)	82.0	14.9	3.1	87.3	12.0	0.6
25. Moro response, phase II (adduction, flexion of arms)	70.8	25.9	3.2	81.7	17.6	0.8

Table 5. *Raw Motor and Neurological Items at 5 Months for the BLS and AYLS: Frequencies, %*

	BLS (*N*=6590)			AYLS (*N*=1990)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
Fine motor: oculomotor, orofacial						
1. Eye position	97.0	3.0	0.0	98.9	1.0	0.1
2. Eyes, setting-sun sign	98.5	1.5	0.0	98.5	1.5	0.0
3. Eyes, following movement of eyes	92.5	6.6	0.8	98.8	0.9	0.4
4. Eyes, strabismus	92.1	7.8	0.2	92.9	6.2	0.9
5. Eyes, nystagmus	98.4	1.1	0.5	99.7	0.2	0.1
6. Eyes, pupils (shape)	99.2	0.6	0.2	99.1	0.8	0.1
7. Eyes, pupil reaction to light	98.6	0.5	0.8	99.6	0.3	0.2
8. Eyes, pupil reaction to convergence	92.1	1.7	6.3	98.9	0.6	0.6
9. Eyes, fixation	94.7	1.4	4.0	99.3	0.5	0.2
10. Eyes, follow with gaze	93.1	2.0	4.9	99.0	0.7	0.4
11. Eyes, follow with gaze and change of head position	92.1	2.3	5.6	97.7	1.3	1.0
12. Eyes, eye contact	97.0	2.8	0.2	99.1	0.8	0.2
13. Ears, reaction to noise[a]	79.2	19.2	1.6	93.0	5.9	1.1

	BLS (*N*=6590)			AYLS (*N*=1990)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
14. Face muscles	97.8	2.0	0.2	98.6	0.9	0.5
15. Facial expression	91.4	4.7	3.9	97.4	2.5	0.1
16. Mouth and tongue movement	96.5	3.1	0.4	98.7	1.1	0.2
17. Sucking[b]	94.1	1.8	4.0	98.7	1.3	0.1
18. Swallowing[b]	96.1	0.6	3.3	99.5	0.4	0.1
Gross motor: sensorimotor – supine posture						
19. Posture supine - head	86.6	13.0	0.5	95.3	4.5	0.2
20. Posture supine - arms	82.7	14.2	3.1	93.5	5.8	0.7
21. Posture supine - hands	83.3	16.6	0.2	91.0	8.8	0.3
22. Posture supine - torso	85.8	14.1	0.2	98.0	1.9	0.1
23. Posture supine - hips	89.5	10.2	0.4	92.5	7.4	0.1
24. Posture supine - knee	95.5	4.3	0.2	96.0	3.9	0.2
25. Posture supine - feet	85.9	13.8	0.3	93.9	5.9	0.3
Gross motor: sensorimotor - spontaneous motor function, gross motor quality						
26. Spontaneous motor function - quantity	86.9	12.9	0.2	92.2	7.7	0.2

	BLS (*N*=6590)			AYLS (*N*=1990)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
27. Quality of gross motor function, movement pattern	89.9	9.8	0.3	96.4	3.5	0.1
28. Quality of gross motor function, stereotypies	94.9	1.4	3.8	99.0	0.9	0.1
29. Quality of gross motor function, movement sequence	83.6	16.1	0.3	91.6	8.1	0.3
30. Quality of gross motor function, speed of movement	88.8	8.0	3.2	97.0	1.5	1.5
31. Quality of gross motor function, range of movement	91.0	8.8	0.3	94.6	5.2	0.2
32. Sensorimotor, involuntary movements	94.9	4.7	0.4	95.4	4.2	0.5
Fine motor: prehension						
33. Fine motor skills, movement pattern	90.7	9.0	0.3	96.5	2.8	0.7
34. Fine motor skills, movement sequence	77.2	22.5	0.3	89.2	10.4	0.5
35. Fine motor skills, co-movements	78.2	18.2	3.6	93.6	5.6	0.8
Sensitivity						
36. Sensitivity, reaction/response to contract/touch or arms, legs, tummy	91.9	4.3	3.8	98.8	0.9	0.3

	BLS (*N*=6590)			AYLS (*N*=1990)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
Sensorimotor - muscle tone, muscle strength, joints						
37. Muscle tone at rest, obtained from posture	81.9	17.1	1.0	91.4	8.4	0.2
38. Muscle tone at rest, obtained from resistance	80.9	18.0	1.2	84.4	15.3	0.3
39. Muscle tone at activity	82.7	16.9	0.4	87.7	12.0	0.3
40. Peripheral muscle paresis	95.8	0.3	3.8	99.6	0.3	0.1
41. Muscle strength	97.5	2.3	0.2	97.7	2.1	0.2
42. Joint mobility	95.0	4.6	0.4	98.8	0.8	0.4
Reflexes						
43. Knee jerk	80.3	18.9	0.8	88.3	11.1	0.6
44. Achilles tendon	70.3	27.5	2.2	88.8	10.8	0.4
45. Biceps tendon	77.7	20.7	1.6	94.8	4.8	0.4
46. Foot clonus	98.6	0.8	0.6	98.5	1.0	0.5
Sensorimotor - pulling up to sit						
47. Pulling up to sit, head control	91.8	7.9	0.3	92.8	7.0	0.3
48. Pulling up to sit, posture of arms	88.0	11.7	0.3	88.8	10.9	0.3

	BLS (*N*=6590)			AYLS (*N*=1990)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
49. Pulling up to sit, posture of legs	91.3	8.4	0.3	94.3	5.4	0.3
50. Supported or independent sitting, posture	64.6	34.5	0.9	88.0	11.7	0.3
Sensorimotor – vertical, tilted and horizontal suspension, prone position						
51. Vertical suspension, posture	73.7	25.5	0.7	87.6	11.7	0.7
52. Vertical suspension, spontaneous motor function	88.3	10.3	1.3	94.2	4.8	1.0
53. Vertical suspension, muscle tone	81.4	18.3	0.3	89.9	9.4	0.7
54. Tilted suspension, head raising	77.3	22.3	0.3	76.8	22.2	1.0
55. Tilted suspension, thoracic spine raising	70.8	28.9	0.3	70.6	28.5	1.0
56. Horizontal suspension, posture	85.9	13.7	0.3	95.4	3.9	0.7
57. Turning from supine to prone, passive turning	72.2	24.7	3.1	79.7	19.0	1.3
58. Prone position, posture	79.7	19.4	0.9	93.1	6.7	0.2
59. Prone position, head raising	85.0	14.4	0.7	95.6	4.2	0.2
Tactile-kinaesthetic response						

	BLS (*N*=6590)			AYLS (*N*=1990)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
60. Response to touch	95.5	4.3	0.2	96.9	2.6	0.5
61. Response to position changes on surface	90.8	9.1	0.1	95.6	4.2	0.3
62. Response to position changes in space	86.7	13.0	0.2	91.8	8.0	0.2
63. Response while carried on arm	96.8	3.1	0.1	94.6	5.3	0.1

[a] Observed/tested and parent-reported (mainly tested).
[b] Observed/tested and parent-reported (mainly parent-reported).

Table 6. *Raw Motor and Neurological Items at 20 Months for the BLS and AYLS: Frequencies, %*

	BLS (*N*=6,061)			AYLS (*N*=1,926)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
Fine motor: oculomotor, orofacial						
1. Face muscles	97.4	2.1	0.5	98.5	1.2	0.3
2. Facial expression	93.9	6.0	0.1	96.7	3.3	0.0
3. Mouth and tongue movement	97.8	1.8	0.4	99.0	0.9	0.1
4. Eating procedure	96.8	2.9	0.3	98.5	1.3	0.2
5. Eyes, fixation	98.6	0.9	0.5	99.6	0.4	0.1
6. Eyes, eye contact	97.2	2.3	0.4	99.0	0.9	0.1
7. Eyes, eye position at rest	93.7	5.5	0.7	94.3	5.0	0.6
8. Eyes, eye position at fixation	93.1	4.3	2.7	95.4	2.1	2.4
9. Eyes, pupils (shape)	99.2	0.6	0.2	99.4	0.3	0.3
10. Eyes, pupil reaction to light	98.5	0.7	0.8	98.9	0.6	0.5
11. Eyes, pupil reaction to convergence	96.8	1.3	1.9	98.7	0.3	1.1
12. Eyes, forced/abnormal head posture during fixation	66.2	0.7	33.1	97.8	0.3	1.9

	BLS (*N*=6,061)			AYLS (*N*=1,926)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
13. Eyes, following movement to full extent	97.1	0.8	2.1	98.6	0.3	1.1
14. Eyes, following movement, smooth	97.1	2.5	0.4	98.7	0.6	0.7
15. Eyes, nystagmus	99.3	0.6	0.2	99.5	0.1	0.4
16. Eyes, eyelid flutter	99.5	0.3	0.2	99.7	0.0	0.3
17. Eyes, vision, with orientating assessment	97.7	1.6	0.7	98.6	0.4	1.0
18. Eyes, glare sensitivity (assessed by examiner)	97.8	1.5	0.7	92.5	6.1	1.4
19. Ears, hearing (observed during examination)	91.9	4.3	3.8	95.0	1.5	3.5
Gross motor: sitting						
20. Sitting, posture during independent or supported sitting	87.0	10.9	2.1	94.9	4.3	0.8
21. Sitting, posture retention/balance: head	98.6	1.2	0.2	99.2	0.7	0.1
22. Sitting, posture retention/balance: torso	96.6	2.9	0.4	98.1	1.6	0.3
23. Sitting, posture retention/balance: hips	96.0	3.6	0.4	98.0	1.7	0.3

	BLS (*N*=6,061)			AYLS (*N*=1,926)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
24. Sitting, posture retention/balance: lateral support reaction	96.8	2.6	0.6	94.1	1.4	4.5
25. Sitting, posture retention/balance: movement transitions (from lying to sitting, from sitting to standing, from supine to prone and in reverse)	93.7	5.8	0.5	96.6	2.8	0.7
26. Sitting, posture retention/balance: pulling up to sit, head control	93.7	0.9	5.4	95.8	0.8	3.3
Fine motor						
27. Fine motor function, quantity	96.3	2.7	1.0	98.4	1.2	0.4
28. Fine motor function, variable and economic movements	88.4	10.0	1.6	93.4	5.6	1.1
29. Fine motor function, movements symmetric, fluent etc.	89.5	10.0	0.4	93.9	5.6	0.5
30. Fine motor function, co-movements	91.2	8.4	0.4	98.4	0.9	0.6
Gross motor: standing						
31. Standing, posture	80.2	16.8	3.0	81.8	17.1	1.1
32. Standing, posture retention	90.5	6.8	2.6	88.8	9.0	2.2

	BLS (*N*=6,061)			AYLS (*N*=1,926)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
Gross motor: walking						
33. Walking, quality: economic, rhythmic, automated, variable.	89.0	8.1	2.9	94.7	3.9	1.5
34. Walking, movements fluent, stable, harmonious.	84.5	12.4	3.1	91.8	6.5	1.7
35. Walking, moderate pace, variable	91.5	5.2	3.3	96.6	1.8	1.6
36. Walking, posture	77.6	18.8	3.7	84.6	12.9	2.5
37. Walking, posture retention: head	96.6	0.2	3.2	98.4	0.2	1.4
38. Walking, posture retention: torso	95.2	1.7	3.1	98.1	0.6	1.3
39. Walking, posture retention: pelvis	93.5	3.6	2.9	98.0	0.7	1.3
Gross motor: crawling[a]						
40. Crawling, quality: economic, rhythmic, automated, variable	96.8	0.8	2.4	98.5	0.3	1.1
41. Crawling, movements fluent, stable, harmonious	96.6	1.1	2.3	98.4	0.5	1.1
42. Crawling, posture	96.6	1.1	2.3	98.5	0.3	1.2
43. Crawling, posture retention: head	97.4	0.2	2.4	98.9	0.0	1.1

	BLS (*N*=6,061)			AYLS (*N*=1,926)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
44. Crawling, posture retention: torso	97.2	0.4	2.5	98.7	0.2	1.1
45. Crawling, posture retention: pelvis	97.0	0.4	2.5	98.7	0.2	1.2
46. Crawling, raising arm to grab an object and not losing balance	97.3	0.4	2.4	98.7	0.1	1.2
Gross motor: movements, muscle tone						
47. Readiness to jump	92.2	4.0	3.7	87.4	6.5	6.0
48. Involuntary movements	96.5	1.6	1.9	98.0	1.3	0.7
49. Stereotypes	96.5	1.7	1.8	99.6	0.3	0.1
50. Muscle tone at rest, obtained from posture	87.7	10.3	1.9	93.1	5.2	1.6
51. Muscle tone at activity (observed while handling an object, in vertical positions and running fast)	95.1	4.0	0.9	96.6	1.6	1.8
Sensitivity, muscle strength, muscle paresis, joint mobility						
52. Sensitivity (reaction to non-visual contact with a brush on arms, legs, face and tummy)	95.1	4.1	0.8	98.0	0.6	1.3

	BLS (*N*=6,061)			AYLS (*N*=1,926)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
53. Muscle strength	97.7	1.8	0.5	96.3	2.0	1.8
54. Peripheral muscle paresis	99.4	0.4	0.3	99.6	0.3	0.1
55. Joint mobility	97.0	2.3	0.6	98.1	1.6	0.4
Reflexes						
56. Knee jerk	79.2	9.8	11.0	82.1	12.5	5.3
57. Achilles tendon	72.1	8.1	19.8	81.0	10.9	8.1
58. Biceps tendon	60.7	8.3	31.0	85.2	6.9	7.9
Tactile and auditive responses/sensitivity						
59. Reaction to touch[b]	96.3	3.2	0.5	99.6	0.2	0.3
60. Pain sensitivity[b]	95.3	4.3	0.3	94.2	4.7	1.1
61. Response to change of position[b]	94.1	5.4	0.5	91.5	6.6	1.9
62. Quantity of movement (urge to move) during examination	85.7	13.3	1.0	87.6	11.9	0.5
63. Distinct noise sensitivity (according to examiner)	98.3	1.0	0.7	96.8	1.7	1.6

[a] If not walking yet or only walking for 2 months. Thus, if independent walking was achieved, crawling is coded as ‘within the normal range of motor function.
[b] Observed/tested and parent-reported (mainly tested)

Table 7. *Raw Motor and Neurological Items at 56 Months for the BLS and AYLS: Frequencies, %*

	BLS (*N*=5,599)			*AYLS* (N=1,527)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
Fine motor: oculomotor, orofacial						
1. Face, facial muscles	92.8	4.0	3.1	97.0	0.6	2.4
2. Face, lips form to whistle	88.5	4.9	6.6	83.6	10.9	5.6
3. Face, stick out tongue	90.1	2.3	7.5	91.4	1.6	6.9
4. Face, tongue movement	83.2	7.9	8.9	72.7	19.0	8.3
5. Face, mouth and tongue motor function	91.5	4.9	3.6	92.9	4.4	2.8
6. Eyes, eye position at rest	91.8	7.3	0.8	94.9	4.5	0.6
7. Eyes, pupils (shape)	98.4	0.3	1.3	99.2	0.2	0.6
8. Eyes, eye follow movements	94.0	2.4	3.6	96.1	1.8	2.1
9. Eyes, extent of eye follow movements	94.9	0.9	4.1	97.4	0.4	2.2
Sensorimotor: sitting, standing, walking, climbing stairs						
10. Sitting, independent sitting > 5 min.	97.6	1.2	1.2	99.3	0.2	0.5
11. Sitting, posture	89.6	8.3	2.2	98.7	0.8	0.6
12. Sitting, joint mobility	93.8	3.0	3.2	97.5	1.7	0.8

Items	BLS (*N*=5,599) Within normal range	Outside normal range	Missing data	*AYLS* (N=1,527) Within normal range	Outside normal range	Missing data
13. Sitting, balance	92.9	1.6	5.4	98.4	0.8	0.8
14. Sitting, quantity of moving	74.2	24.0	1.8	80.0	17.9	2.1
15. Sitting, muscle strength	90.8	2.9	6.3	95.3	1.6	3.1
16. Standing, independent standing > 5 min	96.7	1.5	1.8	99.0	0.5	0.5
17. Standing, posture	70.8	24.6	4.6	77.0	18.2	4.8
18. Standing, arms extended	84.7	3.7	11.6	85.6	6.5	7.9
19. Standing, arms hanging	80.1	9.4	10.5	84.5	5.4	10.1
20. Standing, finger-nose-test	65.4	22.0	12.6	74.8	16.1	9.1
21. Standing, index finger to examiner's index finger	67.3	18.5	14.2	81.6	10.2	8.3
22. Standing, both tasks (finger-nose-test & index finger to examiner): straight movements	73.8	13.2	13.0	86.3	5.4	8.3
23. Walking, independent walking	98.7	0.9	0.4	99.0	0.5	0.5
24. Walking, posture	85.2	10.7	4.1	93.7	5.1	1.1
25. Walking, movements	88.5	9.3	2.2	95.1	3.6	1.3

Items	BLS (*N*=5,599) Within normal range	Outside normal range	Missing data	*AYLS* (N=1,527) Within normal range	Outside normal range	Missing data
26. Walking, pressure on feet	94.8	2.4	2.8	98.5	0.4	1.1
27. Walking, balance	96.2	1.7	2.1	98.6	0.4	1.1
28. Walking, muscle weakness or paresis	97.1	0.7	2.2	98.6	0.1	1.4
29. Walking, step length	97.9	0.6	1.6	98.8	0.2	1.0
30. Walking, walking speed	95.2	2.3	2.5	97.6	0.7	1.7
31. Walking, running	83.9	11.3	4.8	88.6	8.4	3.1
32. Climbing stairs (5 steps up and down)[a]	77.6	18.3	4.1	71.5	17.1	11.4
33. Climbing stairs (5 steps up and down), posture retention	92.4	2.4	5.2	93.9	0.5	5.6
34. Climbing stairs (5 steps up and down), movement quality	86.5	8.2	5.4	82.2	11.9	5.9
35. Climbing stairs (5 steps up and down), muscle strength	93.8	0.9	5.3	94.4	0.9	4.7
Sensorimotor: Balance testing						
36. Walking on toes: movement quality	85.7	4.3	10.1	93.6	1.4	5.0
37. Walking on toes: compensating movements	79.7	9.9	10.4	93.4	1.3	5.3

Items	BLS (*N*=5,599) Within normal range	Outside normal range	Missing data	*AYLS* (N=1,527) Within normal range	Outside normal range	Missing data
38. Walking on toes: associated muscle tone of arms	72.8	16.7	10.4	89.7	5.1	5.3
39. Walking on heels: movement quality	78.9	10.0	11.1	86.9	7.9	5.1
40. Walking on heels: compensating movements	68.3	19.9	11.9	89.9	4.0	6.1
41. Walking on heels: associated muscle tone of arms	55.6	32.4	12.0	60.1	34.0	5.9
42. One leg balance: compensating movements, right	42.6	46.7	10.7	48.3	46.2	5.5
43. One leg balance: compensating movements, left	40.8	48.6	10.7	46.9	47.7	5.4
44. One leg balance: associated muscle tone of arms, right	67.6	21.5	10.9	84.6	9.8	5.6
45. One leg balance: associated muscle tone of arms, left	66.7	22.4	10.9	84.3	10.1	5.6
46. One leg balance: time (10 sec), right	41.5	48.8	9.8	49.0	45.7	5.3
47. One leg balance: time (10 sec), left	39.8	50.4	9.8	45.8	49.0	5.2

Items	BLS (*N*=5,599) Within normal range	Outside normal range	Missing data	*AYLS* (N=1,527) Within normal range	Outside normal range	Missing data
48. Hopping on one leg: movement quality, right	47.7	39.1	13.2	52.7	41.6	5.8
49. Hopping on one leg: movement quality, left	44.2	42.5	13.3	46.1	47.8	6.1
50. Hopping on one leg: compensating movements, right	33.1	49.5	17.4	56.9	29.6	13.4
51. Hopping on one leg: compensating movements, left	30.4	51.2	18.4	52.3	32.1	15.6
52. Hopping on one leg: associated muscle tone of arms, right	53.5	28.9	17.6	70.1	16.5	13.4
53. Hopping on one leg: associated muscle tone of arms, left	52.2	29.2	18.6	67.6	17.3	15.1
54. Hopping on one leg: time (10 sec), right	26.6	59.8	13.6	37.4	50.4	12.2
55. Hopping on one leg: time (10 sec), left	22.7	63.1	14.2	28.8	58.1	13.1
56. Jump over cord: movement quality	49.9	39.4	10.7	49.0	44.7	6.3
57. Jump over cord: compensating movements	53.7	33.8	12.5	56.5	35.8	7.6

Items	BLS (*N*=5,599) Within normal range	Outside normal range	Missing data	*AYLS* (N=1,527) Within normal range	Outside normal range	Missing data
58. Jump over cord: associated muscle tone of arms	64.6	22.8	12.6	74.0	18.3	7.6
59. Jump over cord: number of jumps (>6)	46.4	36.0	17.6	40.3	49.8	9.9
60. Balance: movement quality, forwards	80.6	11.6	7.8	89.6	5.0	5.4
61. Balance: movement quality, backwards	49.6	40.3	10.0	59.9	31.9	8.2
62. Balance: compensating movements, forwards	58.7	33.1	8.3	56.0	38.0	5.9
63. Balance: compensating movements, backwards	32.5	55.8	11.7	31.4	53.3	15.3
64. Balance: associated muscle tone of arms, forwards	76.0	15.6	8.4	79.7	14.3	6.0
65. Balance: associated muscle tone of arms, backwards	63.4	24.6	12.0	64.9	20.2	14.9
66. Balance: number of errors, forwards	62.4	21.7	15.9	37.0	52.7	10.3
67. Balance: number of errors, backwards	23.8	59.7	16.5	6.3	77.5	16.2
Sensorimotor: supine position						

Items	BLS (*N*=5,599) Within normal range	Outside normal range	Missing data	*AYLS* (N=1,527) Within normal range	Outside normal range	Missing data
68. Supine position, posture	88.4	1.9	9.7	92.7	1.3	6.0
69. Supine position, joint mobility	86.5	4.2	9.3	93.6	1.1	5.4
70. Supine position, muscle tone	81.3	9.4	9.3	92.9	1.6	5.5
71. Supine position, long-sit	80.8	9.3	9.9	94.5	0.4	5.1
Reflexes						
72. Knee jerk	69.1	18.6	12.2	79.4	17.5	3.1
73. Achilles tendon	79.7	8.1	12.1	82.7	14.2	3.1
74. Biceps tendon	78.5	5.0	16.5	85.9	10.9	3.2
Sensitivity						
75. Sensitivity, tactile	80.1	3.0	17.0	81.7	0.8	17.4
Rapid, rhythmic movements						
76. Hand pro- and supination, rhythm, right	51.5	36.3	12.2	65.4	23.9	10.7
77. Hand pro- and supination, rhythm, left	48.5	39.1	12.4	55.9	32.3	11.8
78. Hand pro- and supination, movement quality, right	69.8	18.0	12.2	63.2	28.1	8.8
79. Hand pro- and supination, movement quality, left	66.6	21.0	12.4	50.3	40.5	9.2

Items	BLS (*N*=5,599) Within normal range	Outside normal range	Missing data	*AYLS* (N=1,527) Within normal range	Outside normal range	Missing data
80. Hand pro- and supination, associated tonic reactions, right	85.7	1.9	12.4	88.6	0.7	10.8
81. Hand pro- and supination, associated tonic reactions, left	85.2	2.2	12.6	87.1	1.1	11.9
82. Hand pro- and supination, contralateral movements, right	64.4	23.1	12.5	73.2	16.1	10.8
83. Hand pro- and supination, contralateral movements, left	59.0	28.2	12.8	66.7	21.4	11.9
84. Hand pro- and supination, time (in sec) for 7 cycles, right[b]	65.4	12.8	21.8	74.8	12.9	12.3
85. Hand pro- and supination, time (in sec) for 7 cycles, left[b]	62.7	15.1	22.2	72.2	14.9	12.9
86. Handtapping, rhythm, synchronous	64.8	23.6	11.5	70.2	21.5	8.4
87. Handtapping, rhythm, alternating	47.8	39.1	13.1	48.7	41.1	10.3
88. Handtapping, movement quality, synchronous	79.7	8.8	11.4	79.8	13.4	6.8
89. Handtapping, movement quality, alternating	69.3	17.8	12.9	71.4	21.1	7.5

Items	BLS (*N*=5,599) Within normal range	Outside normal range	Missing data	*AYLS* (N=1,527) Within normal range	Outside normal range	Missing data
90. Handtapping, associated tonic reactions, synchronous	87.2	1.0	11.8	91.4	0.2	8.4
91. Handtapping, associated tonic reactions, alternating	85.0	1.6	13.4	89.5	0.3	10.3
92. Handtapping, time (in sec) for 10 movements, synchronous[b]	67.3	12.3	20.4	76.9	14.1	9.0
93. Handtapping, time (in sec) for 10 movements, alternating[b]	62.4	13.6	24.1	75.7	13.0	11.3
94. Finger-thumb opposition, rhythm, right	81.7	7.2	11.0	91.2	1.9	6.9
95. Finger-thumb opposition, rhythm, left	80.4	8.4	11.2	90.3	3.0	6.7
96. Finger-thumb opposition, movement quality, right	80.7	8.6	10.7	88.9	4.7	6.4
97. Finger-thumb opposition, movement quality, left	78.8	10.2	11.0	85.1	8.5	6.4
98. Finger-thumb opposition, associated tonic reactions, right	86.9	2.2	10.9	92.8	0.5	6.7
99. Finger-thumb opposition, associated tonic reactions, left	86.3	2.4	11.3	92.7	0.6	6.7

	BLS (*N*=5,599)			*AYLS* (N=1,527)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
100. Finger-thumb opposition, contralateral movements, right	68.7	20.0	11.3	89.1	4.3	6.7
101. Finger-thumb opposition, contralateral movements, left	64.6	23.7	11.8	88.2	5.1	6.7
102. Sequential finger-thumb opposition, rhythm, right	56.3	22.3	21.4	81.7	7.0	11.3
103. Sequential finger-thumb opposition, rhythm, left	54.4	24.0	21.6	79.3	8.6	12.1
104. Sequential finger-thumb opposition, movement quality, right	49.3	36.1	14.6	66.1	26.1	7.8
105. Sequential finger-thumb opposition, movement quality, left	48.2	37.1	14.8	62.0	29.9	8.1
106. Sequential finger-thumb opposition, associated tonic reactions, right	79.9	4.2	15.8	89.4	2.4	8.3
107. Sequential finger-thumb opposition, associated tonic reactions, left	79.4	4.6	16.0	88.8	2.6	8.6
108. Sequential finger-thumb opposition, contralateral movements, right	48.5	35.6	16.0	53.7	37.6	8.6

	BLS (*N*=5,599)			*AYLS* (N=1,527)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
109. Sequential finger-thumb opposition, contralateral movements, left	45.5	38.2	16.2	59.9	31.1	9.0
Fine motor skills						
110. Pinboard, time (in sec), right[b]	73.1	22.3	4.6	81.1	16.8	2.2
111. Pinboard, time (in sec), left[b]	78.1	16.6	4.3	79.0	18.0	3.0
112. Pinboard, goal-directedness, right	47.1	48.7	4.3	53.2	44.5	2.3
113. Pinboard, goal-directedness, left	30.8	63.9	5.3	30.5	65.9	3.6
114. Pinboard, strength	84.9	9.7	5.4	95.9	1.6	2.4
115. Pinboard, movement quality	74.0	22.4	3.6	70.2	27.8	2.0
116. Pinboard, finger position, right	93.5	2.3	4.2	97.3	0.5	2.2
117. Pinboard, finger position, left	91.9	3.1	5.0	95.9	1.0	3.1
118. Pinboard, associated tonic reactions	94.4	1.3	4.4	97.0	1.3	1.8
119. Pinboard, co-movements	86.9	8.5	4.6	96.9	1.3	1.8
120. Drawing, holding pencil: strength	78.5	18.5	3.0	87.3	10.9	1.8
121. Drawing, holding pencil: movement quality	78.9	17.9	3.3	83.6	13.6	2.8

	BLS (*N*=5,599)			*AYLS* (N=1,527)		
Items	Within normal range	Outside normal range	Missing data	Within normal range	Outside normal range	Missing data
122. Drawing, holding a pencil (with 3 fingers)	86.0	10.0	4.0	82.8	14.5	2.7
123. Drawing, co-movements	90.7	6.2	3.1	98.1	0.1	1.8
124. Drawing, associated tonic reactions	95.6	1.1	3.3	97.6	0.6	1.8
125. Cutting out a circle, fluent movements	64.8	20.5	14.7	67.5	28.8	3.8

[a] Observed/tested and parent-reported (mainly observed).
[b] Dichotomised, 85th percentile of the normative group.

Missing data

Missing motor functioning data on item-level were low across all assessment time points (see Tables 4 to 7). However, cases with the majority of motor functioning items for each time point missing were deemed as not suited for missing data imputation (van Ginkel, Sijtsma, van der Ark, & Vermunt, 2010). As this criterion pertained only to a small number of cases relative to respective sample size, those cases were excluded (data sets with more than half of motor functioning items missing: BLS *n*=12 at birth, *n* =1 at 5 months, *n*=4 at 20 months, *n*=361 at 56 months; AYLS: *n*=1 at birth, *n*=0 at 5 months, *n*=0 at 20 months, *n*=72 at 56 months). This resulted in sample numbers of *N*=8,082 at birth, *N*=6,589 at 5 months, *N*=6,057 at 20 months, and *N*=5,238 at 56 months for the BLS, and *N*=2,070 at birth, *N*=1,990 at 5 months, *N*=1,926 at 20 months, and *N*=1,527 at 56 months for the AYLS. All remaining missing data were imputed by simple imputation using a state-of-the-art method for item-level missing data imputation, the two-way imputation method (van Ginkel et al., 2010).

Motor Problem Scores

Based on the sum of motor and neurological items (see Tables 4 to 7) 'outside the normal range', a *motor problem score* was computed for each of the four assessment points at birth, 5, 20 and 56 months, with a higher score indicating more or a higher degree of motor problems (see Table 8).

Table 8. *Raw motor problem scores at birth, 5, 20 and 56 months in the BLS and AYLS*

	N	Range (min - max)	Mean (SD)	
BLS				
Birth/Neonatal	8,082	0 - 25	4.49	(4.35)
5 months	6,589	0 - 59	6.74	(8.42)
20 months	6,057	0 - 56	2.83	(6.20)
56 months	5,238	0 - 111	25.80	(15.77)
AYLS				
Birth/Neonatal	2,070	0 - 24	2.28	(3.13)
5 months	1,990	0 - 51	3.52	(6.20)
20 months	1,926	0 - 52	1.95	(4.50)
56 months	1,527	0 - 87	21.51	(11.90)

Due to a varied number of items used to compute the motor problem score across the different time points (birth: 25 items, 5 months: 63 items, 20 months: 63 items, 56 months: 125 items), scores were converted into z-scores with a mean of 0 and a standard deviation of 1 to allow comparability across ages and assessments. Raw and z-standardized motor problem scores across all four assessment time points (i.e., longitudinal) after missing data imputation are provided in Chapter 3, Table 15.

Study 1

Predictive Measures

Pre-pregnancy, pregnancy and perinatal complications were assessed from standard perinatal survey medical records within 10 days of admission. Data on neonatal characteristics and health (i.e., gestational age, birth weight, head circumference, child sex, smallness for gestational age, and neonatal complications), neonatal course (i.e., neonatal neurological problems, and duration of initial hospitalisation), and early social environment (i.e., family socioeconomic status, family adversity, parent-infant relationships, psychosocial stress, and breastfeeding) were collected prospectively during hospitalisation and at 5 months after the child's birth using information from maternal interview, medical records, and standard research nurse observations. A full description of all predictive measures is provided in Table 9.

Table 9. *Overview of predictors and their descriptions*

Predictor	Description
Pre-/pregnancy and perinatal complications	Prenatal data were coded from medical histories in obstetric units while perinatal data were assessed from survey records (Zander, Holzmann, & Selbmann, 1989) and medical notes assessed prospectively, and combined into sum scores, similar to a previously proposed optimality scoring system (Prechtl, 1968; Riegel, Ohrt, Wolke, & Österlund, 1995).
Pre-pregnancy	Pre-pregnancy complications (0–8 complications): (1) Maternal age < 20 or > 30 years; (2) condition after infertility; (3) condition after ≥abortions; (4) prior preterm birth; (5) prior dead/disabled infant; (6) prior difficult labour; (7) severe illness (kidney disease, diabetes, other illness); (8) no or > two prior labours (Gutbrod, Wolke, Soehne, Ohrt, & Riegel, 2000; Schmid, Schreier, Meyer, & Wolke, 2011).
Pregnancy	Pregnancy complications (0–14 complications): (1) Eph gestosis; (2) anaemia; (3) urinary tract infection; (4) bleeding; (5) foetal retardation and/or pathologic CTG; (6) preterm labour; (7) multiples; (8) nicotine addiction; (9) alcohol and/or drug addiction; (10) check-up started after week 12; (11) no regular check-up; (12) infectious disease; (13) severe illness, hyperaemesis and/or accident; (14) (oligo-)hydramnion (Gutbrod et al., 2000; Schmid et al., 2011).
Perinatal	Perinatal birth complications (0–15 complications): (1) Amnion infectious syndrome; (2) over term; (3) pathologic CTG; (4) acidosis; (5) green amniotic fluid; (6) cord prolapse or other cord complication; (7) transverse lie; (8) breech presentation; (9) prolonged labour; (10) adjustment anomaly; (11) dilation in early labour <3 or >12 h; (12) bearing down pains < 10 or > 60 min; (13) anaesthesia; (14) no spontaneous labour; (15) placenta praevia (Gutbrod et al., 2000; Schmid et al., 2011).
Neonatal characteristics and health	

Predictor	Description
Gestational age	Gestational age was determined from maternal reports of the last menstrual period and serial ultrasounds during pregnancy. In case these initial estimates differed by more than two weeks, postnatal Dubowitz scores were used (Dubowitz, Dubowitz, & Goldberg, 1970).
Birth weight, head circumference, child sex	Birth weight, head circumference and child sex were documented in the birth records.
Small for gestational age	Infants were classified as small for gestational age if they weighed less than the sex specific 10th percentile for their respective gestational age according to the national standard weight charts (1985-1986) (Riegel et al., 1995).
Neonatal complications	Neonatal complications (0–21 complications): (1) Ventilation or intubation; (2) Apgar at 1 min after birth < 9 and at 5 min after birth < 10; (3) buffering and/or volume substitution; (4) cord artery pH ≥ 7.3; (5) outborn (i.e. infant was transported after birth from outside obstetric unit for neonatal care); (6) body temperature ≤ 35°C; (7) artificial aspiration; (8) apnoea/bradycardia; (9)ventilation disorder; (10) hypoglycaemia; (11) heart failure; (12) hyperbilirubinaemia; (13) other metabolic diseases; (14) severe anaemia; (15) sepsis; (16) operation; (17) deficits in development (i.e. neurodevelopmental problems); (18) medication > one time/day; (19) nasogastric feeding; (20) neonatal seizures; (21) cerebral haemorrhage (on ultrasound examination neonatally) (Gutbrod et al., 2000; Schmid et al., 2011).
Neonatal course	
Neonatal neurological problems	Infant neonatal neurological problems were assessed with the Intensity of Neonatal Treatment Index (INTI), which was computed from daily ratings of care level, respiratory support, feeding dependency and neurological status such as mobility, muscle tonus and neurological excitability by specially employed research nurses according to the method of Casaer and Eggermont. Each of the 3 variables were scored daily on 4-point rating scales (0-3), with higher scores indicating worse/more unstable neurological status. The INTI was computed as the mean of daily ratings during the first ten days of life

Predictor	Description
	or until a stable clinical state was reached, depending on which occurred sooner (Casaer & Eggermont, 1985; Gutbrod et al., 2000; Riegel et al., 1995; Schmid et al., 2011).
Duration in hospital	Duration of initial hospitalisation was obtained from neonatal records.
Early social environment	
Socioeconomic status	Family socioeconomic status (SES) at birth was computed as a weighted composite score of parents' education and occupation and grouped as low, middle, and high (Bauer, 1988).
Family adversity	The Family Adversity Index (FAI) covered potential risk factors recorded in eight items (neonatal and 5-month assessments; i.e., early parenthood, overcrowded living space, mother or father without educational qualification or vocational training, for or more children in the family, infant requires home or external care, not social support available, being a single parent or having mental health problems), and was grouped as low, middle, and high (Breeman, Jaekel, Baumann, Bartmann, & Wolke, 2017; Riegel et al., 1995).
Parent-infant relationship	The Parent-Infant Relationship Index (PIRI) assessed attachment-related parental concerns, feelings, and behaviour, and current or anticipated parent-infant relationship problems. The PIRI included eight items that were obtained by a standardized interview with the parents and by study nurses' observations on the neonatal ward and at the 5-month assessment, covering attachment-related parental concerns and feelings, and current or anticipated relationship problems (i.e., (1) mother shows little pleasure when interacting with the child; (2) mother does not yet know the infant; (3 and 4) mother/father visits the infant once a week or less; mother is insecure when taking care of the child at home; (5 and 6) mother/father shows little pleasure when interacting with the child; (7) the probability that these parents develop problems in taking care of the infant is high; (8) mother has trouble building a relationship with the child). Items were combined into a sum score. Because the resulting sum score did not show a normal distribution as most parents reported and demonstrated a good relationship with their infant, the

Predictor	Description
	sum score was recoded into (0) no concerns and (1) some degree of concern regarding the parent-infant relationship (Breeman et al., 2017; Riegel et al., 1995; Schmid et al., 2011).
Psychosocial stress	Family-related problems and worries (14 items), expressed by the main caretaker (mother) during a standardized interview (neonatal and 5-month assessments; for example, recent death of a family member, excess pressure from work on the mother/partner, financial difficulties, behavioural or health problems of a sibling, partnership problems, physical health problems of the mother/partner, mental health problems of the mother/partner, social isolation, mother/partner has not time for own interests, serious conflicts with family or friends), were combined into a Psychosocial Stress Index (PSI) and coded into (0) no psychological stress and (1) some degree of psychological stress (Breeman et al., 2017; Riegel et al., 1995; Schmid et al., 2011).
Breastfeeding	Breastfeeding was recorded during a maternal interview at 5 months and coded into (0) ever breastfed and (1) never breastfed (Breeman et al., 2017; Schmid et al., 2011).

Developmental Outcome

Trajectories of motor problems from birth to 56 months: Using the computed motor problem scores at four time points (birth, 5, 20 and 56 months) a person-centred statistical approach (Latent Class Growth Analysis) was applied that identified groups of children with similar motor development from birth to 56 months (for a detailed description see Chapter 3).

Variables Used as Exclusion Criteria for the Sensitivity Analysis

Exclusion criteria for the sensitivity analysis included any neurological diagnosis at 56 months. Neurological diagnoses were made by a developmental paediatrician at 56 months, and included epilepsy, hydrocephalus (Riegel et al., 1995), cerebral palsy (Hagberg, Hagberg, Olow, & von Wendt, 1989), and blindness or deafness (Wolke & Meyer, 1999).

Study 2

Predictive Measures

Motor problems in infancy: Motor problem scores were computed from extensive and detailed neurological and physical examinations at birth and 5 months (see section 'Motor Functioning' above). Following recommendations from the previous literature (Geuze et al., 2001; Lingam et al., 2010) and using the 15th percentile as the cut-off point, children were classified into being at risk or having probable motor problems.

Potential Moderator

During assessments at 5, 20 and 56 months parents were asked whether and for how long their child had received or was currently receiving physiotherapy, based on Bobath, Vojta, or any other physiotherapeutic method.

Developmental Outcomes in Childhood

Developmental outcomes were obtained at age 6 and 8 years using standardized tests, parent reports and observations by examiners. Outcomes included motor skills (Stott, Moyes, & Henderson, 1984), mental health (Achenbach, 1991), cognitive function (Kaufman & Kaufman, 1983; Melchers & Preuss, 1991) and attention regulation (Jaekel, Wolke, & Bartmann, 2013). All measures are described in detail in Tables 10 and 11.

Table 10. *Description of indicators used for defining motor skill, mental health and cognitive function*

Predictor	Measure	Age (years)	Description of assessments and categorization
Motor skill	Test of Motor Impairment	6 and 8	Fine and gross motor skills were measured using the total score of the Test of Motor Impairment (TOMI) (Stott et al., 1984). The TOMI is a standardized assessment of static and dynamic balance, ball skills, and manual dexterity.
Mental health	Child Behavior Checklist	6 and 8	Mental health problems were rated by parents at 6 and 8 years using the German version of the Child Behavior Checklist (CBCL) (Achenbach, 1991). Each item was rated on a scale from 0 (not true) to 2 (very true or often true) and then summed into a total score with higher scores indicating more mental health problems.
Cognitive function	Kaufman Assessment Battery for Children	6 and 8	Cognitive function, i.e., intelligence, was measured with the German version of the Kaufman Assessment Battery for Children (K-ABC) (Kaufman & Kaufman, 1983; Melchers & Preuss, 1991). The K-ABC simultaneous processing scale is based on five subtests (i.e. Gestalt closure, triangles, matrix analogies, spatial memory, and photo series). None of these subtests measure motor skills.

Table 11. *Description of measures used as indicators of attention regulation*

Child Functioning Domain	Measure	Age (years)	Description of assessments
Attention regulation	Tester's Ratings of Child Behaviour	6 and 8	Child behaviour during a challenging cognitive assessment was evaluated by trained psychological assistants with the Tester's Rating of Child Behaviour (TRCB) (Jaekel, Wolke, et al., 2013). The TRCB encompassed 13 nine-point scale items (1 = very low to 9 = very high) of which 6 items (attention, robustness/endurance, demandingness (reverse coded), cooperativeness, compliance, difficulty (reverse recoded) were combined into a Task Orientation scale based on factor analysis (Jaekel, Wolke, et al., 2013) (*Cronbach's alpha* = 0.90 at 6 years and 0.85 at 8 years). Higher scores on the TRCB TEAM rating indicates better attention skills.
	Team consensus rating	6 and 8	The TEAM rating consists of three dimensions from the TRCB: attention, robustness/endurance and demandingness (reverse coded). An index score of attention was computed (*Cronbach's alpha* = 0.88 at 6 years and 0.84 at 8 years). Higher scores on the TEAM rating indicates better attention skills.
	Child Behavior Checklist	6 and 8	Mothers rated their children's attention problems with the Child Behavior Checklist (CBCL) (Achenbach, 1991). Higher scores on this 11 items subscale indicate more attention problems.

Covariates and Potential Confounders

Covariates and potential confounders included biological and socioeconomic variables at birth. Data on gestational age (GA), birth weight, small for GA, and child sex were obtained from perinatal records at birth. Family socioeconomic status (SES) at birth was defined as low, middle, or high (Riegel et al., 1995).

Variables Used to Account for Imbalances in Baseline Characteristics (Propensity Score Matching)

Baseline characteristics, including early motor problems (see section ‘Motor Functioning’ above), and other covariates, such as child biological characteristics, peri- and neonatal health and medical factors, early social environmental factors, and neurological impairments diagnosed at 56 months (cerebral palsy, epilepsy, hydrocephalus, blindness, deafness). For a detailed description of covariates used for Propensity Score Matching see Table 12.

Table 12. *Overview of covariates and their descriptions used for Propensity Score Matching*

Predictor	Description
Child biological characteristics	
Gestational age	Gestational age was determined from maternal reports of the last menstrual period and serial ultrasounds during pregnancy. In case these initial estimates differed by more than two weeks, postnatal Dubowitz scores were used (Dubowitz et al., 1970).
Birth weight, head circumference, child sex, multiple birth	Birth weight, head circumference, child sex, and multiple birth were documented in the birth records.
Small for gestational age	Infants were classified as small for gestational age if they weighed less than the sex specific 10th percentile for their respective GA according to the national standard weight charts (1985-1986) (Riegel et al., 1995).
Peri- and neonatal health and medical factors	
Peri- and neonatal complications	Prenatal data were coded from medical histories in obstetric units while perinatal data were assessed from survey records (Zander et al., 1989) and medical notes assessed prospectively, and combined into sum scores, similar to a previously proposed optimality scoring system (Prechtl, 1968; Riegel et al., 1995): Pre-pregnancy complications (0–8 complications; e.g., maternal age below 20 or above 30 years, prior preterm birth), pregnancy complications (0–14 complications; e.g., nicotine addiction, anaemia), perinatal birth complications (0–15 complications; e.g., no spontaneous labour, anaesthesia), and neonatal complications (0–21 complications; e.g., sepsis, cerebral haemorrhage, neonatal seizures) (Gutbrod et al., 2000; Schmid et al., 2011).
Neonatal neurological problems	Infant neonatal neurological problems were assessed with the Intensity of Neonatal Treatment Index (INTI), which was computed from daily ratings of care level, respiratory support, feeding

Predictor	Description
	dependency and neurological status such as mobility, muscle tonus and neurological excitability by specially employed research nurses according to the method of Casaer and Eggermont (Casaer & Eggermont, 1985; Gutbrod et al., 2000; Riegel et al., 1995; Schmid et al., 2011).
Duration in hospital	Duration of initial hospitalization was obtained from neonatal records.
Early socio-environmental factors	
Socioeconomic status	Family socioeconomic status (SES) at birth was computed as a weighted composite score of parents' education and occupation and grouped as low, middle, and high (Bauer, 1988).
Breastfeeding	Breastfeeding was recorded during a maternal interview at 5 months and coded into (0) ever breastfed and (1) never breastfed (Breeman et al., 2017; Schmid et al., 2011).
Neurological impairments diagnosed in early childhood	
Severe neurological impairments	Severe neurological impairments were assessed and determined by specially trained project paediatricians at 56 months: cerebral palsy (CP), epilepsy, hydrocephalus, blindness, or deafness (not corrected or insufficiently corrected).

Study 3

Predictive Measures

The two main predictors for this study included trajectories of early motor problems from birth to age 56 months which were computed for Study 1 (see Chapter 3), and VP/VLBW birth.

Developmental Outcomes in Adulthood

Developmental outcomes in adulthood were motor competence and cognitive function. For detailed descriptions see Chapter 5.

Motor competence: As the assessment in adulthood did not include a standardized motor functioning test, a motor competence score was computed using items from different instruments applied to participants during the 26-year assessment that described or indicated motor competence in daily life. These indicators included ‘suboptimal functioning for ambulation and dexterity’, ‘low self-esteem in sports activities’, ‘being poorly coordinated or clumsy’, and ‘not being able to ride a bicycle or to swim’. All indicators are described in detail in Table 13.

Table 13. *Description of indicators for suboptimal motor competence at 26 years.*

Indicator	Instrument	Original item	Original coding	Dichotomisation suboptimal motor competence	Group distribution of suboptimal motor competence	
					Term controls	VP/VLBW
					n = 226	*n* = 192
Suboptimal functioning for ambulation[a]	Health Utility Index (HUI): attribute 'Ambulation'	Ability to walk around the neighbourhood	Interval scale: 1=without difficulty, and without walking equipment to 6=cannot walk at all	Suboptimal function=level 2 and above	0 (0.0%)	2 (1.3%)
Suboptimal functioning for dexterity[a]	Health Utility Index (HUI): attribute 'Dexterity'	Ability to use hands and fingers	Interval scale: 1=full use of two hands and ten fingers 6=Limitations, requires the help of another person for all tasks	Suboptimal function=level 2 and above	1 (0.5%)	4 (2.6%)
Low self-esteem regarding sports[b]	BLS self-esteem questionnaire	'I not good at sports' to 'I am good at sports'	Interval scale: 1 to 25; higher scores indicating being better at sports	< -2 SD versus >= -2 SD (standardized on controls)	9 (4.0%)	15 (8.3%)
Somewhat or very poorly coordinated or clumsy[c]	Young Adult Self-Report (YASR)	'I am poorly coordinated or clumsy'	Likert scale: 0=not true, 1=somewhat true and 2=very true	Somewhat (=1) or very true (=2) *versus* not true (=0)	13 (5.8%)	17 (9.4%)

Indicator	Instrument	Original item	Original coding	Dichotomisation suboptimal motor competence	Group distribution of suboptimal motor competence	
					Term controls	VP/VLBW
					n = 226	*n* = 192
Not able to ride a bicycle[d]	BLS Life Course Interview	'Are you able to ride a bicyle'	Yes *versus* no	n/a	0 (0.0%)	7 (3.6%)
Not able to swim[d]		'Are you able to swim'	Yes *versus* no	n/a	1 (0.4%)	4 (2.1%)

Abbreviations: VP/VLBW=Very Preterm and/or Very Low Birth Weight.
[a] Derived from the Health Utility Index (HUI) (Furlong et al., 1998).
[b] Derived from BLS self-esteem questionnaire, based on the Concepts of Effort and Ability (Nicholls, 1978).
[c] Derived from the Young Adult Self Report (YASR) (Achenbach, 1997).
[d] Derived from the BLS Life Course Interview.

All six indicators were combined into a composite score. As this composite score was not normally distributed and highly skewed towards no motor competence problems it was subsequently dichotomised (0=no motor competence problems, 1=motor competence problems).

Cognitive function: Cognitive function in adulthood was operationalised through a standard measure of general intelligence. General intelligence was assessed with a standardized intelligence (intelligence quotient (IQ) test), the German short version of the Wechsler Adult Intelligence Scale (WAIS III) (von Aster, Neubauer, & Horn, 2009; Wechsler, 1997). Scores from six subtests of the WAIS were converted into an age-normed full-scale IQ score.

Covariates and Potential Confounders

Covariates and potential confounders included cognitive function in childhood, and biological and socioeconomic variables at birth.

Cognitive function in childhood was operationalised through general intelligence at 56 months. Because a standardized intelligence or IQ test was not available at that age, general intelligence was assessed through a composite of three cognitive tasks: (1) the Columbia Mental Maturity Scale (Burgemeister, Blum, & Lorge, 1954; Eggert, 1972), (2) the Active Vocabulary Test (Kiese & Kozielski, 1979), and (3) the Beery-Buktenica Developmental Test of Visual-Motor Integration (Beery, 1982). Applying confirmatory factor analysis, a composite score of general intelligence (i.e., IQ score) was constructed using standardized scores from all children who were assessed with the three cognitive tasks at 56 months (Eves,

Mendonça, Bartmann, & Wolke, 2020). Detailed descriptions and factor loadings of the three cognitive tasks are given in Table 14.

Table 14. *Description of cognitive tasks and factor loadings of the cognitive composite score at 56 months*

Cognitive Task/ Factor	Description of cognitive task	Factor loadings
Columbia Mental Maturity Scale (CMM)	The CMM assesses the general reasoning ability of children between the ages of 3 and 10 years. The CMM scale consists of eight age-specific levels, each contains between 51 and 65 pictorial and figural classification items. The child has to select from a series of drawings the one drawing that is out of place.	0.828
Active Vocabulary Test (AWST)	The AWST evaluates the expressive vocabulary of preschool children. It was developed for German-speaking countries and is similar to the widely used and valid Peabody Picture Vocabulary Test. The AWST consists of 82 drawings, and the child has to name the presented item.	0.728
Beery-Buktenica Developmental Test of Visual-Motor Integration (Beery)	The Beery measures the integration of visual and motor abilities. Fifteen drawings of geometric forms are arranged in order of increasing difficulty that the child is asked to copy. Each drawing is evaluated using predefined scoring criteria, i.e., task solved versus not solved, and a sum score is computed, ranging from 0 to 15. A higher score indicates better performance.	0.654

Data on gestational age (GA), birth weight, small for GA, and child sex were obtained from perinatal records at birth. Family socioeconomic status (SES) at birth was defined as low, middle, or high (Riegel et al., 1995).

Variables Used as Exclusion Criteria for the Sensitivity Analysis

Exclusion criteria for the sensitivity analysis included any neurological impairment at age 56 months. Neurological diagnoses were made by a developmental paediatrician at 56 months, and include epilepsy, hydrocephalus (Riegel et al., 1995), cerebral palsy (Hagberg et al., 1989), and blindness or deafness (Wolke & Meyer, 1999).

Statistical Analyses

Statistical analyses for all three studies were conducted using SPSS Version 22 (IBM SPSS Statistics, IBM Corporation), Mplus 7.31 (Muthén and Muthén, Los Angeles, California), and Stata Version 5.0 (StataCorp LP, College Station, TX, USA). For the three empirical studies conducted and described in this thesis the following statistical methods were used for the main analyses:

- Study 1: Latent Class Growth Analysis (LCGA) and Binary Logistic Regression analysis
- Study 2: Linear Regression analysis and Propensity Score Matching
- Study 3: Poisson Regression analysis, Linear Regression analysis, and Structural Equation Modelling

Chapter 3: Predictors of Early Motor Trajectories from Birth to 5 Years in Neonatal At-Risk and Control Children

Abstract

Aims: To describe motor development in preschool children, to identify perinatal, neonatal, and social environmental risk factors of poor motor development, and to replicate results in a second cohort. Methods: Two prospective samples in Germany (Bavarian Longitudinal Study, BLS) and Finland (Arvo Ylppö Longitudinal Study, AYLS) assessed 4,741 and 1,423 children from birth to 56 months, respectively. Motor functioning was evaluated at birth, and 5, 20 and 56 months. Perinatal, neonatal and social environmental information was collected at birth and 5 months. Results: Two distinct motor trajectories were identified: low (BLS: *n*=4,486 (94.6%), AYLS: *n*=1,391 (97.8%)) and high (BLS: *n*=255 (5.4%), AYLS: *n*=32 (2.2%)) degree of motor problems. High degree of motor problems was predicted by neonatal complications, abnormal neonatal neurological status, duration of hospitalisation, and poor parent-infant relationships. Although neonatal complications and poor parent-infant relationships did not significantly predict high degree of motor problems in the AYLS, the trends identified were similar to those obtained from the BLS. Conclusion: Early identification of children at-risk of motor problems across infancy and toddlerhood may help referring those children to interventions earlier. Modifiable risk factors, such as parent-infant relationships, may be addressed by intervention strategies to prevent children from developing motor problems.

Introduction

The spectrum of motor impairment can range in severity and form, and has significant implications for sensorimotor learning, cognition and social development (Adolph & Franchak, 2017). However, even in the absence of a clinical diagnosis (i.e., cerebral palsy (CP) or developmental coordination disorder (DCD)), motor deficits may have an adverse impact on children's development (Spittle & Orton, 2014).

Most children do not outgrow their motor problems (de Kieviet et al., 2009; Spittle & Orton, 2014) and these may negatively impact on mental health, academic achievement, health-related quality of life and social functioning into adolescence and adulthood (Bornstein et al., 2013; Poole et al., 2017; Poole et al., 2015a). Therefore, it is important to identify children who are at-risk for developing any motor deficits (McIntyre et al., 2011) to enable early support or referral for intervention that may help improve motor functioning or ameliorate developmental problems.

Although recent findings have shown that most treatment or intervention programmes for improving motor skills of children with neurodevelopmental disorders are limited (Preston et al., 2017; Spittle et al., 2015), there is evidence that parent training or interventions involving parents may have positive effects on early motor development (Hughes et al., 2016; Spittle et al., 2015). This is not surprising as motor development is affected by the physical environment, as well as by social and cultural influences. As such, parents may largely influence their child's motor

development (Adolph & Hoch, 2018). However, few observational studies have tested the effects of early social environmental factors on child motor development (Forcada-Guex, Pierrehumbert, Borghini, Moessinger, & Muller-Nix, 2006; Laucht et al., 1997). The results of these studies suggest that in addition to biological and medical risk factors (i.e., pre- and perinatal complications), psychosocial risk factors, such as family adversity and poor parent-infant relationships, can have a detrimental effect on later motor, cognitive and social-emotional development in children born at-risk (e.g., preterm birth).

The present study assessed two large samples of children born across the full gestation spectrum in Germany or Finland who received the same standardized physical and neurological assessments from birth to age 56 months. Identical data on perinatal and neonatal risk factors, and early social environment measures, such as family adversity or early parent-infant-relationships, were collected.

The study aims were: (1) to identify trajectories of motor functioning over the first 5 years of life in neonatal at-risk and control children; (2) to investigate whether parent-infant-relationships influence motor development (i.e., early motor trajectories), in addition to known perinatal, neonatal and other early social environmental risk factors in the Bavarian Longitudinal Study (BLS) in Germany; and (3) to test whether findings are replicated in a second cohort, the Arvo Ylppö Longitudinal Study (AYLS) in Finland.

Methods

Participants and Procedures

Data were collected as part of the prospective Bavarian-Finnish Longitudinal Study (BFLS) (Riegel et al., 1995). The BFLS includes two geographically defined, whole population samples of neonatal at-risk children born in 1985 and 1986 in Southern Bavaria, Germany and in the county of Uusimaa, Finland, who required admission to a children's hospital within the first 10 days after birth (BLS: *n*=7,505; AYLS: *n*=1,536). Healthy infants born at term in the same hospitals were recruited as controls (BLS: *n*=916; AYLS: *n*=658).

Parents were approached within 48 hours of the infant's hospital admission and asked to give written informed consent to participate. Ethical permissions were granted by the ethics committees of the University of Munich Children's Hospital and the Bavarian Health Council (Landesärztekammer Bayern) in Germany, and of the Helsinki City Maternity Hospital, Helsinki University Central Hospital, and Jorvi Hospital in Finland.

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

In Germany, 415 families declined to participate, and 390 children died during hospitalisation or between discharge and 56 months. In Finland, 5 families declined participation, and 67 children died during hospitalisation or between discharge and 56 months. In total *n*=7,616 and *n*=2,122 children were eligible for follow up at age 5 months in Germany and Finland, respectively (Figure 2).

The current study used the BLS as the primary sample and the AYLS as the replication sample.

Measures

Motor Functioning. At birth, 5, 20 and 56 months, an extensive and detailed standardized neurological and physical examination based on Prechtl's neurological examination method (Maas et al., 2000; Prechtl, 1977), was carried out by specially trained developmental paediatricians. Examinations at 5, 20 and 56 months were adapted to include extended and age-related items. All paediatricians attended retraining sessions every two months and were blinded to the child's birth status and medical history. To compute a motor problem score from the data obtained through this examination, items on neurological and motor functioning, such as fine and gross motor skills, oculomotor function, muscle tone, and reflexes were combined and categorised into 'within' and 'outside the normal range' of motor function. Missing motor data on item-level were low across all assessment time points. For details on motor items including missing data see Tables 4 to 7 (Chapter 2). However, cases with the majority of motor functioning items missing were deemed as lacking sufficient information and not suited for missing data imputation (van Ginkel et al., 2010). As this criterion pertained only to a small number of cases relative to the respective sample size, they were excluded (cases with more than half of motor functioning items missing: BLS n=12 at birth, n=1 at 5 months, n=4 at 20 months, n=361 at 56 months; AYLS: n=1 at birth, n=0 at 5 months, n=0 at 20 months, n=72 at 56 months). All remaining missing data were imputed by simple imputation using the two-way imputation method (van Ginkel et al., 2010).

Subsequently, a motor problem score was computed based on the sum of motor functioning 'outside the normal range' (i.e., a higher score indicates more motor problems). As the number of items varied across time, scores were standardized to a mean of 0 and a standard deviation of 1 (z-scores) to allow comparability across ages. Raw and z-standardized motor problem scores for the longitudinal sample are provided in Table 15.

Table 15. *Motor problem scores (raw and z-standardized) from birth to 56 months (longitudinal)*

	BLS (*N*=4,741)		AYLS (*N*=1,423)	
	Raw Mean (SD)		Raw Mean (SD)	
At birth	4.0890	(3.7204)	2.0759	(2.7315)
5 months	6.0276	(6.9313)	2.9424	(4.5531)
20 months	2.1500	(4.0946)	1.5741	(2.6239)
56 months	25.7262	(15.7232)	21.3394	(11.8352)
	Z-Standardized Mean (SD)		Z-Standardized Mean (SD)	
At birth	-0.0925	(0.8549)	-0.0641	(0.8735)
5 months	-0.0843	(0.8233)	-0.0939	(0.7348)
20 months	-0.1100	(0.6601)	-0.0837	(0.5831)
56 months	-0.0044	(0.9969)	-0.0143	(0.9949)

In total, longitudinal data on motor functioning were available for 4,741 (62.3% of eligible children at 5-month follow up) and 1,423 (67.1% of eligible children at 5-month follow up) at-risk and term control children in the BLS and AYLS, respectively (Figure 2).

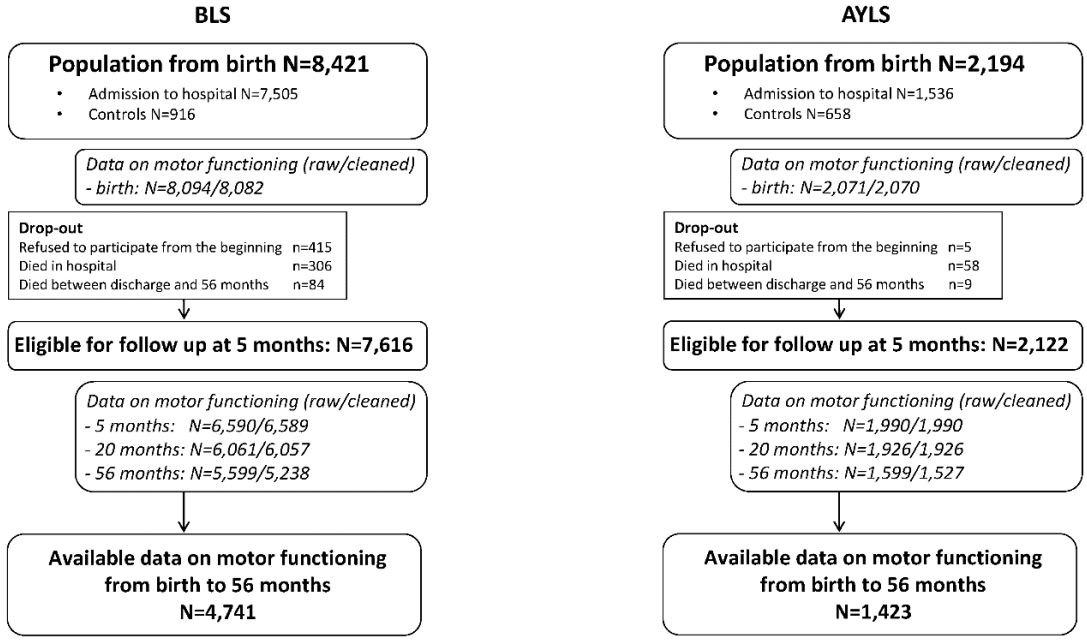

Figure 2. Flow chart BLS and AYLS.

Predictive measures

Pre-pregnancy, pregnancy and perinatal complications were assessed from standard perinatal survey medical records within 10 days of admission. Data on neonatal characteristics and health (i.e., gestational age, birth weight, head circumference, child sex, smallness for gestational age, and neonatal complications), neonatal course (i.e., neonatal neurological problems, and duration of initial hospitalisation), and early social environment (i.e., family socioeconomic status, family adversity, parent-infant relationships, psychosocial stress, and breastfeeding) were collected prospectively during hospitalisation and at 5 months after the child's birth using information from maternal interview, medical records, and standard research nurse observations. For a detailed description of all predictive measures see Table 9 (Chapter 2).

Statistical Analysis

All statistical analyses were performed using SPSS Version 22 (IBM SPSS Statistics, IBM Corporation) and Mplus 7.31 (Muthén and Muthén, Los Angeles, California).

Sample characteristics and attrition analysis (i.e., comparisons with participants who were lost to follow-up or missing/incomplete motor data) were conducted using t-tests for interval scaled variables or chi-square tests for dichotomous variables.

To identify groups of children with similar development of motor functioning over time (motor trajectories), latent class growth analysis (LCGA), a person-centred statistical approach, was performed using Mplus. Within the LCGA, the number of latent classes were estimated, compared, and decided upon according to standard conventions (Jung & Wickrama, 2008; Nylund, Asparouhov, & Muthén , 2007). The optimal number of classes was determined by assessing the Bayesian Information Criterion (BIC), the adjusted BIC, the Parametric Bootstrapped Likelihood Ratio Test (BLRT), the Lo-Mendel-Rubin Likelihood Ratio Test (LMR), and the Vuong-Lo-Mendell-Rubin Likelihood Ratio Test (VLMR) (Nylund et al., 2007). Further, the rule of parsimony and the substantive relevance of a class were taken into account (Jung & Wickrama, 2008). Subsequently, each participant was assigned to the class with the highest probability of membership.

To investigate the relationship between latent classes of motor trajectories and perinatal and neonatal risk factors, logistic regressions were performed using

SPSS. First, univariate regressions were run with all predictors. Next, multivariate regressions were applied using all significant predictors from univariate regressions. Analyses were performed in a stepwise fashion: pre-pregnancy, pregnancy and perinatal complication factors (Model 1), neonatal characteristics and health (Model 2), neonatal course (Model 3), and early social environment factors (Model 4).

All analyses were applied to BLS data first. To test whether results would be replicated, LCGA, univariate regressions, and the final multivariate regression model (Model 4) were repeated with AYLS data.

Additionally, to assess retrospectively whether severe neurological impairments diagnosed at 56 months are associated with the identified motor trajectories, chi-square tests were performed (Appendix E). To rule out that motor trajectories had been influenced by severe neurological impairments (BLS *n*=95 (2.0%), AYLS *n*=15 (1.1%)), regression models were repeated without these children in both cohorts (see Appendix I).

Results

Sample characteristics and dropouts

Sample characteristics (i.e., antenatal, perinatal and neonatal variables) and comparisons with dropouts (i.e., lost to follow-up or missing/incomplete motor data) are provided in Table 16.

BLS. Compared with dropouts, participants had higher perinatal but lower neonatal complication rates. Dropouts were more often male, received more neonatal treatment and on average stayed longer in hospital in comparison to participants.

Overall, dropouts were more often born into families with a low socioeconomic status, higher family adversity, and higher psychosocial stress. Further, they had poorer early parent-infant relationships and were less often breastfed.

AYLS. Dropouts received more neonatal treatment and were born into families with a lower socioeconomic status. In addition, they more frequently had poor early parent-infant relationships and were less often breastfed.

Table 16. *Antenatal, perinatal and neonatal characteristics of BLS and AYLS study participants, and comparisons with dropouts.*

	BLS			AYLS		
	Participants (*N*=4,741)	Dropouts (*N*=2,875)	*p*-value	Participants (*N*=1,423)	Dropouts (*N*=699)	*p*-value
Pre-/pregnancy and perinatal complications						
Pre-pregnancy, mean (SD)	1.11 (0.79)	1.07 (0.79)	.054	1.25 (0.89)	1.18 (0.87)	.081
Pregnancy, mean (SD)	1.37 (1.23)	1.33 (1.24)	.186	1.23 (1.16)	1.31 (1.28)	.176
Perinatal, mean (SD)	3.11 (1.75)	3.01 (1.72)	**.014**	2.87 (1.52)	2.84 (1.53)	.674
Neonatal characteristics and health						
GA (weeks), mean (SD)	37.52 (3.07)	37.54 (3.09)	.807	38.33 (2.82)	38.29 (2.76)	.775
Birth weight (grams), mean (SD)	2830 (788)	2,825 (787)	.798	3295 (784)	3,280 (758)	.677
Head circumference (cm), mean (SD)	33.20 (2.55)	33.18 (2.52)	.643	34.51 (2.34)	34.47 (2.32)	.686
Sex, n (%)			**.039**			.257
Female	2,254 (47.5)	1,297 (45.1)		658 (46.2)	305 (43.6)	
Male	2,487 (52.5)	1,578 (54.9)		765 (53.8)	394 (56.4)	
SGA, n (%)	1,152 (24.3)	737 (25.6)	.191	192 (13.5)	99 (14.2)	.673
Neonatal complications, mean (SD)	3.99 (2.99)	4.23 (3.02)	**.001**	2.18 (2.52)	2.25 (2.56)	.527
Neonatal course						

	BLS			AYLS		
	Participants (*N*=4,741)	Dropouts (*N*=2,875)	*p*-value	Participants (*N*=1,423)	Dropouts (*N*=699)	*p*-value
INTI - Clinical course, mean (SD)	2.36 (2.24)	2.50 (2.31)	**.012**	1.70 (1.96)	1.83 (1.98)	.135
INTI - Neurological status, mean (SD)	2.42 (2.34)	2.62 (2.40)	**<.001**	1.21 (1.59)	1.41 (1.73)	**.010**
Duration in hospital (days), mean (SD)	21.63 (23.48)	23.59 (27.94)	**.002**	8.76 (16.29)	9.47 (18.69)	.370
Early social environment						
SES, n (%)			**<.001**			**<.001**
High	1,039 (21.9)	459 (18.5)		469 (33.4)	183 (27.1)	
Middle	1,893 (40.0)	790 (31.8)		646 (46.0)	294 (43.6)	
Low	1,804 (38.1)	1,237 (49.8)		290 (20.6)	198 (29.3)	
FAI, n (%)						
High FAI (score 2-8)	1,599 (33.9)	971 (40.8)	**<.001**	727 (51.1)	324 (47.4)	.110
Low FAI (score 0)	1,394 (29.6)	585 (24.6)	**<.001**	178 (12.5)	94 (13.7)	.429
Poor PIRI, n (%)	1,554 (34.7)	1,005 (44.9)	**<.001**	174 (12.3)	116 (17.1)	**.003**
High PSI, n (%)	1,300 (27.9)	537 (30.6)	**.035**	421 (29.7)	191 (33.6)	.090
No breastfeeding, n (%)	2,158 (47.3)	1,007 (57.7)	**<.001**	106 (7.7)	61 (11.2)	**.014**

Abbreviations: FAI=Family Adversity Index; GA=gestational age; INTI=Intensity of Neonatal Treatment Index; PIRI=Parent-Infant Relationship Index; PSI=Psychosocial Stress Index; SES=socioeconomic Status; SGA=small for gestational age.

Trajectories of Motor Problems

BLS. LCGA modelling estimated one, two, and three latent classes (trajectories) within motor functioning from birth to 56 months. Model fits BIC, and adjusted BIC decreased gradually with the number of classes, indicating improved model fits (Appendix F). BLRT, LMR, and VLMR were all significant for a 2-class model, while only BLRT continued to be significant for a 3-class model. Considering that not all statistical indicators improved, and the size of classes, the more parsimonious 2-class model was deemed optimal.

AYLS. Following the same statistical indicators, the 2-class model was deemed to offer the best results.

The selected LCGA model identified two motor trajectories within both cohorts (Figure 3): low (BLS: *n*=4,486 (94.6%); AYLS: *n*=1,391 (97.8%)), and high (BLS: *n*=255 (5.4%); AYLS: *n*=32 (2.2%)) degree of motor problems. In both cohorts, motor problem scores differed between trajectories with a large effect size across all four time points (Appendix G).

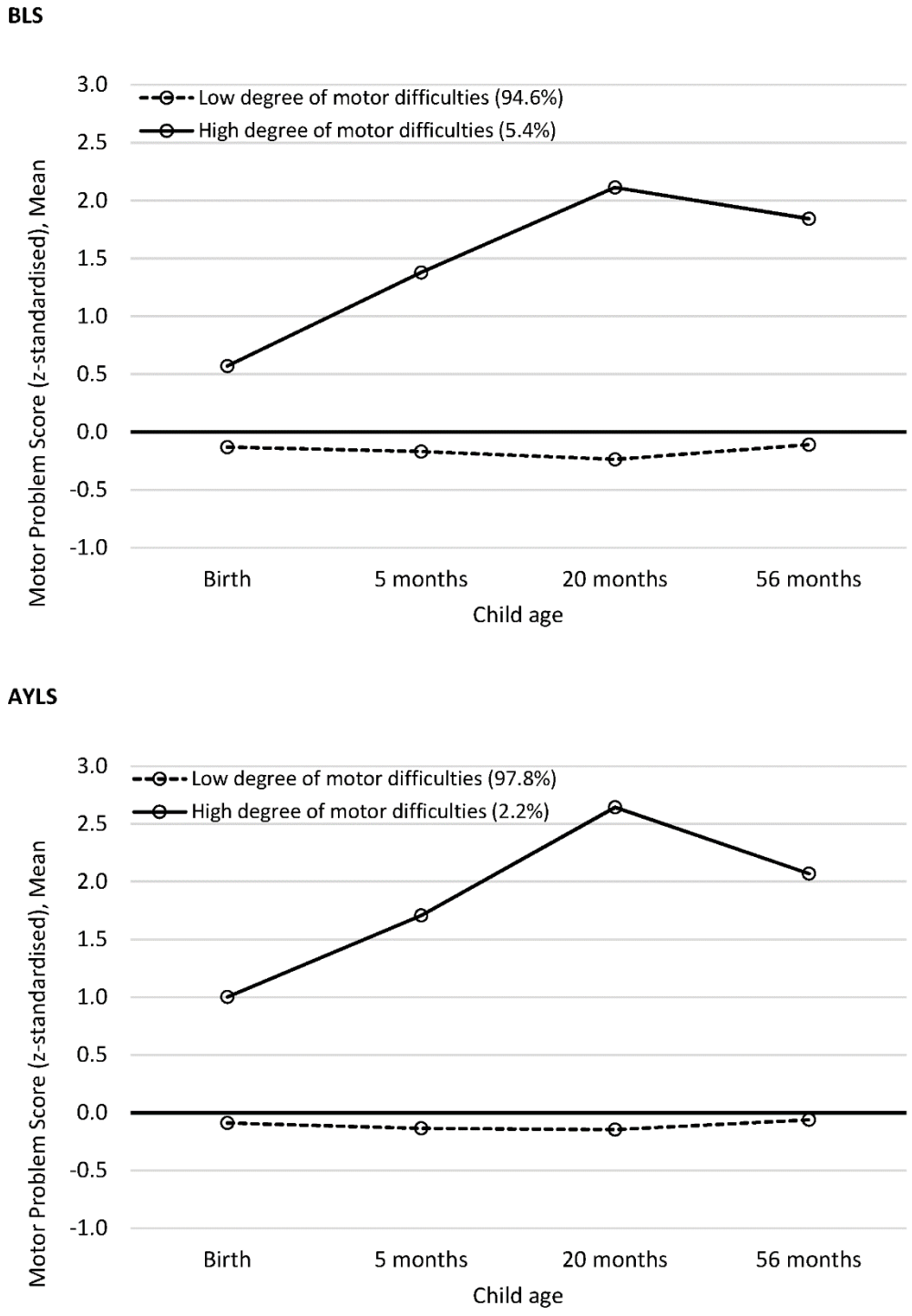

Figure 3. Trajectories of early childhood motor problems: 2-class solution (BLS and AYLS).

Predictors of Motor Trajectories: Unadjusted Models

Table 17 shows the descriptive values and unadjusted estimates of all predictors of motor trajectories.

BLS. Mothers of children with high degree of motor problems were more likely to have more complications before and during pregnancy, and around birth. Children with high degree of motor problems were more often born preterm, with low birth weight, and had a smaller head circumference. Further, they were more often small for gestational age and had more neonatal complications. Children with high degree of motor problems were rated with higher intensity of neonatal treatment scores and stayed in hospital for longer. They were also less often breastfed, more likely to have a family experiencing high adversity, and had poorer parent-infant relationships.

AYLS. Mothers of children with high degree of motor problems were more likely to have pre-pregnancy and pregnancy complications. Children with high degree of motor problems were more likely to be born preterm and with low birth weight, and had more often a smaller head circumference and neonatal complications. Moreover, they were more likely to have higher intensity of neonatal treatment scores and were hospitalized for longer. Additionally, they were more likely to have a family of low socioeconomic status, and a family experiencing more psychosocial stress, and they had poorer parent-infant relationships.

Table 17. *Descriptives and unadjusted estimates[a] of potential predictors of early childhood motor trajectories in the BLS and AYLS.*

	BLS				AYLS			
	Low degree of motor problems trajectory *n*=4,486	High degree of motor problems trajectory *n*=255	*Reference: Low degree of motor problems trajectory* OR (95% CI)	*p*-value	Low degree of motor problems trajectory *n*=1,391	High degree of motor problems trajectory *n*=32	*Reference: Low degree of motor problems trajectory* OR (95% CI)	*p*-value
Pre-/pregnancy and perinatal complications								
Pre-pregnancy, mean (SD)	1.10 (0.78)	1.28 (0.98)	**1.30 (1.12, 1.51)**	**<.001**	1.24 (0.88)	1.72 (1.17)	**1.67 (1.19, 2.33)**	**.003**
Pregnancy, mean (SD)	1.34 (1.22)	1.72 (1.32)	**1.25 (1.14, 1.38)**	**<.001**	1.22 (1.16)	1.53 (1.16)	1.23 (0.94, 1.62)	.139
Perinatal, mean (SD)	3.07 (1.74)	3.81 (1.68)	**1.27 (1.18, 1.36)**	**<.001**	2.86 (1.52)	3.25 (1.55)	1.17 (0.94, 1.45)	.151
Neonatal characteristics and health								
Prematurity (<37 weeks GA), n (%)	1,434 (32.0)	143 (56.1)	**2.72 (2.11, 3.51)**	**<.001**	282 (20.3)	11 (34.4)	2.06 (0.98, 4.32)	.056
Low birth weight (<2500g), n (%)	1,499 (33.4)	158 (62.0)	**3.25 (2.50, 4.21)**	**<.001**	221 (15.9)	11 (34.4)	**2.77 (1.32, 5.83)**	**.007**

	BLS				AYLS			
	Low degree of motor problems trajectory *n*=4,486	High degree of motor problems trajectory *n*=255	*Reference: Low degree of motor problems trajectory* OR (95% CI)	*p*-value	Low degree of motor problems trajectory *n*=1,391	High degree of motor problems trajectory *n*=32	*Reference: Low degree of motor problems trajectory* OR (95% CI)	*p*-value
Head circumference, mean (SD)	33.31 (2.42)	31.37 (3.79)	**0.79 (0.75, 0.82)**	**<.001**	34.55 (2.27)	32.75 (4.21)	**0.81 (0.73, 0.90)**	**<.001**
Male sex, n (%)	2,339 (52.1)	148 (58.0)	1.27 (0.98, 1.64)	.067	746 (53.6)	19 (59.4)	1.26 (0.62, 2.58)	.520
SGA, n (%)	1,057 (23.6)	95 (37.3)	**1.93 (1.48, 2.51)**	**<.001**	187 (13.4)	5 (15.6)	1.19 (0.45, 3.14)	.721
Neonatal complications, mean (SD)	3.84 (2.87)	6.62 (3.82)	**1.30 (1.25, 1.35)**	**<.001**	2.12 (2.43)	4.63 (4.41)	**1.26 (1.16, 1.38)**	**<.001**
Neonatal course								
INTI - Clinical course, mean (SD)	2.27 (2.15)	4.03 (2.89)	**1.33 (1.27, 1.40)**	**<.001**	1.67 (1.94)	3.19 (2.29)	**1.37 (1.18, 1.59)**	**<.001**
INTI - Neurological status, mean (SD)	2.31 (2.28)	4.32 (2.64)	**1.40 (1.32, 1.47)**	**<.001**	1.17 (1.56)	2.98 (2.14)	**1.67 (1.40, 1.99)**	**<.001**
Duration in hospital (10 days), mean (SD)	2.01 (2.04)	4.89 (4.67)	**1.32 (1.27, 1.37)**	**<.001**	0.83 (1.51)	2.74 (4.04)	**1.25 (1.14, 1.37)**	**<.001**

	BLS				AYLS			
	Low degree of motor problems trajectory *n*=4,486	High degree of motor problems trajectory *n*=255	*Reference: Low degree of motor problems trajectory* OR (95% CI)	*p*-value	Low degree of motor problems trajectory *n*=1,391	High degree of motor problems trajectory *n*=32	*Reference: Low degree of motor problems trajectory* OR (95% CI)	*p*-value
Early social environment								
Low SES, n (%)	1,686 (37.6)	118 (46.3)	1.30 (0.98, 1.71)	.066	282 (20.5)	8 (26.7)	2.01 (0.77, 5.26)	.156
High SES, n (%)	999 (22.3)	40 (15.7)	0.74 (0.51, 1.08)	.119	456 (33.2)	13 (43.3)	2.02 (0.86, 4.76)	.109
Low FAI, n (%)	1,342 (30.1)	52 (20.4)	0.74 (0.52, 1.05)	.086	173 (12.4)	5 (15.6)	1.33 (0.46, 3.89)	.600
High FAI, n (%)	1,482 (33.3)	117 (45.9)	**1.50 (1.12, 2.00)**	**.006**	711 (51.1)	16 (50.0)	1.04 (0.48, 2.25)	.926
Poor PIRI, n (%)	1,425 (33.6)	129 (52.7)	**2.19 (1.69, 2.84)**	**<.001**	167 (12.1)	7 (22.6)	2.13 (0.90, 5.01)	.085
High PSI, n (%)	1,231 (27.9)	69 (27.8)	1.00 (0.75, 1.32)	.975	407 (29.4)	14 (46.7)	**2.11 (1.02, 4.35)**	**.045**
No breastfeeding, n (%)	1,986 (46.0)	176 (69.9)	**2.73 (2.07, 3.61)**	**<.001**	102 (7.5)	4 (13.3)	1.88 (0.65, 5.50)	.247

Note. The odds ratios and *p*-values were significant at the 0.05 level. Abbreviations: CI=Confidence Interval, FAI=Family Adversity Index, GA=gestational age, INTI = Intensity of Neonatal Treatment Index; OR=Odds Ratio, PIRI=Parent-Infant Relationship Index, PSI=Psychosocial Stress Index, SES=socioeconomic status, SGA=small for gestational age.

[a] Unadjusted estimates of univariate binomial logistic regression analyses.

Predictors of Motor Trajectories: Adjusted Models

Adjusted estimates of significant predictors of high degree of motor problems in multivariate models are shown in Table 18.

BLS. The results of adjusted stepwise models showed that when pre-pregnancy, pregnancy and perinatal complications were combined into one model (Model 1), all three predictors were associated with motor problems. However, when neonatal health predictors were added (Model 2), only head circumference and neonatal complications remained as significant predictors. In Model 3, neonatal complications, abnormal neonatal neurological status and longer hospitalisation were associated with high degree of motor problems. The final model (Model 4), showed the same associations as in Model 3, with poor parent-infant relationships also predicting high degree of motor problems. All predictors explained 17.4% of the variance in the final model.

AYLS. The final adjusted model (Model 4) with AYLS data showed the same pattern of results as with BLS data. However, only abnormal neonatal neurological status and longer hospitalisation were significantly associated with high degree of motor problems whereas neonatal complications and poor parent-infant relationship ceased to be significant predictors. All predictors explained 19.4% of the variance in Model 4. Results of all stepwise models are shown in Appendix H.

Table 18. *Adjusted estimates[a] of significant predictors of a high degree of motor problems trajectory in the BLS and the AYLS[b].*

	BLS				AYLS
	Model 1	Model 2	Model 3	Model 4	Model 4
Pre-/pregnancy, perinatal complications					
Pre-pregnancy	**1.20 (1.03, 1.40)**	1.13 (0.97, 1.32)	1.14 (0.97, 1.33)	1.15 (0.98, 1.36)	1.28 (0.84, 1.96)
Pregnancy	**1.15 (1.04, 1.27)**	0.97 (0.87, 1.09)	0.97 (0.87, 1.10)	0.92 (0.81, 1.05)	1.04 (0.72, 1.51)
Perinatal	**1.22 (1.13, 1.31)**	1.05 (0.96, 1.15)	1.05 (0.96, 1.15)	1.04 (0.95, 1.14)	0.97 (0.72, 1.29)
Neonatal characteristics and health					
Prematurity (<37 weeks GA)		0.83 (0.55, 1.26)	0.82 (0.53, 1.27)	0.84 (0.53, 1.33)	0.44 (0.11, 1.70)
Low birth weight (<2500g)		1.23 (0.79, 1.91)	1.24 (0.78, 1.97)	1.18 (0.73, 1.91)	1.95 (0.44, 8.68)
Head circumference		**0.92 (0.86, 0.99)**	1.00 (0.93, 1.08)	0.99 (0.91, 1.07)	0.96 (0.78, 1.19)
SGA		1.13 (0.82, 1.56)	1.17 (0.84, 1.62)	1.07 (0.75, 1.51)	0.64 (0.18, 2.24)
Neonatal complications		**1.23 (1.17, 1.29)**	**1.11 (1.03, 1.19)**	**1.11 (1.03, 1.20)**	1.11 (0.90, 1.37)
Neonatal course					

	BLS				AYLS
	Model 1	Model 2	Model 3	Model 4	Model 4
INTI – Clinical course			0.92 (0.83, 1.00)	0.92 (0.83, 1.01)	0.77 (0.54, 1.10)
INTI – Neurological status			**1.21 (1.12, 1.29)**	**1.17 (1.08, 1.26)**	**1.85 (1.38, 2.48)**
Duration in hospital (10 days)			**1.19 (1.13, 1.26)**	**1.17 (1.11, 1.24)**	**1.19 (1.02, 1.39)**
Early social environment					
Low FAI				0.94 (0.64, 1.39)	2.22 (0.68, 7.26)
High FAI				1.34 (0.97, 1.86)	1.19 (0.47, 2.99)
Poor PIRI				**1.55 (1.16, 2.08)**	1.13 (0.40, 3.15)
No breastfeeding				1.34 (0.97, 1.84)	0.40 (0.10, 1.62)

Abbreviations: FAI=Family Adversity Index, GA=gestational age, INTI = Intensity of Neonatal Treatment Index, PIRI=Parent-Infant Relationship Index, SGA=small for gestational age.

[a] Adjusted estimates of multivariate binomial logistic regression analyses (Odds Ratio and 95% Confidence Interval), predictors adjusted for all other variables in the prediction model.

[b] Replication: The same multivariate regression analysis (Model 4) established for BLS data was applied to AYLS data.

The odds ratios and *p*-values were significant at the 0.05 level.

Figure 4 illustrates all four risk factors associated with high degree of motor problems in the final adjusted model for both cohorts: neonatal complications (BLS: OR 1.11, CI 1.03-1.20; AYLS: OR 1.11, CI 0.90-1.37), abnormal neonatal neurological status (BLS: OR 1.17, CI 1.08-1.26; AYLS: OR 1.85, CI 1.38-2.48), duration in hospital (10 days) (BLS: OR 1.17, CI 1.11-1.24; AYLS: OR 1.19, CI 1.02-1.39), and poor parent-infant-relationship (BLS: OR 1.55, CI 1.16-2.08; AYLS: OR 1.13, CI 0.40-3.15).

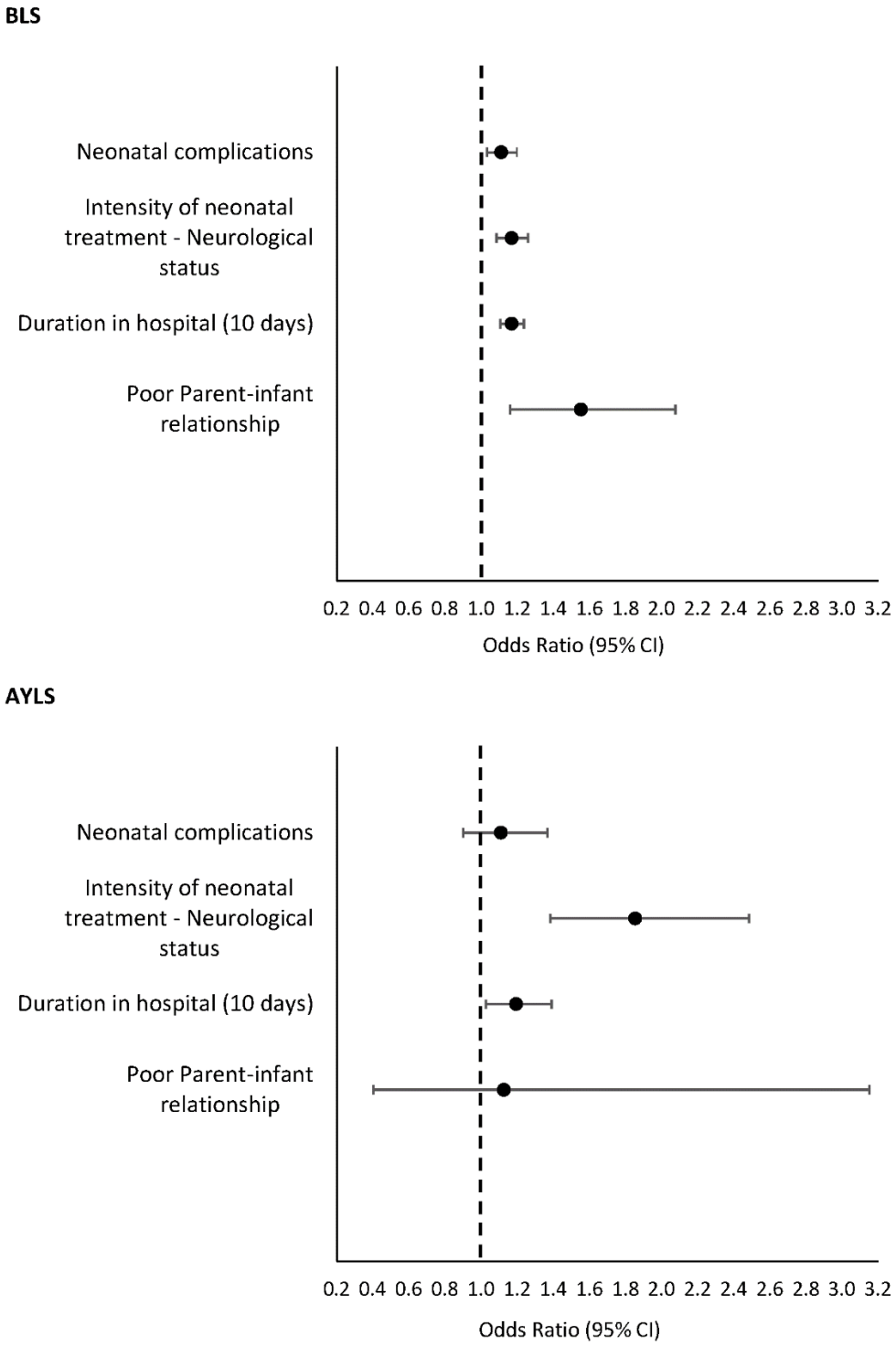

Figure 4. Unique neonatal and early environment predictors of high degree of motor problems trajectory in the BLS and AYLS (adjusted estimates of multivariate binomial logistic regression analyses [Odds Ratio and 95% Confidence Interval])

Discussion

We identified two distinct motor trajectories in this longitudinal study of two samples of at-risk and control children in two countries. These two motor trajectories across the first 5 years of life are described as low and high degree of motor problems. Significant independent predictors of children with high degree of motor problems were neonatal complications, abnormal neonatal neurological status, duration of hospitalisation, and poorer parent-infant relationships in the BLS. The same predictors were identified in the AYLS, however, estimates of neonatal complications and poor parent-infant relationship were not significant at the 0.05 level in multivariate analyses. Nevertheless, the trends were similar to findings obtained from the BLS data, as shown in Figure 4. The differences are likely due to the smaller AYLS sample and smaller group of children with poor motor development, resulting in lower statistical power compared to the larger BLS sample (i.e., the low number of children with poor parent-infant relationships in the AYLS sample; see Table 17). However, there are important differences between the BLS and AYLS sample that may have been contributed to the differences in findings. The AYLS children were more advantaged in terms of neonatal health and neonatal course, compared to BLS children. They were less often born premature, had lower neonatal complication and abnormal neonatal neurological status scores, and stayed in hospital for a shorter period of time (see Table 16).

Results of LCGA show that children's development of motor functioning either followed a low or a high degree of motor problems trajectory across early childhood. Most children in both samples consistently had no or low degree of motor

problems from birth to 56 months, while children in the group with high degree of motor problems demonstrated problems at all four assessments.

Three recent longitudinal studies (Hameed et al., 2017; Heineman et al., 2018; Su et al., 2017) have used LCGA to identify different groups of children with distinct early motor trajectories. Even though more than two groups were identified in these studies, the trajectories represented stable and declining/delayed motor development, with most children exhibiting stable motor development, i.e. average or typically developing motor performance. This is comparable to the two trajectories ascertained in the present study, with the majority of children exhibiting no or low degree of motor problems across early childhood. Thus, despite methodological differences, such as the inclusion of very low birth weight infants (Su et al., 2017) or children born after assisted reproductive techniques (Heineman et al., 2018), and the reliance on parental information to assess motor function (Hameed et al., 2017), our findings are broadly in keeping with previous research.

Interestingly, perinatal risk factors previously identified to predict motor impairment or delayed motor development, i.e. prematurity, low birth weight, smallness for gestational age, male sex (Flensborg-Madsen & Mortensen, 2017; Spittle & Orton, 2014; Su et al., 2017; Zwicker, Yoon, et al., 2013), were only found to be related to poor motor development in univariate but not in multivariate models. Instead, clinical neonatal factors, i.e., complications, abnormal neurological status, duration of hospitalisation, and poor parent- infant relationships emerged as unique predictors of poor motor development. The number and type of risk factors included in previous studies varies considerably. Further, most of these studies have included

preterm children only and had smaller sample sizes compared to the present study. Our finding thus may be explained by a more inclusive approach with broader preconditions, i.e. the inclusion of more comprehensive clinical and early motor-related predictors as well as early social environment factors, the large sample size of both cohorts and the inclusion of children born across the whole gestation spectrum in our analyses.

The data suggest that a higher number of neonatal complications (including seizures, cerebral haemorrhage, and ventilation), ratings of abnormal neonatal neurological status (i.e., increased or decreased mobility, muscle tone or activity/reactivity to hyper-/hypokinesia, hyper-/hypotonia, apathy, coma or hyperexcitability), and longer stay in hospital negatively affect motor outcomes (Pin et al., 2010; Pineda et al., 2013; Zwicker, Yoon, et al., 2013). These early predictors highlight the importance of infants' health and neurological status during the neonatal period. One explanation may be that due to infants' poor health and treatment being paramount, and the stressors that those infants are being exposed to in the NICU environment, normal early movements, motor control and motor learning are impeded or delayed (Pineda et al., 2017; G. C. Smith et al., 2011). Other factors, such as decreased or delayed weight gain and body growth, as well as a constrained environment in the NICU and parental support could play a role (Pineda et al., 2017). Further, processes in brain development (e.g., myelination and synaptogenesis), which are important for motor coordination and functioning, and the integrity of the central nervous system may also be affected by the infant's level of morbidity (Aylward, 2005). Overall, neonatal complications, abnormal neonatal

neurological status, and duration of hospitalisation are useful early medical markers of poor motor development and can be monitored regularly in the neonatal care unit. Importantly, this knowledge would make it possible to inform parents in a timely manner about their child's risk of developing motor problems or delay and enable early referral to interventions.

Most notable, poor early parent-infant relationships increased the infants' risk of early motor problems. As to the reasons and specific mechanisms behind the association between parent-infant relationships and motor development, we can only speculate. Parents are important facilitators of infants' motor learning and development (Adolph & Hoch, 2018). Not only do they provide an appropriate environment (e.g., high chairs to support sitting or crawling tunnels to practice arm and leg movements) (Miquelote, Santos, Cacola, Montebelo, & Gabbard, 2012), they also support and guide their infant verbally and non-verbally (Adolph & Berger, 2015), and help develop muscle strength and gross motor skills (e.g., making noises to encourage the infant to lift its head). As a result, parents influence and determine their child's development. This raises the question, how and why the quality of parent-infant relationships may alter parents' behaviour and perception of their child in regard to how they implement support and guidance for their infants' motor learning and development. Poor parent-infant relationships in the current study were defined by parents not seeing or visiting their child often during the day, and by parents showing little pleasure or confidence in interacting with their infant. This indicates that parents' confidence and belief in their competence to take care and interact with their infant, especially if the infant is perceived as too fragile, may be

an important factor in their ability to create opportunities for their child's motor learning and motor skill practice (Hughes et al., 2016). Parents whose child had been referred to the NICU may even feel less confident and have little opportunity to support and encourage their infant's motor development and learning due to their child's medical condition and care provided through NICU personnel, and the associated stress and anxiety (Holditch-Davis et al., 2015). However, integrating parents while their child is in the NICU and encouraging them to hold their infant, may positively influence motor outcomes (Pineda et al., 2017). A recent meta-analysis found that parenting interventions can positively affect children's motor abilities (Hughes et al., 2016). The authors suggest that such an intervention may alter parents' perception of their preterm born child as being too fragile and may increase parental feelings of competence and self-confidence resulting in positive parent-infant interactions (Forcada-Guex et al., 2006). These findings are important as early parent-infant relationships represent a potentially modifiable factor that can be addressed by support services and in early intervention programmes. Further, previous findings have shown that early parent-infant relationships predict long-term cognitive outcomes (Breeman et al., 2017).

Our findings support future research to investigate whether targeted intervention programmes to improve early parent-infant relationships and to provide parent support in the NICU can lead to significant and long-term improvements in children's motor development. Given the evidence from previous studies that early motor deficits do not diminish over time (Husby et al., 2013), and that poor motor skills in adulthood are associated with mental health problems and lower health-

related quality of life (Husby et al., 2016), the early motor trajectories identified in this current study may help to predict whether children with high degree of motor problems over the first 5 years of life are more likely to have additional problems in other developmental domains across the life span.

The strengths of this study are its prospective longitudinal design, large sample size, the inclusion of children born across the whole gestation spectrum, the assessment of motor functioning via extensive and detailed physical and neurological examinations at four time points, and the uniquely built-in replication with identical data from a second large longitudinal study from a different country. Further, even after excluding children with severe neurological impairments diagnosed at 56 months (sensitivity analysis), the results were similar to our main results. There are also limitations. Although more than 60% of eligible children could be assessed in both cohorts, the dropout was not random. Children who had a poorer health status and a socially disadvantaged family were less likely to continue participation. This may suggest that identified early predictors have an even larger effect on early motor development than reported here. Attrition is a problem in many longitudinal studies. However, simulations have shown that predictions only marginally change even when dropout is selective or correlated with the outcome (Wolke et al., 2009). Further, the participants of both cohorts were born in the mid-80s. Over the last three decades, changes in reproductive medicine and improvements in neonatal practices and care have led to increased survival rates of smaller infants. However, despite these changes, recent findings indicate that the prevalence of neurodevelopmental sequelae, including motor impairments, has not improved (Cheong et al., 2017;

Spittle et al., 2018). Thus, although our results should be cautiously interpreted, they provide a baseline for newer cohorts to investigate whether findings differ for children born after our cohorts.

Conclusion

Our results show distinct pathways of early motor functioning, with a subgroup of children developing a high degree of motor problems in early childhood. In addition to known risk factors, such as neonatal complications, abnormal neonatal neurological status, and duration of hospitalisation, our findings confirm the importance of parent-infant relationships in motor development and should be considered in intervention studies to prevent or ameliorate continued motor problems and possible secondary issues in other developmental domains.

Chapter 4: 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 behaviour 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.

Introduction

Motor impairments, including cerebral palsy (CP) and developmental coordination disorder (DCD), have been found to be associated with adverse developmental outcomes (Spittle & Orton, 2014). Motor functioning assessed in infancy or toddlerhood has been found to be associated with subsequent developmental outcomes, including motor, cognitive and behavioural function, in both healthy and at-risk children, such as those born preterm (Butcher et al., 2009; Hitzert et al., 2014; Piek et al., 2008; Spittle et al., 2013).

Many children with early motor problems are referred for intervention (Herskind et al., 2015). In particular, physiotherapy is a widely used treatment for children with neurological motor dysfunctions (G. T. Brown & Burns, 2001; Spittle & Morgan, 2018). 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 (Aylward, 2009).

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 (see Chapter 3; Baumann, Tresilian, Heinonen, Raikkonen, & Wolke, 2020). 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 (Spittle & Morgan, 2018). 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 (G. T. Brown & Burns, 2001; Spittle & Morgan, 2018).

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 of gestation) or at very low birth weight (<1500g); (2) a subsample of children born at >=32 weeks of 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 (Jaekel, Baumann, & Wolke, 2013). Longitudinal data were available for 1,374 children. In brief, compared to children who were included in the longitudinal analyses, children who dropped out (*N*=169) had a lower gestational age (32.75 *versus* 36.74 weeks, $p<0.001$) and birth weight (1,808 *versus* 2,679 grams, $p<0.001$). Further, dropouts were more frequently classified as being born small for gestational age (33.7 *versus* 24.9%, $p=0.013$) and more often born into families with a lower socioeconomic status (39.5 *versus* 33.1%, p=0.022). However, no significant sex differences were observed (p>0.05).

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 behaviour.

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 (Prechtl, 1977) was carried out by specially trained paediatricians. 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 4 and 5, Chapter 2) 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 (see Chapter 3; Baumann et al., 2020). Guided by current recommendations to differentiate children at risk or with probable motor problems (Blank et al., 2012), 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 19. 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.

Table 19. *Physiotherapy from birth to 56 months (N=372)*

	N (%) or Mean (SD)
Physiotherapy at 5 months	211 (56.7%)
Duration (months), mean (SD) [a]	3.02 (1.78)
Physiotherapy at 20 months	283 (76.1%)
Bobath physiotherapy	196 (52.7%)
Vojta physiotherapy	52 (14.0%)
Other physiotherapy	56 (15.1%)
Duration (months), mean (SD) [b]	8.58 (6.49)
Physiotherapy at 56 months	114 (30.6%)
Bobath physiotherapy	50 (13.4%)
Vojta physiotherapy	27 (7.3%)
Other physiotherapy	51 (13.7%)
Duration (months), mean (SD) [c]	20.23 (20.68)
Physiotherapy from birth to 56 months	
Early physiotherapy (within the first year of life)	324 (87.1%)
Late physiotherapy	48 (12.9%)

[a] Based on *n*=201 due to missing data.
[b] Based on *n*=278 due to missing data.
[c] Based on *n*=80 due to missing data.

Childhood outcomes at 6 and 8 years

Developmental outcomes obtained at 6 and 8 years are described in detail in Tables 10 and 11 (Chapter 2). An overview is given here: *Motor impairment* was evaluated using the Test of Motor Impairment (TOMI) (Stott et al., 1984). *Mental health problems* were assessed via parent reports with the Child Behavior Checklist (CBCL) (Achenbach, 1991). *Cognitive function* was measured with the simultaneous processing scale of the German version of the Kaufman Assessment Battery for Children (K-ABC) (Melchers & Preuss, 1991). 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 Behaviour (TRCB) (Jaekel, Wolke, et al., 2013) task orientation scale, a team consensus rating (TEAM) of attention span, and the attention problem subscale of the Child Behavior Checklist (CBCL) (Achenbach, 1991).

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 (Muthén and Muthén, Los Angeles, California, USA). Measures were used as factor indicators and a standardized factor score was retrieved. Factor loadings are reported in Appendix J.

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 12, Chapter 2). 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 23). 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 (Appendices K and L).

Results

Sample characteristics

Children with infant motor problems had a lower gestational age and birth weight than the comparison group (Table 20). 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.

Table 20. *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=1,171 (85.2%)	*N*=203 (14.8%)		*N*=1,175 (85.5%)	*N*=199 (14.5%)	
Gestational age (weeks)	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 (%). Bold *p*-values were significant at the 0.05 level.

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 21). However, the association between early motor problems and later motor skill was not significant after adjusting for gestational age, SGA, sex, and SES.

Table 21. *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								

	Unadjusted effect				Adjusted effect[a]			
	B	95% CI	*β*	*p*-value	B	95% CI	*β*	*p*-value
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**

Note. Bold *p*-values were significant at the 0.05 level.
[a] Adjusted for gestational age, small for gestational age, male sex, and socioeconomic status.

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 22). 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 months and receipt of physiotherapy for motor skills and cognitive function at age 6 and 8 years.

Table 22. *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:												

	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	-0.59	(-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:												
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

Note. Bold *p*-values were significant at the 0.05 level.

[a] Adjusted for both predictors.

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

Effects of treatment with physiotherapy on childhood outcomes after PSM

After accounting for imbalances in baseline characteristics (see Table 23) 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.

Table 23. *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, %			

	Physiotherapy unmatched: *n*=271 matched: *n*=245	No Physiotherapy unmatched: *n*=800 matched: *n*=768	Standardized bias (%)
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
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			

	Physiotherapy unmatched: *n*=271 matched: *n*=245	No Physiotherapy unmatched: *n*=800 matched: *n*=768	Standardized bias (%)
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 12, Chapter2).

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

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 (Spittle et al., 2013) 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 (Spittle et al., 2013; Su et al., 2017), but in contrast to studies that included healthy low-risk children (Hitzert et al., 2014; Piek et al., 2008). 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 (Jenni et al., 2013). This may result in more catch-up development in low-risk children and a lower stability and poorer predictive value of early motor problems (Jenni et al., 2013). 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 (Denckla, 2005). 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 (Bornstein et al., 2013).

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 (Butcher et al., 2009; Hitzert et al., 2014; Piek et al., 2008; Su et al., 2017). 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 (Pangelinan et al., 2011).

Regarding mental health, previous findings are inconsistent, with some studies having provided evidence for an association between early motor function and later mental health (Hitzert et al., 2014) and others not (Butcher et al., 2009). Children with motor impairments, such as DCD, are more likely to have mental health problems, in particular anxiety, depression and ADHD (Blank et al., 2019). 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 (Lingam et al., 2012). 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 (Laerum et al., 2019).

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)) (Zhang, Ni, & Xu, 2014).

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 (Als, 2009).

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 (G. T. Brown & Burns, 2001; Herskind et al., 2015; Hughes et al., 2016). 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 behaviour can have positive effects on motor development (Hughes et al., 2016). 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 (Spittle & Treyvaud, 2016), 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 (Blank et al., 2019). 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 (Spittle et al., 2018).

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.

Chapter 5: Early Childhood Motor Trajectories Predict Adult Motor and Cognitive Function

Abstract

Very preterm (VP; <32 weeks of gestation) and/or very low birth weight (VLBW; <1500 g) birth has been associated with an increased risk of adverse motor and cognitive outcomes that may persist into adulthood. The aim of this study was to determine whether motor development in the first five years of life is associated with motor and cognitive outcomes in adulthood. A prospective observational study in Germany followed 260 VP/VLBW and 229 term-born individuals from birth into adulthood. Early motor trajectories (i.e., high and low degree of motor problems) were determined from neurological examinations from birth to 56 months. Adult motor and cognitive outcomes were determined from information from multiple instruments and IQ tests, respectively. Associations of VP/VLBW birth and early motor problems on adult outcomes were assessed using regression analyses. VP/VLBW individuals had an increased risk for early motor problems (Relative Risk: 11.77, 95% confidence interval (CI): 4.28, 32.35). Early motor problems were associated with poorer motor competence in adulthood ($\beta = 0.22$, $p < 0.001$), independent of VP/VLBW birth. Adult IQ was predicted by VP/VLBW ($\beta = -0.12$, $p < 0.05$) and child IQ ($\beta = 0.51$, $p < 0.001$), while early motor problems ceased to be associated with adult IQ once participants with a neurological impairment were excluded ($\beta = 0.02$, $p > 0.05$). Motor problems in childhood were homotypically associated with poorer motor competence in adulthood. Similarly, early cognitive

problems were homotypically associated with adult cognitive outcomes. Thus, both motor and cognitive function should be assessed in routine follow-up during childhood.

Introduction

Despite advances in antenatal and neonatal care over recent decades, very preterm birth (VP; gestational age <32 weeks) and/or very low birth weight (VLBW; <1500 g) remain major risk factors for neurodevelopmental sequelae, including motor and cognitive impairments (Allotey et al., 2018; Ream & Lehwald, 2018). Both motor and cognitive impairments can have a profound impact on learning, academic achievement, health, and wellbeing across the lifespan for VP/VLBW individuals (A. Goodman, Joyce, & Smith, 2011; Jaekel & Scott, 2018), and may persist throughout childhood and into adulthood (de Kieviet et al., 2009; Husby et al., 2013; Linsell et al., 2017; Poole et al., 2015a). Furthermore, they are the two most frequent sequelae of VP/VLBW (Wolke, Johnson, & Mendonca, 2019).

According to Piaget and more recent embodied approaches (Adolph & Hoch, 2018), cognitive development in the first two to three years proceeds through sensorimotor interactions between the child and its physical and social environment. Consistent with these ideas, it has been found that a number of cognitive tasks recruit the same brain regions that are used for motor tasks (Pangelinan et al., 2011; Pulvermuller, 2018). Numerous cross-sectional studies have reported an association between motor and cognitive function in typically developing (Abdelkarim et al., 2017; Ludyga, Puhse, Gerber, & Herrmann, 2019; Rigoli, Piek, Kane, & Oosterlaan, 2012; van der Fels et al., 2015) and preterm-born children (Domellof, Johansson, Farooqi, Domellof, & Ronnqvist, 2013; Marlow et al., 2007). This raises a question of whether associations between the motor and cognitive domain will hold in a

longitudinal setting: Does children's early motor development affect their cognitive abilities as they grow into adults? Or is there a homotypic association where early motor development specifically predicts later motor outcomes but not cognition? Several longitudinal studies have shown that early motor problems predict poorer cognitive abilities into school-age, albeit less consistently in preterm than in general or term-born populations (Oudgenoeg-Paz et al., 2017). However, long-term studies that investigate associations between early motor development and later cognitive abilities into adulthood are rare (Flensborg-Madsen & Mortensen, 2015, 2018; Murray et al., 2007; Murray et al., 2006), particularly in preterm populations.

The current study investigated a sample of VP/VLBW and control individuals from birth to adulthood. The study aims were to investigate: (1) whether VP/VLBW birth is associated with early motor development from birth to 56 months (i.e., early motor trajectories), and (2) whether VP/VLBW birth and early motor trajectories are specifically associated with motor competence in adulthood or with adult cognitive function.

Methods

Design and participants

Data were collected as part of the prospective Bavarian Longitudinal Study (BLS) (Riegel et al., 1995). 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 = 7505). The initial cohort included 682 participants born VP/VLBW.

Of these, 411 were alive and eligible for follow-up in adulthood, and 260 (63.3%) participated. Additionally, healthy infants born at term in the same hospitals were recruited as controls (*n* = 916). To be comparable to the VP/VLBW sample, 350 participants of this group who were alive at 6 years were randomly selected as term controls within the stratification variables gender and family socioeconomic status (SES). In adulthood, 308 term-born individuals were eligible for inclusion and 229 (74.4%) participated at 26 years (see Figure 5). The current study used data collected at birth, 5, 20, and 56 months, and 26 years. Participants were assessed for one whole day, including neurological testing in childhood and cognitive testing and detailed interviews at all time points.

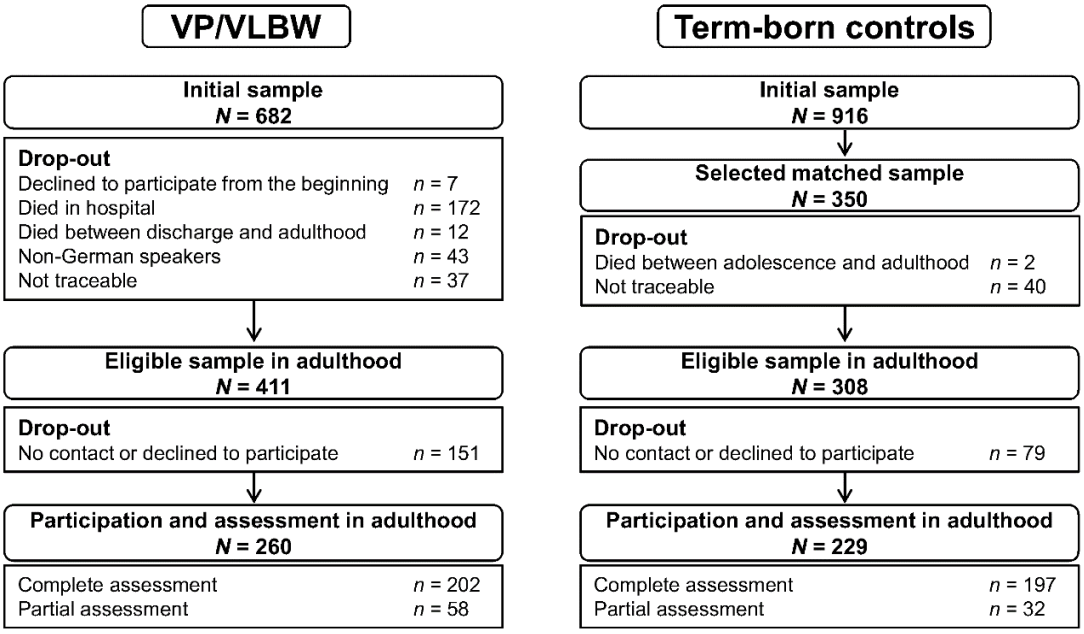

Figure 5. Eligible sample of very preterm and/or very low birth weight (VP/VLBW) and term control participants at age 26 years.

All assessors were blind to participants' characteristics and results of previous assessments. Ethical permissions were granted by the ethics committees of

the University of Munich Children's Hospital and the Bavarian Health Council (Landesärztekammer Bayern). Ethical approval for follow-up in adulthood was granted by the Ethical Board of the University Hospital Bonn (reference # 159/09). Informed written consent was provided initially by parents within 48 h of the infant's hospital admission and all participants gave fully informed written consent for the assessment in adulthood.

Measures

Early motor trajectories

At birth, and at 5, 20, and 56 months, motor functioning was measured via standard neurological and physical examinations based on Prechtl's neurological examination method (Prechtl, 1977). To compute a motor problem score for each age, items on neurological and motor functioning, including fine and gross motor skills, oculomotor function, muscle tone, and reflexes (for example: eye movement, mouth and tongue movement, quantity of spontaneous motor activity, muscle tone at rest, head control while pulling up to sit, posture during sitting, fluent and stable movements while walking, knee jerk reflex), were combined and categorized into 'within' and 'outside the normal range' of motor function. Detailed descriptions of items can be found elsewhere (see Chapter 3; Baumann et al., 2020). Based on the sum of motor functioning 'outside the normal range' a motor problem score was computed, with higher scores indicating more motor problems. Due to the varied number of items across time points (birth: 25 items, 5 months: 63 items, 20 months: 63 items, and 56 months: 125 items), motor problem scores were standardized to a

mean of 0 and a standard deviation of 1 (z-scores), allowing comparability across time points and ages.

Using latent class growth analysis (LCGA), a person-centred statistical approach, two groups of children with a similar development of motor functioning from birth to 56 months (i.e., motor trajectories) were identified. LCGA was applied to the sample available in early childhood, independent of birth status (e.g., preterm birth). The details of the statistical procedure are described elsewhere (see Chapter 3; Baumann et al., 2020). The two motor trajectories described as either high or low degree of motor problems, yielded a binary variable. For the current longitudinal sample 44 (10.5%) and 374 (89.5%) participants had a high and low degree of motor problems in early childhood, respectively.

Outcomes in adulthood

Motor competence

Indicators of motor function were assessed as part of a life course interview and questionnaires with the participants, including suboptimal functioning for ambulation and dexterity, low self-esteem regarding sports, being poorly coordinated or clumsy, and not being able to ride a bicycle or to swim (see Table 13, Chapter 2). Indicators were summed into a composite score. Due to high skewness, the score was dichotomized: 0 (high motor competence) and 1 (low motor competence). Data on adult motor competence were available for 418 participants.

Cognitive function

General intelligence was assessed with the German short version of the Wechsler Adult Intelligence Scale (WAIS III) (von Aster et al., 2009; Wechsler, 1997). Raw scores for six subtests of the WAIS (i.e., vocabulary, similarities, letter-number-sequence, block design, matrix reasoning, and digit symbol coding) were converted into an age-normed full-scale IQ score (Eryigit Madzwamuse, Baumann, Jaekel, Bartmann, & Wolke, 2015). Data on adult IQ were available for 354 participants.

Covariates and potential confounds

Data on gestational age (GA, weeks), birth weight (grams), and sex (1 = male, 0 = female) were obtained from perinatal records at birth. Children with a birth weight of less than the sex specific 10^{th} percentile for GA were classified as small for GA (SGA) (Eryigit Madzwamuse et al., 2015). Family socioeconomic status (SES) at birth was defined and categorized as 1 (low), 2 (middle), or 3 (high) (Riegel et al., 1995).

IQ at 56 months was assessed through a composite of three cognitive tasks (the Columbia Mental Maturity Scale (Burgemeister et al., 1954; Eggert, 1972), the Active Vocabulary Test (Kiese & Kozielski, 1979), and the Beery–Buktenica Developmental Test of Visual-Motor Integration (Beery, 1982)).

Diagnoses of a range of mild to severe neurological impairments were made by a specially trained developmental paediatrician at 56 months, and included epilepsy, hydrocephalus (Riegel et al., 1995), cerebral palsy (CP; four stages: 1 = more pronounced in fast-paced movement, impairment has a hardly noticeable

negative impact (mildest CP); 2 = possible to walk but with noticeable negative impact, additional impairment to the motor function of the hand; 3 = walking is not possible; 4 = no active movement at all (most severe CP)) (Hagberg et al., 1989), and blindness, or deafness (not corrected or insufficiently corrected) (Wolke & Meyer, 1999).

Statistical analyses

All statistical analyses were performed using SPSS Version 22 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA) and Stata Version 15.0 (StataCorp LLC, College Station, TX, USA). Differences between VP/VLBW and term-born individuals and those that dropped out or were excluded due to missing data on adult outcomes, were tested with a *t*-test for continuous variables and chi-square test for categorical variables. Statistical significance was set at $p < 0.05$.

In addition to the computation of frequencies and group differences, the relative risk (RR) with 95% confidence interval (CI) was calculated to test whether VP/VLBW individuals more often had a trajectory of high degree of motor problems in early childhood (reference: low degree of motor problems) compared to term-born participants. RR was subsequently adjusted for potential confounds of motor outcomes (Wolke et al., 2019), such as SGA, multiple births, child sex, family SES at birth, and IQ at 56 months.

The weight least square estimation (WLSMV) in Mplus 7 (Muthén and Muthén , Los Angeles, California, USA) was used for structural equation modelling (SEM). Fit of the models was tested using chi-square test of model fit, the root mean

squared error of approximation (RMSEA), and the comparative fit index (CFI). Model fits were considered good with RMSEA below 0.06 and CFI above 0.95 (Hu & Bentler, 1999). SEM was applied to test direct and indirect effects of early motor problems and VP/VLBW on motor and cognitive outcomes in adulthood. The SEM model additionally included IQ at 56 months and was controlled for potential confounds.

To rule out the possibility that the tested longitudinal associations had been influenced by a neurological impairment (n = 25; Table 24), a sensitivity analysis was carried out where the SEM model was repeated excluding individuals with a diagnosed neurological impairment in childhood (i.e., epilepsy, hydrocephalus, CP, blindness, or deafness).

Results

VP/VLBW participants were born with lower GA and birth weight than term-born controls (Table 24). Further, VP/VLBW adults were more often multiples and born SGA. While there were no group differences in regard to sex, VP/VLBW participants were more often born into families of lower and middle SES. At age 56 months, VP/VLBW individuals were more frequently diagnosed with CP and had lower IQ scores. In adulthood, VP/VLBW participants had lower motor competence and lower IQ scores compared to term-born adults (Table 24).

Compared to VP/VLBW participants, VP/VLBW dropouts had lower birth weight and lower IQ scores in childhood. Control dropouts were more often males,

had a lower familial socioeconomic status and lower IQ scores than participating controls.

Table 24. *Comparison of participating preterm and term control adults and those that dropped out on neonatal characteristics, early childhood function, and motor competence and cognitive function in adulthood.*

	Participants			Dropouts			
	Term Controls	VP/VLBW		Term Controls		VP/VLBW	
	n = 226	*n* = 192	*p*-value[a]	*N=82*	*p*-value[b]	*N=219*	*p*-value[c]
Neonatal Characteristics							
Gestational Age (GA), in weeks, mean (SD)	39.66 (1.16)	30.51 (2.11)	**<0.001**	39.66 (1.16)	0.664	30.55 (2.45)	0.851
Birth Weight (BW), in grams, mean (SD)	3367 (441)	1344 (328)	**<0.001**	3428 (458)	0.290	1265 (284)	**0.009**
Small for GA <10%, *n* (%)	23 (10.2)	73 (38.0)	**<0.001**	8 (9.8)	0.914	103 (47.0)	0.065
Multiple, *n* (%)	6 (2.7)	50 (26.0)	**<0.001**	6 (7.3)	0.062	53 (24.2)	0.667
Sex, *n* (%)			0.059		**0.039**		0.115
Male	105 (46.5)	107 (55.7)		49 (59.8)		105 (47.9)	
Female	121 (53.5)	85 (44.3)		33 (40.2)		114 (52.1)	
Socioeconomic Status at Birth, *n* (%)			**0.010**		**<.001**		0.239
High	77 (34.1)	42 (21.9)		15 (18.3)		39 (17.9)	
Middle	95 (42.0)	85 (44.3)		27 (32.9)		88 (40.4)	
Low	54 (23.9)	65 (33.9)		40 (48.8)		91 (41.7)	

	Participants			Dropouts			
	Term Controls	VP/VLBW		Term Controls		VP/VLBW	
	n = 226	*n* = 192	*p*-value[a]	*N=82*	*p*-value[b]	*N=219*	*p*-value[c]
Early Childhood Function							
Early Motor Trajectories, *n* (%)			**<0.001**		0.259		0.515
Low Degree of Difficulties	222 (98.2)	152 (79.2)		71 (100.0)		72 (75.8)	
High Degree of Difficulties	4 (1.8)	40 (20.8)		0 (0.0)		23 (24.2)	
General Intelligence (IQ) at 56 Months, Mean (SD)	101.92 (12.94)	87.92 (19.82)	**<0.001**	98.10 (14.16)	**0.029**	76.88 (24.57)	**<0.001**
Neurological Impairments at 56 Months, *n* (%)	2 (0.9)	23 (12.0)	**<0.001**	1 (1.2)	0.792	29 (13.2)	0.701
Epilepsy	1 (0.4)	2 (1.0)	0.470	0 (0.0)	0.546	6 (2.7)	0.214
Hydrocephalus	0 (0.0)	2 (1.0)	0.124	0 (0.0)	n/a	5 (2.3)	0.332
Cerebral Palsy (CP)	0 (0.0)	20 (10.4)		0 (0.0)		27 (17.0)	
CP Stage 1	0 (0.0)	10 (5.2)		0 (0.0)		4 (2.5)	
CP Stage 2	0 (0.0)	7 (3.6)	**<0.001**	0 (0.0)	n/a	7 (4.4)	0.072
CP Stage 3	0 (0.0)	3 (1.6)		0 (0.0)		13 (8.2)	
CP Stage 4	0 (0.0)	0 (0.0)		0 (0.0)		3 (1.9)	
Blindness	0 (0.0)	1 (0.5)	0.227	0 (0.0)	n/a	2 (1.3)	0.455

	Participants			Dropouts			
	Term Controls	VP/VLBW		Term Controls		VP/VLBW	
	n = 226	*n* = 192	*p*-value[a]	*N=82*	*p*-value[b]	*N=219*	*p*-value[c]
Deafness	1 (0.4)	0 (0.0)	0.356	1 (0.4)	0.447	0 (0.0)	n/a
Adulthood Outcomes at 26 Years				n/a		n/a	
Motor Competence, *n* (%)			**0.003**	n/a		n/a	
High Motor Competence	204 (90.3)	154 (80.2)					
Low Motor Competence	22 (9.7)	38 (19.8)					
Cognitive Function, Mean (SD)				n/a		n/a.	
General Intelligence (Full-Scale IQ)	102.62 (12.57)	91.21 (17.05)	**<0.001**				

Note. Bold *p*-values were significant at the 0.05 level; Abbreviations: SD=standard deviation, VP/VLBW=very preterm and/or very low birth weight.

[a] Compares term controls and VP/VLBW; [b] Compares participating and dropout term control; [c] Compares participating and dropout VP/VLBW.

VP/VLBW birth and early motor problems

Compared to term-born individuals, VP/VLBW participants were more likely to have motor problems from birth to 56 months (RR: 11.77, 95% CI: 4.28–32.35). This increased risk remained after adjusting for confounds (adjusted RR: 8.32, 95% CI: 2.83–24.44; significant covariates: multiple birth and IQ at 56 months).

After excluding participants with a neurological impairment (VP/VLBW: n = 23; term controls: n = 2), VP/VLBW participants still had a substantially increased risk for early motor problems (RR: 6.96, 95% CI: 2.43–19.92), compared to term-born individuals; even when adjusting for potential confounds (adjusted RR: 4.47, 95% CI: 1.45–13.77; significant covariates: multiple birth and IQ at 56 months).

Effects of VP/VLBW birth and early motor problems on motor and cognitive outcomes in adulthood

SEM results (Model 1) showed that individuals with early motor problems were more likely to exhibit lower motor competence in adulthood (β = 0.22, p < 0.001), while VP/VLBW was not associated with adult motor competence (β = 0.13, p = 0.151), after accounting for IQ at 56 months, SGA, multiple births, child sex, and SES (Table 25 and Figure 6). Further, child sex (male) negatively affected motor competence at 26 years (β = −0.16, p = 0.032). VP/VLBW (β = 0.35, p < 0.001) and multiple births (β = −0.19, p = 0.002) were associated with early motor problems.

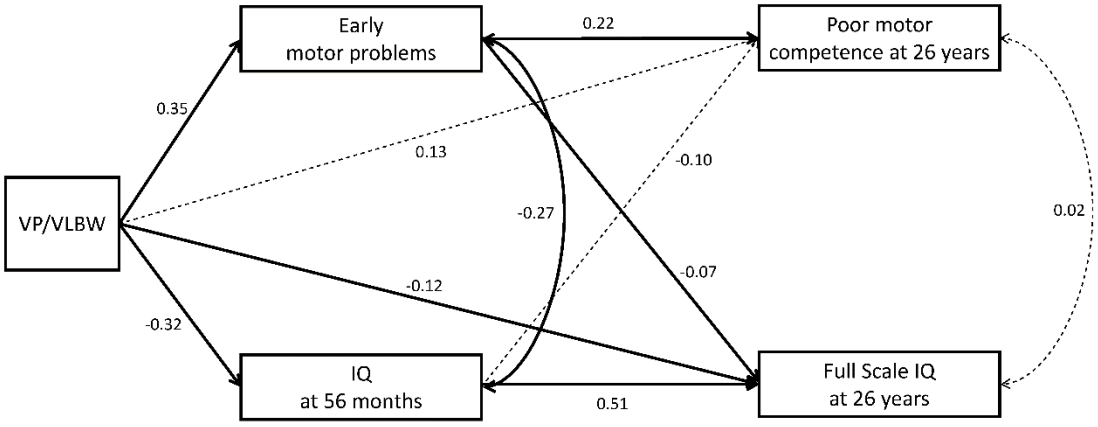

Figure 6. Structural equation model showing direct and indirect effects of VP/VLBW and early motor problem trajectories on motor competence and IQ at 26 years (Model 1).
Bold lines represent hypothesized effects, solid lines represent significant effects, and dashed lines represent non-significant effects (standardized regression coefficients β). Effects of interest are shown. Effects of covariates and error terms are not presented to enhance readability. For effects of confounds see Table 25.

Adult IQ was associated with early cognitive abilities ($\beta = 0.51$, $p < 0.001$) and was negatively affected by VP/VLBW and early motor problems ($\beta = -0.12$, $p = 0.044$ and $\beta = -0.07$, $p = 0.010$, respectively). The effects of VP/VLBW on adult IQ were partly mediated by early motor problems ($\beta = -0.03$, $p = 0.023$). Moreover, SES was associated with both child and adult IQ, but not with any of the other covariates (Table 25).

Table 25. *Regression coefficients using structural equation modelling (Model 1).*

	Unstandardized			Standardized		
	B	Standard Error	95% CI	*β*	*p*-value	R^2
Direct Effects						
Motor Competence at 26 years						0.14
Motor problems from Birth to 56 months	0.77	0.22	(0.41, 1.13)	0.22	**<0.001**	
IQ at 56 Months	−0.11	0.07	(−0.23, 0.01)	−0.10	0.137	
VP/VLBW	0.28	0.20	(−0.05, 0.60)	0.13	0.151	
SGA	0.03	0.20	(−0.29, 0.35)	0.01	0.884	
Multiple Births	0.13	0.24	(−0.26, 0.53)	0.04	0.582	
Sex (Male)	−0.35	0.17	(−0.62, −0.07)	−0.16	**0.032**	
SES Low	−0.05	0.20	(−0.37, 0.27)	−0.02	0.794	
SES High	0.28	0.20	(−0.05, 0.60)	0.12	0.162	
Motor problems from Birth to 56 months						0.13
VP/VLBW	0.22	0.05	(0.14, 0.30)	0.35	**<0.001**	
SGA	0.03	0.03	(−0.02, 0.08)	0.05	0.291	
Multiple Births	−0.17	0.06	(−0.26, −0.08)	−0.19	**0.002**	
Sex (Male)	0.00	0.03	(−0.05, 0.05)	0.00	0.979	
SES Low	0.01	0.03	(−0.04, 0.07)	0.02	0.724	
SES High	−0.03	0.04	(−0.10, 0.04)	−0.04	0.482	
Full-Scale IQ at 26 years						0.47
Motor problems from Birth to 56 months	−0.24	0.09	(−0.39, −0.08)	−0.07	**0.010**	
IQ at 56 months	0.51	0.04	(0.44, 0.58)	0.51	**<0.001**	
VP/VLBW	−0.25	0.12	(−0.45, −0.04)	−0.12	**0.044**	
SGA	−0.09	0.12	(−0.28, 0.10)	−0.04	0.424	

	Unstandardized			Standardized		
	B	Standard Error	95% CI	β	p-value	R^2
Multiple Births	0.11	0.13	(−0.10, 0.32)	0.04	0.384	
Sex (Male)	0.15	0.08	(0.01, 0.28)	0.07	0.075	
SES Low	−0.12	0.10	(−0.28, 0.04)	−0.05	0.220	
SES High	0.35	0.11	(0.17, 0.53)	0.16	**0.001**	
IQ at 56 months						0.25
VP/VLBW	−0.64	0.11	(−0.81, −0.46)	−0.32	**<0.001**	
SGA	−0.20	0.11	(−0.38, −0.03)	−0.09	0.059	
Multiple Births	−0.02	0.13	(−0.22, 0.19)	−0.00	0.922	
Sex (Male)	−0.01	0.09	(−0.16, 0.13)	−0.01	0.883	
SES Low	−0.45	0.11	(−0.63, −0.27)	−0.20	**<0.001**	
SES High	0.34	0.11	(0.17, 0.52)	0.16	**0.001**	
Indirect Effects						
Full-Scale IQ at 26 years via Motor problems from Birth to 56 months	−0.05	0.02	(−0.09, −0.01)	−0.03	**0.023**	
From VP/VLBW						

Note. Bold *p*-values were significant at the 0.05 level; Abbreviations: SGA=small for gestational age, SES=socioeconomic status.

Measures of motor and cognitive function were associated in childhood (r = −0.27, $p < 0.001$) but not in adulthood (r = 0.02, p = 0.810). All predictors explained 13% of the variance in early motor problems and 14% in adult motor competence, 25% in child IQ, and 47% in adult IQ. Model fits suggest a fully saturated model and indicate a good statistical model fit once non-significant paths were removed (χ^2 (2) = 4.795, p = 0.091; CFI = 0.989; RMSEA = 0.058).

After excluding participants with neurological impairments (Model 2), the results of SEM model 2 (Table 26 and Figure 7) showed that early motor problems (β = 0.13, p = 0.029) were still associated with lower motor competence in adulthood but VP/VLBW was not (β = 0.10, p = 0.311), after controlling for IQ at 56 months, SGA, multiple births, child sex, and SES. VP/VLBW (β = 0.24, p = 0.001) and multiple births were associated with early motor problems (β = −0.16, p = 0.050).

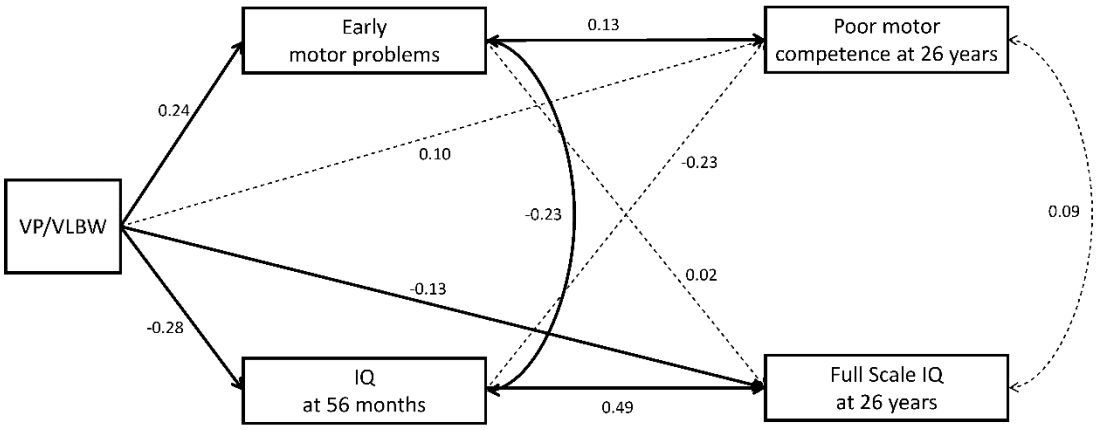

Figure 7. Structural equation model showing direct and indirect effects of VP/VLBW and early motor problems trajectories on motor competence and IQ at 26 years (excluding participants with neurological impairment, Model 2).
Bold lines represent hypothesized effects, solid lines represent significant effects, and dashed lines represent non-significant effects (standardized regression coefficients β). Effects of interest are shown. Effects of covariates and error terms are not presented to enhance readability. For effects of confounds see Table 26.

Adult IQ was predicted by child IQ (β = 0.49, p < 0.001) and VP/VLBW (β = −0.13, p = 0.044), but was not affected by early motor problems (β = 0.02, p = 0.520). Moreover, the effects of VP/VLBW on adult IQ was not mediated by early motor problems (β = 0.00, p = 0.527). Family SES affected both child and adult IQ (Table 26).

Associations between motor and cognitive function were found in childhood ($r = -0.23$, $p < 0.001$) but not in adulthood ($r = 0.09$, $p = 0.810$). All predictors explained 9% of the variance in early motor problems and 8% in adult motor competence. Moreover, 24% and 42% of the variance in childhood and adult IQ were explained, respectively. After removing non-significant paths, the fit values of the fully saturated model indicated a good statistical model fit (χ^2 (3) = 3.493, p = 0.322; CFI = 0.997; RMSEA = 0.020).

Table 26. *Regression coefficients using structural equation modelling (excluding participants with neurological impairment, Model 2).*

	Unstandardized			Standardized		
	B	Standard Error	95% CI	B	*p*-value	R^2
Direct Effects						
Motor Competence at 26 years	0.57	0.26	(0.13, 1.00)	0.13	0.029	0.08
Motor problems from Birth to 56 months	−0.09	0.08	(−0.21, 0.04)	−0.08	0.253	
IQ at 56 Months	0.21	0.21	(−0.13, 0.55)	0.10	0.311	
VP/VLBW	−0.07	0.22	(−0.43, 0.28)	−0.03	0.732	
SGA	0.12	0.27	(−0.32, 0.56)	0.04	0.653	
Multiple Births	−0.26	0.18	(−0.56, 0.04)	−0.13	0.142	
Sex (Male)	0.12	0.21	(−0.23, 0.47)	0.05	0.566	
SES Low	0.38	0.22	(0.02, 0.73)	0.16	0.076	
SES High						
Motor problems from Birth to 56 months	0.12	0.04	(0.06, 0.18)	0.24	0.001	
VP/VLBW	0.05	0.03	(−0.00, 0.09)	0.08	0.103	0.09
SGA	−0.12	0.06	(−0.21, −0.02)	−0.16	0.050	
Multiple Births	0.01	0.03	(−0.03, 0.06)	0.02	0.675	
Sex (Male)	0.04	0.03	(−0.01, 0.08)	0.07	0.151	
	−0.01	0.04	(−0.07, 0.05)	−0.01	0.850	

	Unstandardized			Standardized		
	B	Standard Error	95% CI	B	*p*-value	R^2
SES Low						
SES High						
Full-Scale IQ at 26 years						0.42
Motor problems from Birth to 56 months	0.07	0.11	(−0.10, 0.24)	0.02	0.520	
IQ at 56 months	0.49	0.05	(0.41, 0.56)	0.49	<0.001	
VP/VLBW	−0.26	0.13	(−0.47, −0.05)	−0.13	0.044	
SGA	−0.10	0.13	(−0.32, 0.11)	−0.04	0.433	
Multiple Births	0.14	0.15	(−0.10, 0.38)	0.05	0.345	
Sex (Male)	0.12	0.09	(−0.03, 0.27)	0.06	0.171	
SES Low	−0.21	0.11	(−0.39, −0.02)	−0.09	0.069	
SES High	0.32	0.11	(0.14, 0.51)	0.15	0.003	
IQ at 56 months						0.24
VP/VLBW	−0.57	0.11	(−0.75, −0.38)	−0.28	<0.001	
SGA	−0.16	0.11	(−0.35, 0.02)	−0.07	0.149	
Multiple Births	−0.12	0.13	(−0.33, 0.10)	−0.04	0.362	
Sex (Male)	−0.04	0.09	(−0.20, 0.11)	−0.02	0.664	
SES Low	−0.50	0.11	(−0.68, −0.31)	−0.22	<0.001	
SES High	0.33	0.11	(0.15, 0.52)	0.15	0.002	
Indirect Effects						
Full-Scale IQ at 26 years via Motor problems from Birth to 56 months	0.01	0.01	(−0.01, 0.03)	0.00	0.527	
From VP/VLBW						

Note. Bold *p*-values were significant at the 0.05 level.

Discussion

This prospective longitudinal study found that motor problems in early childhood were associated with later motor competence. Furthermore, early motor problems had a weak association with IQ in adulthood that was independent of the effects of VP/VLBW birth, and present after controlling for small for GA, multiple births, sex (male), family SES at birth, and preschool cognitive abilities (i.e., IQ at 56 months). However, once individuals with a neurological impairment at 56 months (which mostly included mild, stage 1 and 2 CP) were excluded, only the longitudinal associations between early motor problems and motor competence remained, but those with cognitive outcomes in adulthood were no longer significant.

The current findings show that children born VP/VLBW have a higher risk of motor problems during the preschool years, compared to term-born individuals. Once individuals with a neurological impairment were excluded, the risk was substantially reduced but VP/VLBW participants were still four times more likely to experience early motor problems. Similar prevalence rates for motor impairments in preterm children without CP have been reported previously (Spittle & Orton, 2014; Williams et al., 2010).

Both VP/VLBW and term-born individuals with motor problems in infancy and toddlerhood (including those without neurological impairment) still had lower motor competence in adulthood (Cousins & Smyth, 2003; Husby et al., 2013; Poole et al., 2015b). Some previous studies have found that early motor development or aspects of early motor function are predictive of later motor skills in preterm (Burns et al., 2004; Su et al., 2017), but not in healthy term-born children (Ghassabian et al., 2016; Hitzert et al., 2014; Piek et al., 2008). In contrast, other studies reported

persistent motor problems from middle childhood to adulthood, in both preterm (Husby et al., 2013; Poole et al., 2015b) and term populations (Cousins & Smyth, 2003; Losse et al., 1991). In this study, persistent lower motor function was determined across four time points (from birth to 56 months), resulting in consistent long-term associations between early motor function and adult motor competence in both preterm- and term-born individuals. Rather than identifying individuals with persistent early motor problems, previous studies often took a snapshot, i.e., one single measure of motor functioning at a single time point.

In accordance with previous work, VP/VLBW birth and childhood IQ were associated with IQ in adulthood (Breeman, Jaekel, Baumann, Bartmann, & Wolke, 2015; Linsell et al., 2017). In addition to VP/VLBW birth and child IQ, early motor problems showed significant association with adult IQ. This may not be surprising as IQ, particularly performance IQ, is reliant on aspects of motor function or motor skills (Gillberg & Kadesjo, 2003), and associations between motor functioning and cognitive outcomes have been demonstrated in previous studies of preterm children (Foulder-Hughes & Cooke, 2003; Geldof et al., 2016). Importantly, the longitudinal associations between early motor problems and adult IQ in the current study were independent of childhood IQ and therefore cannot be solely attributed to an early link between motor and cognitive function (Figure 6). In adulthood, motor competence and IQ were not correlated, indicating that they measure two independent constructs. This may be explained by previously proposed concepts or theories of differentiation and integration, which posit that basic skills are integrated into new and higher-level functions. This can be manifested by a developmental path

from motor to sensorimotor to cognitive function (Aylward, 2009; Keenan et al., 2016). In adulthood, IQ assesses higher abstract logical reasoning and cognitive functioning that is not dependent on sensorimotor skills (as in early childhood). Considering the link between early motor problems and adult IQ found here (Figure 6), this may speak against this concept, and instead suggests global long-term associations between both domains, i.e., motor problems in early childhood predicting both motor competence and IQ in adulthood. However, once individuals who were diagnosed with a neurological impairment were excluded from analysis (Figure 7), early motor problems no longer predicted adult IQ. The most frequent neurological impairment was mild CP, which is often caused by bleeding in the brain such as periventricular leukomalacia that may affect wider areas of white matter rather than just the motor neurons and alteration of brain development (Williams, Hyde, & Spittle, 2014). Thus, both motor and cognitive abilities may share the same underlying cause. In contrast, in those without major neurological impairment, motor and cognitive function are related to different brain areas during development, i.e., differentiation, so that IQ in adulthood was not affected by early motor problems. As a result, the predictive models for both the motor and the cognitive domain were homotypic. Thus, early motor problems identified in the current study may serve as a predictor of later problems in motor competence in all children. In children who had been diagnosed with a neurological impairment, the prediction from early motor problems may be extended to short- and long-term problems in other developmental domains, such as academic achievement, mental health, and social functioning

(Bornstein et al., 2013; Butcher et al., 2009; Murray et al., 2007; Taanila et al., 2005).

Overall, the findings of the current study suggest that motor competence in adulthood is independently, directly, and thus homotypically, predicted by early motor problems, while adult cognitive function is associated with early cognitive function and VP/VLBW birth. Motor and cognitive deficits have been identified as the most frequent adverse sequelae with the highest effect sizes differentiating VP/VLBW from term-born children and adults (Wolke et al., 2019). Therefore, it is important to test both motor and cognitive function as early as possible to identify children at risk for motor and cognitive sequelae.

The current study has several strengths. It is a prospective long-term follow-up study of a large whole population sample of VP/VLBW and term-born individuals recruited in the same hospitals using data based on age-appropriate physical and neurological examinations to assess early motor functioning, and reliable and valid tests to assess IQ in adulthood. There were some limitations to the current study. Although 47% of the eligible VP/VLBW and term-born individuals had complete data from birth to 26 years, the dropout was not random, as low SES families were less likely to continue participation (Eryigit Madzwamuse et al., 2015). As social factors are a major reason for dropout in most longitudinal studies, we controlled for family SES at birth in our analyses. However, to ascertain the validity of the results, it would be important to replicate the findings in a larger sample. Furthermore, whether the results of this study generalize beyond our at-risk sample requires testing.

Conclusions

Our results demonstrate that preterm-born individuals have a high risk of early motor problems. Early motor problems and cognitive problems uniquely predict later motor competence and IQ in adulthood, respectively. In children with neurological impairment, both motor and cognitive function are likely to be affected not only in childhood but also into adulthood. The results further demonstrate that while motor and cognitive functions are related in childhood, they differentiate into adulthood and are no longer related. The findings highlight the importance of testing motor and cognitive function in all children early on and to follow up the children that are identified to be at risk for adverse motor and cognitive outcomes.

Chapter 6: General Discussion

The general aim of this thesis was to track early motor functioning and to highlight the importance of early motor development and how it is associated with children's medium and long-term development and functioning across different psychological domains. Specific objectives were:

1) To investigate predictors and risk factors of poor motor development during the first 5 years of life,
2) To evaluate associations between motor problems in infancy and developmental outcomes into school-age and how physiotherapy may alter this relationship, and
3) To answer the question of whether early motor development is associated with motor competence and general cognitive function in adulthood.

The purpose of this chapter and general discussion is to give a summary of the results from all three empirical studies that were carried out as part of this thesis. The main findings, potential implications and the importance to the research field of motor development will be discussed, including limitations for each study that were not or only briefly discussed in the previous chapters. Further, suggestions for future research will be made that have arisen from the findings and limitations of the three empirical studies.

Summary of Results

Study 1 (Chapter 3)

Study 1 had three aims: First, to track motor functioning across an early age range (birth to 56 months) and to identify motor trajectories. Second, to conduct a comprehensive investigation of precursors and risk factors of early motor problems in a large population-based sample of at-risk and healthy control children. Third, to test whether the findings can be replicated in a second similar cohort in another country. In addition to known biological, medical and child health factors, several social-environmental factors, including family adversity and including early parent-infant relationships, were considered.

Study 1 identified two distinct trajectories of motor functioning from birth to 56 months of age in both cohorts: 1) low degree of motor problems and 2) high degree of motor problems. While most children (~ 95%) exhibited a low degree of motor problems, the smaller proportion were found to have a high degree of motor problems. This matches findings from previous research reporting a prevalence rate of 5 to 6% for non-CP motor impairment in the general population (Blank et al., 2019; Spittle & Orton, 2014). Further, a high degree of early motor problems across early childhood was not only predicted by biological or child health factors (i.e., neonatal complications, abnormal neonatal neurological status, and duration of hospitalisation), but also, and with an equal magnitude, by early social-environmental factors (i.e., parent-infant relationship).

The identified biological and child health or medical factors (i.e., neonatal complications, abnormal neonatal neurological status, and duration of

hospitalisation) could be used by clinicians and health care professionals to monitor children's early motor development. And as a possible implication, children with motor problems may benefit from early intervention programmes that include parents and focus on parent-infant relationships. In sum, these findings are important for identification and prognosis of motor problems, and for the design and implementation of early intervention programmes that aim to prevent or ameliorate motor problems, or improve early motor development and thereby positively affect or prevent other developmental and functional problems and secondary issues that are associated with poor motor development.

While in both cohorts two groups of children with distinctly different trajectories of early motor functioning emerged, it is noteworthy that these trajectories followed a similar pattern across time, in particular for the group that experienced a high degree of motor problems. That is, motor problems in that group clearly increased from birth up to 20 months but then decreased by the age of 56 months. But how can this be explained? Does the age of 20 months signify an important developmental period or phase? One explanation may be that developmental tests at younger ages have a wider range of error which can result in tests not reliably picking up developmental functions or skills (Aylward, 2009). Another explanation could be that while some basic motor function may be 'normal' initially, children may not (fully) integrate these functions into more advanced or complex skills at a subsequent age (Aylward, 2009; Piek et al., 2008). In other words, at the time children enter toddlerhood motor skills and tasks become more complex and diverse so that difficulties may become more apparent. The period

between infancy and toddlerhood may therefore be particularly important for targeted and age-appropriate intervention, treatment and support services.

As laid out in the introduction of this thesis, previous studies have shown that biological factors, such as gestational age and birth weight, may be more important than environmental factors for motor development (Laucht et al., 1997), but that children with a high biological risk (i.e., children born preterm or with low birth weight) may benefit from a high stimulating or positive psychosocial environment as it may help improve motor and cognitive outcomes in these children (Levy-Shiff et al., 1994; Weisglas-Kuperus, Baerts, Smrkovsky, & Sauer, 1993). The results from study 1, show that this may also be true for all children.

In study 1 we comprehensively investigated biological, child health and social-environmental risk factors for early motor impairment. However, it may also be important to consider other biological factors, i.e., brain features and neural pathways that could explain underlying mechanisms leading to motor impairment. Over the past decade, there has been considerable progress in neuroimaging studies with findings showing that multiple brain areas, including white and grey matter abnormalities, are associated with motor impairments in early childhood (Spittle, Boyd, Inder, & Doyle, 2009; Woodward, Anderson, Austin, Howard, & Inder, 2006). However, allowing for the motor plasticity during the first year of life, there is mounting evidence that these deficits can be overcome by an appropriate and supportive environment (Anderson et al., 2020; Herskind et al., 2015; Johnston, 2009; Kolb et al., 2017; Lobo & Galloway, 2012; Milgrom et al., 2010; Ustad et al., 2016).

Study 2 (Chapter 4)

The primary aim of Study 2 was to investigate whether motor problems assessed in infancy (i.e., at birth and at 5 months), are associated with various developmental outcomes at school-age. Because children who are at risk of developmental difficulties (e.g., children born preterm) often receive treatment or intervention, a secondary aim was to investigate whether associations between early motor problems and later developmental outcomes were altered by early treatment with physiotherapy.

The findings showed that motor problems in infancy can negatively affect subsequent developmental outcomes across a wide range of domains and functions, including motor skill, cognitive function, and attention regulation, but not mental health. However, after accounting for imbalances in covariates and baseline characteristics, such as initial infant motor scores and neurological impairments, it was demonstrated that treatment with physiotherapy did not alter associations between early motor problems and subsequent outcomes. The main finding was that motor problems measured as early as at birth and 5 months can have long-lasting effects on a range of developmental outcomes in both at-risk and term born children. Secondly, it was found that treatment with physiotherapy had no beneficial effect in relation to the outcomes assessed. These results have important implications for the prognosis of developmental outcomes for infants with motor problems. Early assessment or screening for motor problems may be used to identify children who are at risk for subsequent developmental problems. The findings may also be important for planning and design of early intervention or treatment. Further, the

finding from Study 2 together with findings from study 1 demonstrating that poor parent-infant relationships are an important but modifiable risk factor for early motor problems, early intervention or treatment should take results from early assessments into account to allow for targeted and age-appropriate interventions that involve parents and focus on parenting training and parent-infant relationships.

The conclusions that can be drawn concerning the effectiveness of treatment with physiotherapy are rather limited due to the design of Study 2. Nevertheless, it is important to consider interventions or treatment in an observational study as many children, particularly children at risk for developmental delay or difficulties, are often referred to it. Almost a third of all children in Study 2 received physiotherapy. However, a large proportion of those children had no motor problems, according to applied criteria to determine them (~ 70%). This raises the question of why physiotherapy was prescribed in spite of that. Unfortunately, this cannot be answered without speculation. On the other hand, if the majority of children failed to meet the criteria for motor problems it may not be surprising that treatment with physiotherapy was not found to have a beneficial effect.

Alongside the identification and application of age-appropriate activities (Hughes et al., 2016), other aspects that may be important and should be considered in regards to physiotherapy are timing, duration and frequency of treatment (Blauw-Hospers & Hadders-Algra, 2005; Orton et al., 2009; Spittle et al., 2015). The timing of treatment is dependent on when developmental problems become apparent or are being diagnosed (Blauw-Hospers & Hadders-Algra, 2005) which in cases of non-CP related motor impairments, for example, do not happen before preschool or school-

age. Further, while the effectiveness of treatment or intervention may be reliant and likely influenced by compliance of the child and the child's family, as well as on the dose, i.e., the frequency and amount of treatment given to the child (Orton et al., 2009; Spittle et al., 2015) there is some evidence that differently organised treatment (i.e., intermittent versus continuous physiotherapy) does not affect outcomes (Christiansen & Lange, 2008). Although information on the duration of physiotherapy was available for Study 2, the quality of these data was limited due to a considerable amount of missing data. However, analysis that included cases with information on duration of physiotherapy did not change the results.

Study 3 (Chapter 5)

The aims of Study 3 were to ascertain whether VP/VLBW children have an increased risk for early motor problems, and whether early motor problems are associated with long-term motor outcomes into adulthood. Further, given that motor and cognitive function are closely related on a sensorimotor basis (at least in childhood), it was investigated whether early motor problems negatively affect cognitive functioning in adulthood.

Study 3 supported previous research by showing that children born VP/VLBW had a four times higher risk for early motor problems, compared to their term born counterparts. Longitudinal studies that investigate motor development into adulthood are still rare, in particular studies that span preschool-age to adulthood. Further, there are only very few studies that examine associations between early motor development and adult cognitive function and how associations between

motor and cognitive function change over time. The results of Study 3 not only underpin prior research that children with poor early motor development do not outgrow their difficulties; but more importantly, findings demonstrate that while early motor development is homotypically associated with adult motor competence, cognitive function seems to be more differentiated and specific in adulthood and may thus rely more on higher-order cognitive functioning and less on sensorimotor elements. This means that early motor problems, despite a close relationship with concurrent cognitive function, do not necessarily result in lower cognitive function in adulthood, at least not in individuals who did not have any neurological impairments that can include severe motor problems, such as CP, in childhood. In contrast, there is no evidence that children with lower IQ or learning disabilities, experience poorer motor competence in adulthood; at least not according to the motor measure used in Study 3. However, it may be possible that these individuals would show much poorer motor competence in activities that require greater motor functioning and skill, for example, playing sports or a musical instrument, rock climbing or dancing. Unfortunately, a standardized motor test that assesses the quality of motor functioning in adulthood was not available for this study. The motor measure was instead based on a composite score that assesses motor competence in daily life (see Chapter 2, page 95). It may therefore be important to investigate longitudinal associations between motor and cognitive function further in a future study with a standardized motor measure in adulthood that is at par with the cognitive/IQ measure, in particular because children with lower IQ or learning abilities may rely on motor skills more than others as they are more likely to take up vocations that

require motor skills (Smits-Engelsman & Hill, 2012). Overall, because there seem to be different pathways, it is important to monitor and follow up children's motor and cognitive performance.

Longitudinal studies in term and preterm children have demonstrated a link between early motor skills and later cognitive function (for a review, see Oudgenoeg-Paz et al., 2017). There is evidence that motor functions are associated with the performance part of IQ and with specific higher-order cognitive functions, that is, executive function, in children and adolescents (Cook et al., 2019; Foulder-Hughes & Cooke, 2003; Piek et al., 2004; Rigoli et al., 2012; Tseng, Henderson, Chow, & Yao, 2004). This seems plausible as executive functions and skills, such as sustained attention, working memory and impulse control are needed for daily fine and gross motor tasks, particularly if the motor task is complex (van der Fels et al., 2015).

Preliminary analyses that were carried out for Study 3 not only examined full-scale IQ as an outcome but also included both subscales, i.e., verbal and performance IQ, and a battery of executive functioning measures that assessed visual scanning and sustained attention, selective attention, verbal inhibition, cognitive flexibility, divergent thinking and verbal processing speed. As expected, early motor problems were associated with performance IQ and a task that measured visual scanning and sustained attention (even when taking into account early childhood IQ and other covariates such as VP/VLBW birth, SGA, multiple birth, male sex and family SES), but there was no association with verbal IQ or other executive function tasks. However, once participants with neurological impairments were removed the

associations diminished and were no longer significant. These results thus perfectly reflected homotypic motor and cognitive pathways ascertained in Study 3 and presented in Chapter 5.

Given the temporal associations between early motor and adult cognitive function in Study 3, it may be tempting to assume a causal inference between motor and cognitive function. Strong evidence for causal inference can only be established with a RCT or with a specifically designed experiment to test for causality. However, it is possible to assume causality from observational cohort data, albeit with limitations, in a well-designed study that allows for confounding factors. Replications and studies that combine data from multiple cohorts in a meta-analytical design can support the assumption of causal inference (VanderWeele, 2021). To ascertain the association between early motor development and adult cognitive function, Study 3 should therefore be replicated with data from another longitudinal cohort or through combining observational data from multiple longitudinal cohorts in a meta-analytic design. Importantly, these replication studies should control for potential confounding factors and should take into account cognitive function at baseline to rule out reverse association (Oudgenoeg-Paz et al., 2017; VanderWeele, 2021).

Directions for Future Research

Motivated by the findings of the three empirical studies conducted as part of this thesis, this section will propose future studies that address gaps and questions that have not or not sufficiently been addressed or answered yet.

Predictors of Early Motor Impairment: A Replication of Study 1

The primary strength of Study 1 has been its 'in-built' replication of findings in another cohort in another country, which substantiated the overall results. However, as discussed in Chapter 3, it would nonetheless be important to replicate the study in a more recent, contemporary cohort to facilitate comparability across datasets and eras and to ascertain whether changes in medical and neonatal care since the mid-80s (including assisted ventilation, administration of antenatal and postnatal glucocorticoids and postnatal surfactant therapy (Philip, 2012)) that have led to more children born premature survive (Wilson-Costello, Friedman, Minich, Fanaroff, & Hack, 2005), result in different findings. However, findings from a recent study showing that despite reduced incidence rates of CP in extremely preterm children from 1991 to 2005, non-CP motor impairments have increased, may speak against such a hypothesis (Cheong, Spittle, Burnett, Anderson, & Doyle, 2020; Spittle et al., 2018). That is, the increase in numbers of children surviving seems not to have led to an equally reduced rated of motor impairments and other developmental sequelae. It may therefore be possible that the identified prognostic or risk factors of early motor problems in Study 1 would remain unchanged or similarly important in a contemporary cohort. Although an exact replication of Study 1 may not be possible in a contemporary cohort, a partial replication in one, or across multiple contemporary cohorts using a meta-analytical approach, could help ascertaining the findings of Study 1. This replication study could focus on identifying motor trajectories across childhood and/or peri- and neonatal predictors

(including social-environmental data, such as parental socioeconomic status and parental mental health) of early motor impairment.

Further, although preterm birth-related mortality rates have been decreasing in middle- and low-income countries, disparities with high income countries still exist (Benfer et al., 2018), particularly regarding the availability and utilisation of medical and neonatal care (Blencowe et al., 2012; Rahman et al., 2019), as well as childrearing practices which are recognised as highly influential in early motor development (Adolph & Hoch, 2018). Importantly, middle- and low-income countries account for the majority (approximately 60%) of preterm births worldwide (Blencowe et al., 2012). Therefore, in order to extent and test the generalisability of findings in Study 1 beyond high income countries, it would be important to investigate prognostic and risk factors of child motor impairment in a middle- or low-income country.

Early Motor Problems and Consequences for Educational Achievement, Wealth and Social Functioning

Both Study 2 and Study 3 have addressed longitudinal links of early motor problems with other developmental domains, including cognitive function, attention regulation and mental health. These findings may indicate that early motor problems measured in infancy and toddlerhood can be helpful to flag potential problems and to identify children who are at risk for developing long-term difficulties – not only in the cognitive domain, but also in other, related, domains and functions, for example

academic achievement (Bornstein et al., 2013). This should therefore be investigated in future studies.

As outlined in the introduction of this thesis, motor impairments can affect and have long-lasting consequences for other developmental and functional outcomes, such as academic or educational achievement, social functioning (i.e., social relationships and support, social activities and participation), and health-related quality of life that can persist into adulthood (Husby et al., 2016; Karras et al., 2019; Lingam et al., 2010; Poole et al., 2017). Even though these functions may seem further afield from the motor domain than cognition they are similarly built on and steeped in motor behaviour and skills. It is therefore important to carefully differentiate and describe functions and skills across developmental domains.

Compared to term born individuals, preterm born children have consistently been reported to have a greater risk for motor impairments (Marlow et al., 2007; Spittle & Orton, 2014; Williams et al., 2010) that seems to persist into adolescence and adulthood (de Kieviet et al., 2009; Husby et al., 2013). This not only suggests the existence of a *preterm motor phenotype,* that is may further be characterised by different patterns of motor functions (Bracewell & Marlow, 2002) as well as by different developmental comorbidities and pathways, compared to their term born counterparts (Bolk et al., 2018). This should be taken into account in future investigations of associations between motor and other psychological functions.

The following two sections briefly describe ideas for future longitudinal investigations into associations between early motor problems and subsequent

outcomes. In order to strengthen the design and increase statistical power of such an investigation, data from multiple cohorts could be included. For example, data from cohort studies that are part of the RECAP preterm consortium of European studies (https://recap-preterm.eu/) and the APIC consortium that also includes non-European studies (https://www.apic-preterm.org). A number of cohort studies of these consortia have collected data on motor skills or motor impairment in childhood (6 to 8 years of age) as well as data on education, wealth and social functioning in adulthood, including the BLS (Germany), EPICure (UK), NTNU (Norway), and VICS (Australia). Combining and harmonisation data from these studies allows for an investigation of both cohort and participant level factors with individual participant data (IPD) meta-analysis using a linear mixed model approach.

Early Motor Problems and Educational Achievement

There is evidence that motor problems in childhood, and even as early as infancy, can have detrimental and long-lasting effects on academic and educational success, as well as on employment and income (Bornstein et al., 2013; Dewey et al., 2002; Lingam et al., 2010; Mathiasen, Hansen, Anderson, & Greisen, 2009; Michelsen et al., 2005; Poole et al., 2017). However, it is important to note that some studies had a cross-sectional design, and that classification, severity and measures of motor impairment as well as measures of educational attainment varied widely across studies. Measures of educational attainment, for example, including tests of academic achievement (e.g., letter-word identification, comprehension and calculation), years of education, and reading, writing and spelling skills. Given that some of these measures, in particular reading and writing are in essence motor skills,

it is difficult to differentiate between motor and academic skills. In sum, the interpretation of previous findings is rather limited and there still remain significant gaps in the knowledge and understanding of long-term associations between early motor problems and educational and occupational achievement. Thus, it would be important to conduct such a longitudinal investigation and to additionally test whether early motor problems translate into adverse socioeconomic status or lower wealth in adulthood, which is likely associated with lower educational achievement. Further, given that it has been shown that preterm birth is associated with educational and socioeconomic difficulties (Bilgin, Mendonca, & Wolke, 2018), it would be important to examine whether preterm birth compounds these problems.

Early Motor Problems and Social Functioning

Cross-sectional studies have demonstrated associations between motor problems and social functions, skills and participation in school-aged children and adolescents (Cantell, Smyth, & Ahonen, 1994; Chen & Cohn, 2003; Dewey et al., 2002; Goulardins et al., 2018; Izadi-Najafabadi et al., 2019; Lingam et al., 2010). Further, it has been reported (though not consistently) that children and adolescents with motor problems perceive themselves less socially accepted and supported, and less often engage in social physical play, and are about two times more likely to experience bullying victimisation or being ostracised (Bejerot & Humble, 2013; Bejerot, Plenty, Humble, & Humble, 2013; Piek, Barrett, Allen, Jones, & Louise, 2005; Piek, Dworcan, Barrett, & Coleman, 2000; Torn et al., 2015). These difficulties are associated or may lead to lower perceived self-worth and self-esteem, loneliness, and depressive symptoms (Campbell et al., 2012; Skinner & Piek, 2001).

Given that this topic has been researched primarily in cross-sectional studies, which do not allow for conclusions in regards to causality, it would be important to investigate peer relationships and its consequences for children with early motor problems using a longitudinal design incorporating a multidimensional approach that includes positive and negative aspects of peer relationships, for example, information on participation in activities with peers, making and keeping friends, number of friends and bullying victimisation. This would not only extend previous research in terms of methodological design, but would also help understand and describe longitudinal associations and outcomes of early motor impairment. This knowledge would be an important asset for the planning and design of interventions and treatment programmes.

The Pattern of Comorbidities

In Study 2 and 3 we have primarily focussed on investigating longitudinal and not comorbid associations between motor and other developmental domains and functions. As described in the introduction chapter of this thesis, comorbidities often occur with motor impairment which have a similar or even greater impact on children's functioning. This is not surprising as motor functioning and motor behaviour permeates other developmental domains and functions throughout development and the life-span and indeed represent the (only) means to navigate every day activities and life. Although associations between motor impairment and different developmental and functional domains and skills have been reported in numerous studies, only a few studies have attempted to investigate multiple comorbidities of motor impairment (Bolk et al., 2018; Dewey et al., 2002; Husby et

al., 2016; King-Dowling et al., 2015; Lingam et al., 2010; Poole et al., 2017). However, what these studies could not, or failed to describe, is the pattern or profiling of comorbidities (Tallet & Wilson, 2020). This information would be particularly important for health care professionals and families to understand the different implications of motor impairment and for the planning of intervention and treatment. Therefore, in order to investigate and describe the pattern of comorbidities in young children with motor problems the following questions should be addressed in a future study:

1) What is the number of developmental domains and skills that are affected besides motor problems?
2) Are comorbidities additive, i.e. do children with co-morbid problems have worse outcomes than those who have 'pure' motor problems?
3) Does the pattern of comorbidities change over time across time (e.g., from childhood to adolescence and/or from adolescence to adulthood) in terms of both the number and effect size?

Biological and Environmental Factors That May Influence the Pathway from Early Motor Problems to Long-Term Outcomes

The results of Study 1 demonstrated that early parent-infant relationships can significantly influence the course of early motor development. And although Study 2 showed that treatment with physiotherapy had no effect on the association between motor problems in infancy and school-aged motor, cognitive and attentional function, there is evidence that interventions can positively influence motor

development, particularly if they are activity-based and involve parents as facilitators (Hughes et al., 2016). Further, in Study 3, it was demonstrated that in contrast to IQ, preterm birth directly affected early motor problems but not motor competence in young adulthood.

Thus, in all three studies environmental (i.e., parent-infant relationships and treatment with physiotherapy) or biological (i.e. preterm birth) factors were present or occurred in infancy and differently affected the developmental pathway of motor functioning or subsequent outcomes of other developmental domains. This is in accordance with previous work suggesting that there are several biological (e.g., prematurity and growth), functional (e.g., regulatory problems, such as crying, sleeping or feeding problems) and environmental factors (e.g., familial socioeconomic status, parenting, nutrition, and intervention or treatment) that can affect child development, including motor development (Jaekel & Scott, 2018; Pridham, Brown, Clark, Sondel, & Green, 2002; Raghuram et al., 2017).

As to the role of environmental and biological factors in the three empirical studies: In Study 1, poor early parent-infant relationship was a predictor (or stressor) of early motor trajectories. In contrast, in Study 2, motor problems in infancy were regarded as an initial ‘stressor’ for subsequent developmental outcomes, while treatment with physiotherapy was investigated as a factor that potentially could alleviate the negative effects of early motor problems on subsequent school-aged outcomes. And in Study 3, prematurity was regarded and examined as a primary ‘stressor’ of long-term motor and cognitive development. This raises the question of whether these or other biological or environmental factors can change the course of

motor development or influence negative effects of early motor problems on developmental or functional outcomes across different periods or stages of life. Or in other words: What is the pathway of long-term outcomes of children with early motor problems? And what possible developmental and environmental factors may positively or negatively influence this pathway?

Several studies have sought to answer these (or related) questions by investigating the effect of biological and/or environmental factors on developmental outcomes. For example, it has been found that sensitive and stimulating parenting can positively influence cognitive, academic and behavioural outcomes in toddlers (Jaffee, 2007), young children (Treyvaud et al., 2016) and adolescents (Wolke, Jaekel, Hall, & Baumann, 2013) who are at risk for neurodevelopmental problems, but also in healthy controls. Based on these studies as well as on the findings of the empirical studies that are part of this thesis, future work should investigate whether sensitive and stimulating parenting may act as a protective or resiliency factor and positively influence motor functioning and other developmental outcomes throughout childhood and beyond. Further, it should be tested whether a combination with targeted and age-appropriate intervention and treatment might lead to even stronger positive effects.

Another environmental factor that has been reported to alter developmental pathways from early motor problems to subsequent outcomes is bullying victimisation. Despite exceptions (Piek et al., 2005), it has frequently been demonstrated that children with motor problems have a higher risk for being bullied by their peers (Bejerot & Humble, 2013; Bejerot et al., 2013; Torn et al., 2015),

particularly verbally, for example through name-calling and insults, and through being socially excluded and ostracised (Campbell et al., 2012), which may occur in addition to social skill problems (Bejerot, 2011). Further, children who are experiencing motor problems, or both motor problems and peer victimisation, are more likely to be depressed (Campbell et al., 2012; Lingam et al., 2012; Piek, Barrett, Smith, Rigoli, & Gasson, 2010; Piek et al., 2007).

As a causal framework to explain the influence of environmental factors, particularly on the pathway between motor problems and subsequent internalising problems, the environmental stress hypothesis has been put forward. The environmental stress hypothesis, posits that motor problems and internalising problems are associated via multiple mediating and moderating psychosocial factors (or environmental stressors), for example, peer problems, being bullied, low self-esteem, low academic achievement (Mancini et al., 2016). However, while there is some evidence to support this conceptual framework, it is mostly supported by cross-sectional or correlational research (Mancini, Rigoli, Roberts, & Piek, 2019). This conceptual framework therefore needs further investigation in a future longitudinal study with the aim to unravel mechanisms and to identify environmental factors that influence developmental pathways between motor problems and other developmental or functional outcomes.

The Effect of Early Interventions on Parents and Their Emotional Wellbeing

Although we were not able to show a beneficial effect of treatment with physiotherapy on subsequent motor and cognitive outcomes in Study 2, the concept

of this study may be used to develop a future investigation into potential positive effects of intervention or treatment on parents' mental health and wellbeing.

Parents of children who are at risk for developmental problems often experience stress as well as anxiety and/or depressive symptoms (S. L. Edwards & Sarwark, 2005; Holditch-Davis et al., 2015; Treyvaud, Lee, Doyle, & Anderson, 2014), due to concerns about their children's diverse developmental and functional problems, including motor and academic difficulties, self-care, emotional and peer problems (Missiuna et al., 2007; Stephenson & Chesson, 2008).

To aid prognosis and to facilitate timely referral to intervention or treatment, screening and follow-up examinations are recommended (S. L. Edwards & Sarwark, 2005; Novak et al., 2017; Spittle et al., 2015). As demonstrated by prior research (Hughes et al., 2016; Spittle et al., 2015) as well as by findings in Study 2 there is still a lack of evidence for a sustained and long-lasting effect of early interventions on motor skill development and other developmental outcomes beyond preschool or school-age. However, there is some evidence that early interventions may have a positive effect on parents' mental health and wellbeing (Benzies, Magill-Evans, Hayden, & Ballantyne, 2013; S. L. Edwards & Sarwark, 2005; Spittle et al., 2016; Spittle & Treyvaud, 2016). In this vein, a recent study (A. D. Edwards et al., 2018) found that although routine MRI was not significantly better to predict neurodevelopmental problems in preterm infants compared to ultrasound, the parents of children who had MRI were less anxious. These are important findings because they demonstrate a positive 'side-effect' of intervention.

Drawing on these findings that parents of children who receive treatment (or a perceived superior treatment) may experience improved mental health outcomes Study 2 should be extended or developed into testing whether parents of children who received physiotherapy would have better or improved mental health and wellbeing outcomes than the parents whose children were not treated with physiotherapy. This would increase the understanding of the 'wider' effects of intervention and treatment, such as physiotherapy. Further, this could be helpful for the planning of interventions and treatment – not only for the children but also for parents of children who are at risk for developmental delay or problems.

Concluding Remarks

The purpose of this thesis was to examine and track early motor functioning and to demonstrate its central importance in overall child development. To this end, three empirical studies were carried out to identify perinatal and neonatal risk factors of poor early motor development and to investigate medium and long-term consequences of early motor problems. The key messages and main conclusions are as follows:

- While the majority of children did not exhibit motor problems during the preschool years, early motor problems were independently predicted by child health and social-environmental factors, that is, neonatal complications, abnormal neonatal neurological status, duration of hospitalisation and poor parent-infant relationships. As a possible implication, children with early

motor problems may benefit from interventions that include parents and focus on parent-infant relationships (Study 1).

- Motor problems in early infancy are associated with school-aged motor, cognitive and attention difficulties, but not with mental health issues. Receipt of physiotherapy, however, seems not to influence these associations and can therefore not be credited with a beneficial effect (Study 2).
- Consistent motor problems across the first five years of life have long-term effects on adult motor competence. Similarly, early cognitive function is associated with adult IQ. Children who experience early motor problems and neurological impairments are likely to have motor and cognitive problems in adulthood. It is therefore important to follow up both early motor and cognitive difficulties, particularly in at-risk children (Study 3).

The work in this thesis demonstrates that early motor functioning is ubiquitous and highly pervasive, and affects and is affected by other developmental domains and functions. This is because all psychological domains and functions require or are imbued with motor functions and skills. While motor development is dependent and rooted in the physical body and its functions, not least those of the brain and nervous system – it also is very much influenced by experience and the social and physical environment. Particularly, in early childhood parents are facilitators who enable, shape and support their child's motor functioning and learning. It has been shown that early motor functioning is central and a building block for subsequent developmental outcomes into school-age and adulthood.

The main implications from the three empirical studies presented in this thesis are that children, and particularly children at risk for motor problems may benefit from early testing or screening of motor functions, as it can have far-reaching consequences across diverse psychological domains and time, particularly during important periods of development and life transitions. Given the importance of early motor development, neonatal complications and neurological problems should be monitored, and the involvement of parents in infant care, even for the most vulnerable (e.g., preterm born children) should be supported and implemented in early intervention and treatment programs.

Despite increasing research focussing on motor development and its consequences, the study of motor development is still lagging behind other research fields (e.g., cognitive, emotional and social development). However, the findings reported in this thesis, along with others in the literature, demonstrate that early motor development has significant and important implications for general child development and long-term developmental outcomes in other domains. Thus, researchers who study child development should recognize the contribution of motoric factors and their role in the development of cognitive and social functioning.

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Appendices

Appendix A. Motor and Neurological Items at Birth (All Categories).

Items	Item Categories
Fine motor: oculomotor, orofacial	
1. Pupils (shape)	1 'symmetrical, round, medium wide' 2 'irregular outline' 3 'left pupil smaller' 4 'right pupil smaller'
2. Pupil reaction to light	1 'normal' 2 'incomplete right' 3 'incomplete left' 4 'delayed right' 5 'delayed left' 6 'incomplete right & left' 7 'incomplete & delayed right' 8 'incomplete left & delayed right' 9 'delayed right & left' 10 'delayed right & other' 11 'delayed right & left & other' 12 'incomplete right and left and delayed right & left' 13 'incomplete right and left and delayed right & left and other' 14 'no reaction'
3. Eye position	1 'normal' 2 'strabismus right'

Items	Item Categories
	3 'strabismus left'
	4 'nystagmus right'
	5 'nystagmus left'
	6 'setting sun right'
	7 'setting sun left'
	8 'strab right & left'
	9 'nyst right & left'
	10 'sett right & left'
	11 'strab/nys right'
	12 'strab right, nys left'
	13 'strab/nys left'
	14 'strab right & other'
	15 'strab left & other'
	16 'nys right & other'
	17 'nys left & other'
	18 'sett right & other'
	19 'strab right & left, nys right'
	20 'strab right & left, nys left'
	21 'strab & nys right'
	22 'strab right, sett right & left'
	23 'strab left, ny right & left'
	24 'nys right, sett right & left'
	25 'strab left, sett right & left'
	26 'strab right & left, other'
	27 'nys right & left, other'
	28 'sett right & left, other'

Items	Item Categories
	29 'strab right & left, nys right & left' 30 'strab right & left, sett right & left' 31 'nys right & left, sett right & left' 32 'strab right & left, nys right, other' 33 'strab right & left, nys right & left, sett right & left, other' 34 'strab left, nys right & left, sett right & left' 35 'strab right & left, nys right & left, sett right & left'
4. Fixate & follow eye movement	1 'yes' 2 'no' 3 'incomplete'
5. Ears (reaction to a loud acoustic noise)	1 'yes' 2 'problematic' 3 'no reaction'
6. Facial expression	1 'normal, symmetric, variable, normal facial muscles tone' 2 'abnormal'.
7. Glabella reflex	1 'immediate, symmetric' 2 'left weak' 3 'left absent' 4 'right weak' 5 'right absent' 6 'right absent, left weak' 7 'both sides weak' 8 'both sides absent'
8. Sucking	1 'rhythmic, strong' 2 'weak' 3 'absent'

Items	Item Categories
9. Swallowing	1 'yes, undisturbed' 2 'disturbed' 3 'absent'
Gross motor: sensorimotor	
10. Posture in supine position	1 'normal' 2 'abnormal: head' 3 'abnormal: torso' 4 'abnormal: arms' 5 'abnormal: legs' 6 'abnormal: head & torso' 7 'abnormal: head & arms' 8 'abnormal: head & legs' 9 'abnormal: torso & arms' 10 'abnormal: torso & legs' 11 'abnormal: arms & legs' 12 'abnormal: head, torso & arms' 13 'abnormal: head, torso & legs' 14 'abnormal: head, arms & legs' 15 'abnormal: torso, arms & legs' 16 'abnormal: head, torso, arms & legs'.
11. Quantity of spontaneous motor activity	1 'moderate movements/activity' 2 'increased' 3 'decrease' 4 'no spontaneous motor activity'
12. Movement pattern	1 'normal' 2 'right arm abnormal'

Items	Item Categories
	3 'left arm abnormal' 4 'right leg abnormal' 5 'left leg abnormal' 6 'both arms abnormal' 7 'right arm and leg abnormal' 8 'left arm and leg abnormal' 9 'both legs abnormal' 10 'both arms and right leg abnormal' 11 'both arms and left leg abnormal' 12 'right arm and both legs abnormal' 13 'left arm and both legs abnormal' 14 'both arms and legs abnormal'
13. Movement sequence	1 'normal' 2 'high-amplitude' 3 'predominant sudden movement out of position' 4 'predominant sudden movement out of position, high-amplitude' 5 'weak, slow' 6 'weak, slow, high-amplitude' 7 'other and high-amplitude'
14. Involuntary movements	1 'normal' 2 'subtle tremor' 3 'gross tremor' 4 'myoclonus' 5 'seizures' 6 'subtle and gross tremor' 7 'subtle tremor and myoclonus'

Items	Item Categories
	8 'subtle tremor and seizures' 9 'subtle tremor and other' 10 'gross tremor and myoclonus' 11 'gross tremor and seizures' 12 'gross tremor and other' 13 'myoclonus and seizures' 14 'myoclonus and other' 15 'seizures and other' 16 'subtle and gross tremor & myoclonus' 17 'subtle and gross tremor & seizures' 18 'subtle and gross tremor & other' 19 'subtle tremor, myoclonus & seizures' 20 'gross tremor, myoclonus & seizures' 21 'gross tremor, seizures & other' 22 'gross tremor, myoclonus & other' 23 'subtle and gross tremor, myoclonus & seizures' 24 'subtle and gross tremor, seizures & other' 25 'gross tremor, myoclonus, seizures & other'
15. Muscle tone at rest, posture	1 'normal' 2 'arms decreased' 3 'arms increased' 4 'legs decreased' 5 'legs increased' 6 'torso decreased' 7 'torso increased' 8 'arms and legs decreased'

Items	Item Categories
	9 'arms decreased, legs increased' 10 'arms increased, legs decreased' 11 'arms and legs increased' 12 'arms and torso decreased' 13 'arms decreased, torso increased' 14 'arms increased, torso decreased' 15 'arms and torso increased' 16 'legs and torso decreased' 17 'legs decreased, torso increased' 18 'legs increased, torso decreased' 19 'legs and torso increased' 20 'arms, legs and torso decreased' 21 'arms and legs decreased, torso increased' 22 'arms and torso decreased, legs increased' 23 'arms, legs and torso increased' 24 'arms and legs increased, torso decreased' 25 'arms and torso increased, legs decreased'.
16. Muscle tone at rest, resistance against passive movement	1 'normal' 2 'head decreased' 3 'head increased' 4 'torso decreased' 5 'torso increased' 6 'arms decreased' 7 'arms increased' 8 'legs decreased' 9 'legs increased'

Items	Item Categories
	10 'head and torso decreased'
	11 'head and torso increased'
	12 'head and arms decreased'
	13 'head decreased, arms increased'
	14 'head and arms increased'
	15 'head and legs decreased'
	16 'head decreased, legs increased'
	17 'head increased, legs decreased'
	18 'head and legs increased'
	19 'torso and arms decreased'
	20 'torso and arms increased'
	21 'torso and legs decreased'
	22 'torso decreased, legs increased'
	23 'torso increased, legs decreased'
	24 'torso and legs increased'
	25 'arms and legs decreased'
	26 'arms decreased, legs increased'
	27 'arms increased, legs decreased'
	28 'arms and legs increased'
	29 'head, torso and arms decreased'
	30 'head and torso decreased, arms increased'
	31 'head, torso and arms increased'
	32 'head, torso and legs decreased'
	33 'head and torso decreased, legs increased'
	34 'head decreased, torso and legs increased'
	35 'head and legs increased, torso decreased'

Items	Item Categories
	36 'head and torso increased, legs decreased' 37 'head, torso and legs increased' 38 'head, arms and legs decreased' 39 'head and arms decreased, legs increased' 40 'head decreased, arms and legs increased' 41 'head increased, arms and legs decreased' 42 'head, arms and legs increased' 43 'torso, arms and legs decreased' 44 'torso and arms decreased, legs increased' 45 'torso decreased, arms and legs increased' 46 'torso, arms and legs increased' 47 'head, torso, arms and legs decreased' 48 'head, torso and arms decreased, legs increased' 49 'head, torso and legs decreased, arms increased' 50 'head, arms and legs decreased, torso increased' 51 'head and torso decreased, arms and legs increased' 52 'head decreased, torso, arms and legs increased' 53 'head increased, torso, arms and legs, decreased' 54 'head and torso increased, arms and legs decreased' 55 'head, arms and legs increased, torso decreased' 56 'head, torso and arms increased, legs decreased' 57 'head, torso and legs increased, arms decreased' 58 'head, torso, arms and legs increased'
17. Head control	1 'normal' 2 'head hangs down passively'

Items	Item Categories
18. Arm position/posture	1 'symmetric, slightly bent' 2 'flabby'
Reaction/Reflexes/Responses	
19. Grasping reaction hands	1 'immediate, symmetric, moderate' 2 'weak' 3 'increased' 4 'absent' 5 'discontinuous with tremor'
20. Grasping reaction feet	1 'immediate, symmetric, moderate' 2 'weak' 3 'increased' 4 'absent' 5 'discontinuous with tremor'
21. Knee jerk/patellar reflex	1 'immediate, symmetric, moderate' 2 'increased' 3 'weakened' 4 'absent'
22. Achilles tendon reflex	1 'immediate, symmetric, moderate' 2 'increased' 3 'weakened' 4 'absent'
23. Biceps reflex	1 'immediate, symmetric, moderate' 2 'increased' 3 'weakened' 4 'absent'

Items	Item Categories
24. Moro response, phase I (adduction, extension of arms)	1 'normal' 2 'increased' 3 'weakened' 4 'absent'
25. Moro response, phase II (adduction, flexion of arms)	1 'normal' 2 'increased' 3 'weakened' 4 'absent'

Note. For the computation of the motor functioning score all items were categorised into ‘within’ (=1) and ‘outside the normal range’ (>1).

Appendix B. Motor and Neurological Items at 5 months (All Categories).

Items	Item Categories
Fine motor: oculomotor, orofacial	
1. Eye position	1 'normal' 2 'abnormal'
2. Eyes, setting-sun sign	1 'normal' 2 'unclear' 3 'certain'
3. Eyes, following movement of eyes	1 'normal' 2 'uncoordinated'
4. Eyes, strabismus	1 'normal' 2 'slightly inconstant right' 3 'slightly constant right' 4 'slightly inconstant left' 5 'convergent' 6 'divergent' 7 'slightly inconstant right & left' 8 'slightly inconstant right & convergent' 9 'slightly constant right & convergent' 10 'distinctly inconstant right & convergent' 11 'distinctly constant right & convergent' 12 'slightly inconstant right & convergent' 13 'slightly constant right & convergent' 14 'slightly inconstant left & convergent' 15 'slightly constant left & convergent' 16 'distinctly inconstant left & convergent'

Items	Item Categories
	17 'distinctly constant left & convergent' 18 'slightly inconstant left & divergent' 19 'slightly constant left & divergent' 20 'distinctly inconstant left & divergent' 21 'slightly inconstant right and left & convergent' 22 'slightly constant right and left & convergent' 23 'distinctly inconstant right and left & convergent' 24 'distinctly constant right and left & convergent' 25 'slightly inconstant right and distinctly inconstant left & convergent' 26 'slightly constant right and distinctly constant left & convergent' 27 'distinctly inconstant right and slightly inconstant left & convergent' 28 'distinctly constant right and slightly constant left & convergent' 29 'distinctly inconstant right and distinctly constant left & convergent' 30 'distinctly constant right and slightly inconstant left & convergent' 31 'slightly constant right and slightly inconstant left & convergent' 32 'distinctly constant right and distinctly inconstant left & convergent' 33 'slightly inconstant right and slightly inconstant left & divergent' 34 'distinctly inconstant right and slightly inconstant left & divergent' 35 'distinctly inconstant right and distinctly inconstant left & convergent and divergent' 36 'distinctly constant right and distinctly constant left & convergent and divergent'
5. Eyes, nystagmus	1 'normal' 2 'inconstant' 3 'constant' 4 'horizontal' 5 'inconstant & horizontal' 6 'constant & horizontal'

Items	Item Categories
	7 'inconstant & vertical' 8 'constant & vertical' 9 'inconstant, horizontal & vertical'
6. Eyes, pupils (shape)	1 'normal' 2 'not round right' 3 'narrow left' 4 'wide right' 5 'wide left' 6 'narrow right & left' 7 'wide right & left' 8 'narrow right & wide left'
7. Eyes, pupil reaction to light	1 'normal' 2 'delayed right' 3 'delayed left' 4 'delayed right & left' 5 'absent right & left'
8. Eyes, pupil reaction to convergence	1 'normal' 2 'delayed right' 3 'delayed left' 4 'absent right' 5 'absent left' 6 'delayed right & left' 7 'absent right & left' 8 'delayed right & absent left'
9. Eyes, fixation	1 'normal' 2 'unclear'

Items	Item Categories
	3 'absent'
10. Eyes, follow with gaze	1 'normal' 2 'left 45 degree' 3 'left absent' 4 'right 45 degree' 5 'right 45 degree, left absent' 6 'right absent' 7 'right absent, left 45 degree' 8 'right and left absent'
11. Eyes, follow with gaze and change of head position	1 'normal' 2 'left 45 degree' 3 'left absent' 4 'right 45 degree' 5 'right 45 degree, left absent' 6 'right absent' 7 'right absent, left 45 degree' 8 'right and left absent'
12. Eyes, eye contact	1 'normal' 2 'short' 3 'unclear' 4 'absent' 5 'short & other' 6 'unclear & other'
13. Ears, reaction to noise	1 'normal' 2 'vague reaction' 3 'vague reaction & other'

Items	Item Categories
	4 'pays attention' 5 'pays attention & other' 6 'absent' 7 'absent & other'
14. Face muscles	1 'normal' 2 'weak paresis right' 3 'hypotonic left' 4 'hypertonic left' 5 'weak paresis left' 6 'uncoordinated movement' 7 'hypotonic right & left' 8 'hypertonic right & left' 9 'weak paresis right & left' 10 'hypertonic left & other' 11 'weak paresis right & other' 12 'hypotonic right and left & uncoordinated movement' 13 'hypertonic right and left & uncoordinated movement' 14 'hypotonic right and left & uncoordinated movement & other'
15. Facial expression	1 'normal, variable, age-appropriate differentiation' 2 'poor facial expression' 3 'poor facial expression and other'
16. Mouth and tongue movement	1 'normal' 2 'uncoordinated' 3 'monotonous' 4 'uncoordinated & monotonous' 5 'uncoordinated & other'

Items	Item Categories
	6 'monotonous & other'
17. Sucking	1 'normal' 2 'uncoordinated' 3 'weak' 4 'absent' 5 'weak & other'
18. Swallowing	1 'normal' 2 'abnormal'
Gross motor: sensorimotor – supine posture	
19. Posture supine - head.	1 'normal' 2 'slightly retroflexed ' 3 'opisthotonos' 4 'preferred turn left' 5 'preferred turn right' 6 'preferred inclination left' 7 'preferred inclination right' 8 'slightly retroflexed & preferred turn left' 9 'slightly retroflexed & preferred turn right' 10 'opisthotonos & preferred turn left' 11 'opisthotonos & preferred turn right' 12 'slightly retroflexed & preferred inclination left' 13 'slightly retroflexed & preferred inclination right' 14 'opisthotonos & preferred inclination right' 15 'slightly retroflexed & other' 16 'opisthotonos & other' 17 'preferred turn left & inclination left'

Items	Item Categories
	18 'preferred turn left & inclination right' 19 'preferred turn right & inclination left' 20 'preferred turn right & inclination right' 21 'preferred turn left & other' 22 'preferred turn right & other' 23 'slightly retroflexed & preferred turn left & preferred inclination left' 24 'slightly retroflexed & preferred turn right & preferred inclination right' 25 'slightly retroflexed & preferred turn right & preferred inclination left' 26 'opisthotonos & preferred turn left & preferred inclination left' 27 'opisthotonos & preferred turn left & preferred inclination right' 28 'opisthotonos & preferred turn right & preferred inclination right' 29 'opisthotonos & preferred turn right & preferred inclination left' 30 'opisthotonos & preferred turn left & other' 31 'opisthotonos & preferred turn right & other' 32 'preferred turn left & preferred inclination right & other'
20. Posture supine - arms.	1 'normal' 2 'extended right' 3 'extended left' 4 'flexed right' 5 'flexed left' 6 'rotated inward right' 7 'rotated inward left' 8 'rotated outward right' 9 'weak, resting and flexed right' 10 'weak, resting and flexed left' 11 'shoulder retraction right'

Items	Item Categories
	12 'shoulder retraction left' 13 'extended right & left' 14 'extended right & flexed left' 15 'extended right & rotated inward right' 16 'extended right & rotated inward left' 17 'extended right & rotated outward right' 18 'extended right & weak, resting, flexed right' 19 'extended right & shoulder retracted right' 20 'extended right & other' 21 'extended left & flexed right' 22 'extended left & rotated inward left' 23 'extended left & rotated outward left' 24 'extended left & other' 25 'flexed right & left' 26 'flexed right & rotated inward right' 27 'flexed right & rotated outward right' 28 'flexed right & shoulder retracted right' 29 'flexed left & rotated outward right' 30 'flexed left & shoulder retracted left' 31 'rotated inward right & left' 32 'rotated inward left & rotated outward right' 33 'rotated inward left & shoulder retracted left' 34 'rotated inward left & other' 35 'rotated outward right & left' 36 'rotated outward right & shoulder retracted right' 37 'rotated outward right & shoulder retracted left'

Items	Item Categories
	38 'weak, resting and flexed right & left'
	39 'shoulder retraction right & left'
	40 'extended right & left & rotated outward right'
	41 'extended right & left & rotated outward left'
	42 'extended right & left & shoulder retracted right'
	43 'extended right & left & other'
	44 'extended right & flexed left & other'
	45 'extended right & rotated inward right & shoulder retraction left'
	46 'extended right & weak, resting, flexed left & other'
	47 'extended left & rotated inward left & shoulder retracted left'
	48 'extended left & rotated inward left & other'
	49 'extended left & rotated outward left & weak resting flexed right'
	50 'extended left & shoulder retracted right & left'
	51 'extended left & shoulder retracted left & other'
	52 'flexed right & left & shoulder retracted right'
	53 'flexed right & left & shoulder retracted left'
	54 'flexed right & left & other'
	55 'flexed right & rotated inward right & shoulder retracted right'
	56 'flexed right & rotated outward right & left'
	57 'flexed right & shoulder retracted right & left'
	58 'flexed left & rotated inward left & shoulder retracted left'
	59 'flexed left & shoulder retracted right & left'
	60 'rotated inward right & left & other'
	61 'rotated inward left & weak, resting, flexed right & left'
	62 'rotated inward left & shoulder retracted right & left'
	63 'rotated outward right & left & other'

Items	Item Categories
	64 'rotated outward left & shoulder retracted right & left'
	65 'shoulder retraction right & left & other'
	66 'weak, resting, flexed right & left & shoulder retracted right'
	67 'extended right & left & rotated inward right & left'
	68 'extended right & left & rotated outward right & left'
	69 'extended right & left & shoulder retraction right & left'
	70 'extended right & rotated inward right & shoulder retraction right & left'
	71 'extended right & rotated outward right & shoulder retraction right & other'
	72 'extended right & shoulder retraction right & left & other'
	73 'extended left & flexed right & weak, resting and flexed right & shoulder retraction right'
	74 'extended left & rotated inward left & shoulder retracted right & left'
	75 'extended left & rotated outward left & shoulder retracted right & left'
	76 'flexed right & left & rotated inward right & left'
	77 'flexed right & left & rotated outward right & left'
	78 'flexed right & left & shoulder retraction right & left'
	79 'rotated inward right & left & shoulder retraction right & left'
	80 'rotated inward right & left & weak, resting flexed right & left'
	81 'rotated outward right & left & weak, resting flexed right & left'
	82 'rotated outward right & left & shoulder retraction right & left'
	83 'weak, resting and flexed right & left & shoulder retraction right & left'
	84 'extended right & left & flexed right & left & other'
	85 'extended right & left & rotated outward right & left & other'
	86 'extended right & left & rotated inward left & shoulder retraction right & left'
	87 'extended right & left & rotated outward right & shoulder retraction right & left'
	88 'extended right & left & shoulder retraction right & left & other'
	89 'extended left & flexed right & rotated inward left & shoulder retraction right & left'

Items	Item Categories
	90 'extended left & flexed right & rotated outward left & shoulder retraction right & left' 91 'flexed right & left & shoulder retraction right & left & other' 92 'flexed left & rotated inward right & left & shoulder retraction right & left' 93 'rotated outward right & left & shoulder retraction right & left & other' 94 'extended right & left & rotated inward right & left & shoulder retraction right & left' 95 'extended right & left & rotated outward right & left & shoulder retraction right & left' 96 'flexed right & left & rotated inward right & left & shoulder retraction right & left' 97 'flexed right & left & rotated outward right & left & shoulder retraction right & left' 98 'rotated outward right & left & weak, resting, flexed right & left & shoulder retraction right & left' 99 'extended right & left & rotated outward right & left & shoulder retraction right & left & other'
21. Posture supine - hands	1 'normal' 2 'loosely open right' 3 'loosely open left' 4 'slightly fisted right' 5 'distinctly fisted right' 6 'slightly fisted left' 7 'distinctly fisted left' 8 'adducted thumb right' 9 'adducted thumb left' 10 'loosely open right & left' 11 'slightly fisted right & left' 12 'distinctly fisted right & left' 13 'adducted thumb right & left' 14 'loosely open right & slightly fisted left'

Items	Item Categories
	15 'loosely open right & distinctly fisted left'
	16 'loosely open left & slightly fisted right'
	17 'loosely open left & adducted thumb left'
	18 'slightly fisted right & distinctly fisted left'
	19 'distinctly fisted right & slightly fisted left'
	20 'slightly fisted right & adducted thumb right'
	21 'distinctly fisted right & adducted thumb right'
	22 'slightly fisted right & other'
	23 'slightly fisted left & adducted thumb left'
	24 'distinctly fisted left & adducted thumb left'
	25 'distinctly fisted left & other'
	26 'adducted thumb right & other'
	27 'adducted thumb left & other'
	28 'loosely open right & left & adducted thumb right'
	29 'loosely open right & left & adducted thumb left'
	30 'loosely open right & slightly fisted left & adducted thumb left'
	31 'loosely open right & distinctly fisted left & adducted thumb left'
	32 'slightly fisted right & left & adducted thumb right'
	33 'slightly fisted right & left & adducted thumb left'
	34 'slightly fisted right & left & other'
	35 'distinctly fisted right & left & other'
	36 'slightly fisted right & distinctly fisted left & adducted thumb left'
	37 'slightly fisted right & distinctly fisted left & other'
	38 'slightly fisted right & adducted thumb right & left'
	39 'distinctly fisted right & slightly fisted left & adducted thumb right'
	40 'distinctly fisted right & adducted thumb right & left'

Items	Item Categories
	41 'distinctly fisted right & adducted thumb right & other' 42 'slightly fisted left & adducted thumb right & left' 43 'distinctly fisted left & adducted thumb right & left' 44 'adducted thumb right & left & other' 45 'loosely open right & left & adducted thumb right & left' 46 'slightly fisted right & left & adducted thumb right & left' 47 'distinctly fisted right & left & adducted thumb right & left' 48 'slightly fisted right & distinctly fisted left & adducted thumb right & left' 49 'distinctly fisted right & slightly fisted left & adducted thumb right & left' 50 'loosely open right & left & slightly fisted right & left & other' 51 'loosely open right & left & adducted thumb right & left & other' 52 'slightly fisted right & left & adducted thumb right & left & other' 53 'distinctly fisted right & slightly fisted left & adducted thumb right & left & other' 54 'distinctly fisted right & left & adducted thumb right & left & other'
22. Posture supine - torso	1 'normal' 2 'instable' 3 'weakly lying on' 4 'right convex' 5 'left convex' 6 'hyperextended' 7 'instable & weakly lying on' 8 'instable & right convex' 9 'instable & left convex' 10 'instable & hyperextended' 11 'instable & other' 12 'weakly & right convex'

Items	Item Categories
	13 'weakly & left convex' 14 'weakly & hyperextended' 15 'weakly & other' 16 'right convex & hyperextended' 17 'right convex & other' 18 'left convex & hyperextended' 19 'left convex & other' 20 'hyperextended & other' 21 'instable & weakly lying on & right convex' 22 'instable & right convex & left convex' 23 'instable & right convex & hyperextended' 24 'instable & left convex & hyperextended' 25 'weakly lying on & right convex & left convex' 26 'weakly lying on & right convex & hyperextended'
23. Posture supine - hips	1 'normal' 2 'bent (left/right slightly/distinctly)' 3 'stretched (left/right slightly/distinctly)' 4 'adducted (left/right slightly/distinctly)' 5 'abducted (left/right slightly/distinctly)' 6 'rotated inward (left/right slightly/distinctly)' 7 'rotated outward (left/right slightly/distinctly)' 8 'bent & stretched' 9 'bent & adducted' 10 'bent & abducted' 11 'bent & rotated inward' 12 'bent & rotated outward'

Items	Item Categories
	13 'bent & other' 14 'stretched & adducted' 15 'stretched & abducted' 16 'stretched & rotated inward' 17 'stretched & rotated outward' 18 'stretched & other' 19 'adducted & abducted' 20 'adducted & rotated inward' 21 'adducted & other' 22 'abducted & rotated inward' 23 'abducted & rotated outward' 24 'abducted & other' 25 'rotated outward & other' 26 'bent, stretched & rotated outward' 27 'bent, adducted & rotated inward' 28 'bent, adducted & rotated outward' 29 'bent, adducted & other' 30 'bent, abducted & rotated outward' 31 'bent, abducted & other' 32 'bent, rotated inward & outward' 33 'bent, rotated outward & other' 34 'stretched, adducted & rotated inward' 35 'stretched, adducted & rotated outward' 36 'stretched, adducted & other' 37 'stretched, abducted & rotated inward' 38 'stretched, abducted & rotated outward'

Items	Item Categories
	39 'abducted, rotated outward & other' 40 'bent, abducted, rotated outward & other' 41 'stretched, adducted, rotated inward & other' 42 'stretched, abducted, rotated outward & other' 43 'bent, stretched, adducted, rotated outward & other' 44 'bent, stretched, abducted, rotated inward & outward'
24. Posture supine - knee	1 'normal' 2 'stretched right' 3 'stretched left' 4 'bent left' 5 'stretched right & left' 6 'stretched left & bent right' 7 'bent right & left' 8 'bent left & other' 9 'stretched right & left, other' 10 'bent right & left, other'
25. Posture supine - feet	1 'normal' 2 'forefoot adducted (left/right slightly/distinctly)' 3 'forefoot abducted (left/right slightly/distinctly)' 4 'feet plantar flexed (left/right slightly/distinctly)' 5 'feet supinated (left/right slightly/distinctly)' 6 'feet pronated (left/right slightly/distinctly)' 7 'forefoot adducted & abducted' 8 'forefoot adducted & feet plantar flexed' 9 'forefoot adducted & feet supinated' 10 'forefoot adducted & feet pronated'

Items	Item Categories
	11 'forefoot adducted & other' 12 'forefoot abducted & feet plantar flexed' 13 'forefoot abducted & feet supinate' 14 'forefoot abducted & feet pronated' 15 'forefoot abducted & other' 16 'feet plantar flexed & supinated' 17 'feet plantar flexed & pronate' 18 'feet plantar flexed & other' 19 'feet supinated & pronated' 20 'feet supinated & other' 21 'forefoot adducted, abducted & feet plantar flexed' 22 'forefoot adducted, abducted & feet supinated' 23 'forefoot adducted, feet plantar flexed & supinated' 24 'forefoot adducted, feet plantar flexed & pronated' 25 'forefoot adducted, feet plantar flexed & other' 26 'forefoot adducted, feet supinated & pronated' 27 'forefoot adducted, feet supinated & other' 28 'forefoot abducted, feet plantar flexed & supinated' 29 'forefoot abducted, feet plantar flexed & pronated' 30 'forefoot abducted, feet plantar flexed & other' 31 'forefoot abducted, feet supinated & other' 32 'forefoot abducted, feet pronated & other' 33 'feet plantar flexed, supinated & other' 34 'feet plantar flexed, pronated & other' 35 'forefoot adducted, abducted, feet plantar flexed & supinated' 36 'forefoot adducted, feet plantar flexed, supinated & other'

Items	Item Categories
	37 'forefoot adducted, feet plantar flexed, pronated & other' 38 'forefoot abducted, feet plantar flexed, supinated & other' 39 'forefoot abducted, feet plantar flexed, pronated & other' 40 'forefoot adducted, abducted, feet plantar flexed, supinated & pronated'
Gross motor: sensorimotor - spontaneous motor function, gross motor quality	
26. Spontaneous motor function - quantity	1 'normal' 2 'movement<25% right arm' 3 'movement<25% left arm' 4 'movement<25% left leg' 5 'movement>75% left arm' 6 'movement>75% right leg' 7 'movement>75% left leg' 8 'movement<25% both arms' 9 'movement<25% both legs' 10 'movement>75% both arms' 11 'movement>75% both legs' 12 'movement<25% both arms & legs' 13 'movement>75% both arms & legs' 14 'movement<25% right arm & leg' 15 'movement<25% left arm & leg' 16 'movement<25% left leg & other' 17 'movement>75% right arm & leg' 18 'movement<25% right arm & both legs' 19 'movement<25% right arm & leg, >75% left leg' 20 'movement<25% left arm & both legs'

Items	Item Categories
	21 'movement<25% both legs & other' 22 'movement>75% both arms & right leg' 23 'movement>75% right arm & leg & other' 24 'movement>75% left arm & both legs' 25 'movement>75% both legs & other' 26 'movement<25% both arms & >75% both legs' 27 'movement<25% left arm & leg & >75% right arm & leg' 28 'movement<25% both legs & >75% both both arms' 29 'movement>75% left arm, both legs & other' 30 'movement<25% both arms & legs & other' 31 'movement<25% left leg & >75% both arms & legs' 32 'movement>75% both arms & legs & other'
27. Quality of gross motor function, movement pattern.	1 'normal' 2 'synchronous extension legs' 3 'synchronous extension arms' 4 'invariable/atavistic movement of legs' 5 'invariable/atavistic movement of arms' 6 'synchronous extension legs & arms' 7 'synchronous extension & invariable/atavistic movement of legs' 8 'synchronous extension legs & invariable/atavistic movement of arms' 9 'synchronous extension legs & other' 10 'synchronous extension arms & invariable/atavistic movement of legs' 11 'synchronous extension & invariable/atavistic movement of arms' 12 'synchronous extension arms & other' 13 'invariable/atavistic movement of legs & arms' 14 'invariable/atavistic movement of legs & other'

Items	Item Categories
	15 'invariable/atavistic movement of arms & other' 16 'synchronous extension legs, arms & invariable/atavistic movement of legs' 17 'synchronous extension legs, arms & other' 18 'synchronous extension legs, invariable/atavistic movement of legs & arms' 19 'synchronous extension arms, invariable/atavistic movement of legs & arms' 20 'invariable/atavistic movement of legs, arms & other' 21 'synchronous extension legs, arms & invariable/atavistic movement of legs, arms' 22 'synchronous extension legs, arms, invariable/atavistic movement of legs & other' 23 'synchronous extension arms, invariable/atavistic movement of legs, arms & other' 24 'synchronous extension legs, arms, invariable/atavistic movement of legs, arms & other'
28. Quality of gross motor function, stereotypies.	1 'normal' 2 'rarely' 3 'often'
29. Quality of gross motor function, movement sequence.	1 'normal' 2 'disturbed by hypertonia arms (left/right slightly/distinctly)' 3 'disturbed by hypertonia legs (left/right slightly/distinctly)' 4 'excessive movements arms (left/right slightly/distinctly)' 5 'excessive movements legs (left/right slightly/distinctly)' 6 'change of movement not smooth arms (left/right slightly/distinctly)' 7 'change of movement not smooth legs (left/right slightly/distinctly)' 8 'disturbed by hypertonia arms & legs' 9 'disturbed by hypertonia & excessive movements arms' 10 'disturbed by hypertonia arms & excessive movement legs' 11 'disturbed by hypertonia arms & change of movement not smooth arms' 12 'disturbed by hypertonia arms & change of movement not smooth legs' 13 'disturbed by hypertonia arms & other'

Items	Item Categories
	14 'disturbed by hypertonia legs & excessive movements arms' 15 'disturbed by hypertonia legs & excessive movements legs' 16 'disturbed by hypertonia legs & change of movement not smooth arms' 17 'disturbed by hypertonia legs & change of movement not smooth legs' 18 'disturbed by hypertonia legs & other' 19 'excessive movements arms & legs' 20 'excessive movements & change of movement not smooth arms' 21 'excessive movements arms & change of movement not smooth legs' 22 'excessive movements arms & other' 23 'excessive movements legs & change of movement not smooth arms' 24 'excessive movements & change of movement not smooth legs' 25 'excessive movements legs & other' 26 'change of movement not smooth arms & legs' 27 'change of movement not smooth arms & other' 28 'change of movement not smooth legs & other' 29 'disturbed by hypertonia arms, legs & excessive movements arms' 30 'disturbed by hypertonia arms, legs & excessive movements legs' 31 'disturbed by hypertonia arms, leg & change of movement not smooth arms' 32 'disturbed by hypertonia arms, legs & change of movement not smooth legs' 33 'disturbed by hypertonia arms, legs & other' 34 'disturbed by hypertonia legs & excessive movements arms, legs' 35 'disturbed by hypertonia legs, excessive movements arms & change of movement not smooth arms' 36 'disturbed by hypertonia legs, excessive movements arms & other' 37 'excessive movements arms, legs & change of movement not smooth arms' 38 'excessive movements arms, legs & change of movement not smooth legs'

Items	Item Categories
	39 'excessive movements arms, legs & other' 40 'excessive movements legs & change of movement not smooth arms, legs' 41 'change of movement not smooth arms, legs & other' 42 'disturbed by hypertonia, excessive movements & change of movement not smooth arms' 43 'disturbed by hypertonia, excessive movements arms & legs' 44 'disturbed by hypertonia, excessive movements arms & other' 45 'disturbed by hypertonia arms, change of movement not smooth arms & legs' 46 'disturbed by hypertonia arms, excessive movement & change of movement not smooth legs' 47 'disturbed by hypertonia arms, change of movement not smooth arms & other' 48 'disturbed by hypertonia legs & change of movement not smooth arms, legs' 49 'excessive movements arms & change of movement not smooth arms, legs' 50 'excessive movements & change of movement not smooth arms & other' 51 'excessive movements & change of movement not smooth legs & other' 52 'disturbed by hypertonia arms, legs & excessive movements arms, legs' 53 'disturbed by hypertonia arms, legs, excessive movements arms, change of movement not smooth arms' 54 'disturbed by hypertonia arms, legs & excessive movements arms, change of movement not smooth legs' 55 'disturbed by hypertonia arms, legs & change of movement not smooth arms & legs' 56 'excessive movement arms, legs & change of movement not smooth arms & legs' 57 'disturbed by hypertonia arms, excessive movement legs & change of movement not smooth arms & legs' 58 'disturbed by hypertonia arms, legs & excessive movement, change of movement not smooth legs' 59 'disturbed by hypertonia, excessive movements arms & change of movement not smooth arms, legs'

Items	Item Categories
	60 'disturbed by hypertonia, excessive movements & change of movement not smooth arms & other' 61 'disturbed by hypertonia legs, excessive movements arms & change of movement not smooth arms & legs' 62 'disturbed by hypertonia, excessive movements arms, legs & change of movement not smooth arms' 63 'disturbed by hypertonia arms & legs, excessive movements arms & change of movement not smooth arms & legs' 64 'disturbed by hypertonia, excessive movements arms & legs & change of movement not smooth legs' 65 'disturbed by hypertonia arms & legs, excessive movements, change of movement not smooth arms & other' 66 'disturbed by hypertonia, change of movement not smooth arms & legs & other' 67 'disturbed by hypertonia arms, excessive movements & change of movement not smooth arms & legs' 68 'disturbed by hypertonia legs, excessive movements & change of movement not smooth arms & legs' 69 'disturbed by hypertonia, excessive movements & change of movement not smooth arms & legs'
30. Quality of gross motor function, speed of movement.	1 'normal' 2 'low right' 3 'low left' 4 'high right' 5 'high right & left' 6 'low left, high right'

Items	Item Categories
31. Quality of gross motor function, range of movement.	1 'normal' 2 'high amplitude arms right' 3 'high amplitude arms left' 4 'high amplitude legs right' 5 'low amplitude arms right' 6 'low amplitude arms left' 7 'low amplitude legs right' 8 'low amplitude legs left' 9 'high amplitude arms right & left' 10 'high amplitude legs right & left' 11 'low amplitude arms right & left' 12 'low amplitude legs right & left' 13 'high amplitude arms and legs right/left' 14 'low amplitude arms and legs right/left' 15 'high amplitude arms right/left & low amplitude legs right/left' 16 'high amplitude arms & legs right' 17 'high amplitude arms right & legs right/left' 18 'high amplitude arms left & legs right/left' 19 'high amplitude arms left & low amplitude legs right/left' 20 'high amplitude arms left & low amplitude legs left' 21 'high amplitude legs right/left & low amplitude arms right/left' 22 'high amplitude legs right/left & low amplitude arms right' 23 'high amplitude legs left & low amplitude arms right/left' 24 'high amplitude legs left & low amplitude arms right/left, legs right' 25 'low amplitude arms & legs right' 26 'low amplitude arms right, legs right/left'

Items	Item Categories
	27 'low amplitude arms & legs left' 28 'low amplitude arms left, legs right' 29 'low amplitude arms left, legs right/left'
32. Sensorimotor, involuntary movements.	1 'normal' 2 'slight tremor whilst arousal' 3 'slight tremor constantly' 4 'strong tremor, slightly' 5 'strong tremor, slightly & whilst spontaneous movement' 6 'strong tremor, distinctly & whilst spontaneous movement' 7 'slight tremor whilst arousal & strong tremor whilst spontaneous movement' 8 'slight tremor whilst arousal & athetoid movement' 9 'slight tremor whilst arousal & other' 10 'slight tremor whilst arousal, strong tremor, slightly' 11 'slight tremor whilst arousal, strong tremor, slightly & whilst spontaneous movement' 12 'slight tremor whilst arousal, strong tremor, slightly & whilst muscle stretching' 13 'slight tremor whilst arousal, strong tremor, distinctly, whilst spontaneous movement & athetoid movement' 14 'slight tremor all the time, strong tremor whilst spontaneous movement' 15 'slight tremor all the time, strong tremor distinctly, whilst spontaneous movement, muscle stretching & cramps' 16 'strong tremor, slightly, whilst muscle stretching' 17 'strong tremor, slightly, whilst spontaneous movement & muscle stretching' 18 'strong tremor, slightly, whilst spontaneous movement & cramps' 19 'strong tremor, distinctly, whilst muscle stretching' 20 'strong tremor, distinctly & cramps' 21 'strong tremor, distinctly & other'

Items	Item Categories
	22 'strong tremor, distinctly, whilst spontaneous movement & cramps' 23 'strong tremor, distinctly, whilst spontaneous & athetoid movements' 24 'strong tremor, distinctly, whilst spontaneous movements & other' 25 'strong tremor, distinctly, whilst spontaneous movement, muscle stretching & cramps' 26 'strong tremor, distinctly, whilst spontaneous movement, muscle stretching & athetoid movements' 27 'cramps' 28 'cramps & athetoid movements' 29 'athetoid movements' 30 'athetoid movements & other'
Fine motor: prehension	
33. Fine motor skills, movement pattern	1 'normal' 2 'monotonous' 3 'mostly synchronous' 4 'monotonous & mostly synchronous' 5 'monotonous & other' 6 'mostly synchronous & other'
34. Fine motor skills, movement sequence	1 'normal' 2 'excessive movements (left/right slightly/distinctly)' 3 'inadequate strength (left/right slightly/distinctly)' 4 'slow (left/right slightly/distinctly)' 5 'disturbed due to hypertonia (left/right slightly/distinctly)' 6 'excessive movements & inadequate strength' 7 'excessive movements & slow' 8 'excessive movements & disturbed due to hypertonia' 9 'excessive movements & other'

Items	Item Categories
	10 'inadequate strength & slow' 11 'inadequate strength & disturbed due to hypertonia' 12 'inadequate strength & other' 13 'slow & disturbed due to hypertonia' 14 'slow & other' 15 'disturbed due to hypertonia & other' 16 'excessive movements, inadequate strength & disturbed due to hypertonia' 17 'inadequate strength, slow & disturbed due to hypertonia' 18 'excessive movements, inadequate strength & slow' 19 'excessive movements, inadequate strength & other' 20 'excessive movements, slow & disturbed due to hypertonia' 21 'excessive movements, slow & other' 22 'excessive movements, disturbed due to hypertonia & other' 23 'inadequate strength, slow & other' 24 'inadequate strength, disturbed by hypertonia & other' 25 'slow, disturbed due to hypertonia & other' 26 'excessive movements, inadequate strength, slow & disturbed due to hypertonia' 27 'excessive movements, inadequate strength, slow & other' 28 'excessive movements, inadequate strength, disturbed due to hypertonia & other' 29 'inadequate strength, slow, disturbed due to hypertonia & other'
35. Fine motor skills, co-movements	1 'normal' 2 'frequent loose fisting (left/right slightly/distinctly)' 3 'hypertonic fisting contralateral (left/right slightly/distinctly)' 4 'mirror movements (left/right slightly/distinctly)' 5 'frequent loose fisting & hypertonic fisting contralateral' 6 'frequent loose fisting & mirror movements'

Items	Item Categories
	7 'frequent loose fisting & other' 8 'hypertonic fisting contralateral & mirror movements' 9 'hypertonic fisting contralateral & other' 10 'mirror movements & other' 11 'frequent loose fisting, hypertonic fisting contralateral & mirror movements' 12 'frequent loose fisting, hypertonic fisting contralateral & other'
Sensitivity	
36. Sensitivity, reaction/response to contract/touch or arms, legs, tummy.	1 'normal' 2 'excessive response' 3 'delayed response' 4 'weak response' 5 'no response' 6 'excessive response & other' 7 'delayed & weak response' 8 'weak & no response' 9 'weak response & other' 10 'delayed, weak & no response'
Sensorimotor - muscle tone, muscle strength, joints	
37. Muscle tone at rest, obtained from posture	1 'normal' 2 'torso (slightly/distinctly increased/decreased)' 3 'right arm (slightly/distinctly increased/decreased)' 4 'left arm (slightly/distinctly increased/decreased)' 5 'right leg (slightly/distinctly increased/decreased)' 6 'left leg (slightly/distinctly increased/decreased)' 7 'torso & right arm'

Items	Item Categories
	8 'torso & left arm' 9 'torso & left leg' 10 'torso, right arm & right leg' 11 'torso & both arms' 12 'torso & both legs' 13 'torso, both arms & left leg' 14 'torso, right arm & both legs' 15 'torso, left arm & both legs' 16 'both arms' 17 'right arm & right leg' 18 'right arm & left leg' 19 ' left arm & left leg' 20 'left arm & right leg' 21 'both arms & right leg' 22 'right arm & both legs' 23 'left arm & both legs' 24 'both arms & both legs' 25 'both legs' 26 'torso, both arms and both legs'
38. Muscle tone at rest, obtained from resistance	1 'normal' 2 'neck (slightly/distinctly increased/decreased)' 3 'torso (slightly/distinctly increased/decreased)' 4 'right arm (slightly/distinctly increased/decreased)' 5 'left arm (slightly/distinctly increased/decreased)' 6 'right leg (slightly/distinctly increased/decreased)' 7 'left leg (slightly/distinctly increased/decreased)'

Items	Item Categories
	8 'neck & torso' 9 'both arms' 10 'right arm, right leg' 11 'right arm, right leg' 12 'left arm, left leg' 13 'both legs' 14 'right arm, both legs' 15 'left arm, both legs' 16 'neck, torso & right arm' 17 'neck, torso & left arm' 18 'neck, torso & right leg' 19 'neck & both arms' 20 'neck & both legs' 21 'torso, right arm' 22 'torso, left arm' 23 'torso, right leg' 24 'torso, left arm, right leg' 25 'torso, left arm, left leg' 26 'torso, both arms' 27 'torso, both legs' 28 'torso, both arms, left leg' 29 'torso, both arms, both legs' 30 'neck & torso & both arms' 31 'neck & torso & both legs' 32 'neck, torso, right arm, right leg' 33 'neck, torso, left arm, right leg'

Items	Item Categories
	34 'both arms, left leg' 35 'both arms & both legs' 36 'neck, torso, both arms & right leg' 37 'neck, torso, both arms & left leg' 38 'neck, both arms & both legs' 39 'neck, torso, both arms & both legs'
39. Muscle tone at activity.	1 'normal' 2 'neck (slightly/distinctly increased/decreased)' 3 'torso (slightly/distinctly increased/decreased)' 4 'right arm (slightly/distinctly increased/decreased)' 5 'left arm (slightly/distinctly increased/decreased)' 6 'right leg (slightly/distinctly increased/decreased)' 7 'left leg (slightly/distinctly increased/decreased)' 8 'neck & torso' 9 'neck & right arm' 10 'both arms' 11 'right arm, right leg' 12 'left arm, right leg' 13 'left arm, left leg' 14 'both legs' 15 'both arms, right leg' 16 'right arm, both legs' 17 'left arm, both legs' 18 'neck, torso & right arm' 19 'neck & both arms' 20 'neck & both legs'

Items	Item Categories
	21 'neck, right arm, right leg' 22 'neck, left arm, right leg' 23 'neck, torso, left arm, left leg' 24 'torso, right arm' 25 'torso, left arm' 26 'torso, right arm, right leg' 27 'torso, both arms' 28 'torso, both legs' 29 'torso, both arms, left leg' 30 'torso, right arm, both legs' 31 'torso, left arm, both legs' 32 'torso, both arms, both legs' 33 'neck & torso & both arms' 34 'neck & torso & both legs' 35 'neck, torso, right arm, right leg' 36 'both arms, left leg' 37 'both arms & both legs' 38 'neck, torso, both arms & right leg' 39 'neck, torso, right arm, both legs' 40 'neck, torso, left arm, both legs' 41 'neck, both arms & both legs' 42 'neck, torso, both arms & both legs'
40. Peripheral muscle paresis.	1 'normal' 2 'muscle paresis'
41. Muscle strength.	1 'normal'

Items	Item Categories
	2 'slight muscle weakness' 3 'distinct muscle weakness'
42. Joint mobility.	1 'normal' 2 'increased' 3 'contractures' 4 'limited by other reason' 5 'increased & limited by other reason' 6 'contractures & other'
Reflexes	
43. Knee jerk	1 'immediate, moderate response right & left' 2 'slightly or distinctly increased right & left' 3 'decreased right & left' 4 'broadened right & left' 5 'slightly or distinctly increased & broadened right & left' 6 'absent right & left' 7 'immediate right, slightly or distinctly increased left' 8 'immediate right, decreased left' 9 'immediate right, slightly or distinctly increased & broadened left' 10 'immediate right, absent left' 11 'slightly or distinctly increased right, immediate left' 12 'slightly or distinctly increased right, decreased left' 13 'slightly or distinctly increased right, slightly or distinctly increased & broadened left' 14 'decreased right, immediate left' 15 'decreased right, slightly or distinctly increased left' 16 'decreased right, absent left' 17 'slightly or distinctly increased & broadened right, slightly or distinctly increased left'

Items	Item Categories
	18 'slightly or distinctly increased & broadened right, broadened left' 19 'absent right, immediate left' 20 'absent right, decreased left' 21 'immediate right, unclear or missing left' 22 'slightly or distinctly increased right, unclear or missing left' 23 'unclear or missing right, immediate left' 24 'unclear or missing right, slightly or distinctly increased left' 25 'unclear or missing right, decreased left' 26 'unclear or missing right, broadened left' 27 'unclear or missing right, slightly or distinctly increased & broadened left' 28 'unclear or missing right, absent left'
44. Achilles tendon	1 'immediate, moderate response right & left' 2 'slightly or distinctly increased right & left' 3 'decreased right & left' 4 'broadened right & left' 5 'slightly or distinctly increased & broadened right & left' 6 'absent right & left' 7 'immediate right, slightly or distinctly increased left' 8 'immediate right, decreased left' 9 'immediate right, slightly or distinctly increased & broadened left' 10 'immediate right, absent left' 11 'slightly or distinctly increased right, immediate left' 12 'decreased right, immediate left' 13 'decreased right, slightly or distinctly increased left' 14 'decreased right, absent left' 15 'absent right, immediate left'

Items	Item Categories
	16 'absent right, decreased left' 17 'immediate right, unclear or missing left' 18 'slightly or distinctly increased right, unclear or missing left' 19 'decreased right, unclear or missing left' 20 'absent right, unclear or missing left' 21 'unclear or missing right, immediate left' 22 'unclear or missing right, slightly or distinctly increased left' 23 'unclear or missing right, decreased left' 24 'unclear or missing right, broadened left' 25 'unclear or missing right, slightly or distinctly increased & broadened left' 26 'unclear or missing right, absent left'
45. Biceps tendon	1 'immediate, moderate response right & left' 2 'slightly or distinctly increased right & left' 3 'decreased right & left' 4 'broadened right & left' 5 'slightly or distinctly increased & broadened right & left' 6 'absent right & left' 7 'immediate right, slightly or distinctly increased left' 8 'immediate right, decreased left' 9 'immediate right, slightly or distinctly increased & broadened left' 10 'immediate right, absent left' 11 'slightly or distinctly increased right, immediate left' 12 'slightly or distinctly increased right, slightly or distinctly increased & absent left' 13 'decreased right, immediate left' 14 'decreased right, slightly or distinctly increased left' 15 'decreased right, absent left'

Items	Item Categories
	16 'absent right, immediate left' 17 'absent right, decreased left' 18 'immediate right, unclear or missing left' 19 'slightly or distinctly increased right, unclear or missing left' 20 'unclear or missing right, immediate left' 21 'unclear or missing right, slightly or distinctly increased left' 22 'unclear or missing right, absent left'
46. Foot clonus	1 'no' 2 'yes, right' 3 'yes, left' 4 'yes, right & left'
Sensorimotor - pulling up to sit	
47. Pulling up to sit, head control.	1 'normal, stable in body lateral axis' 2 'beginning' 3 'absent' 4 'opisthotonus' 5 'beginning & opisthotonus' 6 'beginning & other' 7 'absent & opisthotonus' 8 'opisthotonus & other'
48. Pulling up to sit, posture of arms.	1 'normal, symmetric, slightly bent' 2 'bending absent right' 3 'bending absent left' 4 'strong bending right' 5 'strong bending left' 6 'bending absent right & left'

Items	Item Categories
	7 'strong bending right & left' 8 'bending absent left & other' 9 'strong bending left & other' 10 'bending absent right/left & other' 11 'strong bending right/left & other'
49. Pulling up to sit, posture of legs.	1 'normal, symmetric, slightly bent hips, abducted' 2 'hypertone stretching right' 3 'hypertone stretching left' 4 'hips weak right' 5 'hips weak left' 6 'hypertone stretching right & left' 7 'hips weak right & left' 8 'hypertone stretching left & hips weak right' 9 'hypertone stretching right & other' 10 'hypertone stretching left & other' 11 'hips weak right & other' 12 'hypertone stretching right/left & other' 13 'hips weak right/left & other'
50. Supported or independent sitting, posture.	1 'normal, symmetric, hips bent 90 degrees, stable head control, torso up in axis.' 2 'asymmetry: head inclined or turned (right or left & preferred or all the time) or body weight (right or left pelvis)' 3 'beginning or absent posture retention: head control or torso straightening' 4 'abnormal posture: thorathic spine kyphotic/convex (left/right); lumbar spine kyphotic/lordosis; torso/hip extension' 5 'asymmetry & beginning or absent posture retention' 6 'asymmetry & abnormal posture'

Items	Item Categories
	7 'asymmetry & other' 8 'beginning or absent posture retention & abnormal posture' 9 'beginning or absent posture retention & other' 10 'abnormal posture & other' 11 'asymmetry, beginning or absent posture retention & abnormal posture' 12 'asymmetry & beginning or absent posture retention & other' 13 'asymmetry, abnormal posture & other' 14 'beginning or absent posture retention, abnormal posture & other' 15 'asymmetry, beginning or absent posture retention, abnormal posture & other'
Sensorimotor – vertical, tilted and horizontal suspension, prone position	
51. Vertical suspension, posture.	1 'normal, symmetric, relaxed, variable' 2 'stretching, adduction, rotation legs, plantar flexion feet or limp hanging legs' 3 'torso posture convex (left or right)' 4 'arms strongly bent, pronated or extended right or left (slightly or distinctly)' 5 'legs/feet & torso' 6 'legs/feet & arms' 7 'legs/feet & other' 8 'torso & arms' 9 'torso & other' 10 'arms & other' 11 'legs/feet & torso & arms' 12 'legs/feet & torso & other' 13 'legs/feet & arms& other' 14 'torso & arms & other' 15 'legs/feet & torso & arms & other'

Items	Item Categories
52. Vertical suspension, spontaneous motor function.	1 'normal' 2 'monoform kicking right' 3 'monoform kicking left' 4 'synchronous leg flection and extension movements' 5 'monoform kicking right & left' 6 'monoform kicking right & synchronous leg flection and extension movements' 7 'monoform kicking left & synchronous leg flection and extension movements' 8 'monoform kicking right and left & synchronous leg flection and extension movements'
53. Vertical suspension, muscle tone	1 'normal, moderate' 2 'adductor activity, right or left (slightly/distinctly)' 3 'arms hypertonic, right or left (slightly/distinctly)' 4 'arms hypotonic, right or left' 5 'torso hypotonic' 6 'legs hypotonic, right or left' 7 'adductor activity & arms hypertonic' 8 'adductor activity & arms hypotonic' 9 'adductor activity & torso hypotonic' 10 'adductor activity & legs hypotonic' 11 'adductor activity & other' 12 'arms hypertonic & torso hypotonic' 13 'arms hypertonic & legs hypotonic' 14 'arms hypertonic & other' 15 'arms hypotonic & torso hypotonic' 16 'arms hypotonic & legs hypotonic' 17 'torso hypotonic & legs hypotonic' 18 'torso hypotonic & other'

Items	Item Categories
	19 'adductor activity & arms hypertonic & torso hypotonic' 20 'adductor activity & arms hypertonic & other' 21 'adductor activity & arms hypotonic & torso hypotonic' 22 'arms hypertonic & torso hypotonic & legs hypotonic' 23 'arms hypotonic & torso hypotonic & legs hypotonic' 24 'arms hypotonic & torso hypotonic & other' 25 'arms hypotonic & legs hypotonic & other' 26 'adductor activity & arms hypotonic & torso hypotonic & legs hypotonic' 27 'adductor activity & arms hypotonic & torso hypotonic & other' 28 'adductor activity & arms hypertonic & torso hypotonic & legs hypotonic'
54. Tilted suspension, head raising.	1 'normal' 2 'beginning whilst tilting right' 3 'beginning whilst tilting left' 4 'absent whilst tilting right' 5 'absent whilst tilting left' 6 'beginning whilst tilting right & left' 7 'absent whilst tilting right & left' 8 'beginning whilst tilting right & absent whilst tilting left' 9 'beginning whilst tilting left & absent whilst tilting right' 10 'beginning whilst tilting right and left & other' 11 'absent whilst tilting right and left & other' 12 'beginning whilst tilting right & other' 13 'beginning whilst tilting left & other' 14 'absent whilst tilting left & other' 15 'beginning whilst tilting right, absent whilst tilting left & other'

Items	Item Categories
55. Tilted suspension, thoracic spine raising.	1 'normal' 2 'beginning whilst tilting right' 3 'beginning whilst tilting left' 4 'absent whilst tilting right' 5 'absent whilst tilting left' 6 'beginning whilst tilting right & left' 7 'absent whilst tilting right & left' 8 'beginning whilst tilting right & absent whilst tilting left' 9 'beginning whilst tilting left & absent whilst tilting right' 10 'beginning whilst tilting right and left & other' 11 'absent whilst tilting right and left & other' 12 'beginning whilst tilting right & other' 13 'beginning whilst tilting left & other' 14 'beginning whilst tilting left, absent whilst tilting right & other'
56. Horizontal suspension, posture.	1 'normal' 2 'convex right' 3 'convex left' 4 'torso hypertonic' 5 'torso limp' 6 'convex right & torso hypertonic' 7 'convex right & torso limp' 8 'convex left & torso hypertonic' 9 'convex left & torso limp' 10 'convex right & other' 11 'convex left & other' 12 'torso hypertonic & other'

Items	Item Categories
	13 'torso limp & other' 14 'convex right, torso limp & other' 15 'convex left, torso limp & other' 16 'convex left, torso hypertonic & other'
57. Turning from supine to prone, passive turning.	1 'normal/promptly' 2 'beginning right' 3 'beginning left' 4 'absent right' 5 'absent left' 6 'beginning right & left' 7 'absent right & left' 8 'beginning right & absent left' 9 'beginning left & absent right' 10 'beginning right, left & other' 11 'beginning right, absent left & other' 12 'absent right, left & other' 13 'beginning right & other' 14 'beginning left & other' 15 'absent left & other'
58. Prone position, posture.	1 'normal' 2 ' instable' 3 'cannot hold posture' 4 'body weight on right side' 5 'body weight on left side' 6 'torso convex right' 7 'torso convex left'

Items	Item Categories
	8 'arm position asymmetric' 9 'leg position asymmetric' 10 'instable & body weight on right side' 11 'instable & body weight on left side' 12 'instable & torso convex right or left' 13 'instable & arm or leg position asymmetric' 14 'instable, body weight on both sides & torso convex right or left' 15 'instable, body weight on both sides & arm or leg position asymmetric' 16 'instable, torso convex right or left & arm or leg position asymmetric' 17 'instable, body weight on both sides, torso convex right or left & arm or leg position asymmetric' 18 'cannot hold posture & body weight on both sides' 19 'cannot hold posture, torso convex right or left' 20 'cannot hold posture & arm or leg position asymmetric' 21 'cannot hold posture, body weight on both sides & torso convex right or left' 22 'cannot hold posture, body weight on both sides & arm or leg position asymmetric' 23 'cannot hold posture, torso convex right or left & arm or leg position asymmetric' 24 'cannot hold posture, body weight on both sides, torso convex right or left & arm or leg position asymmetric' 25 'body weight on both sides & torso convex right or left' 26 'body weight on both sides & arm or leg position asymmetric' 27 'torso convex right or left & arm or leg position asymmetric' 28 'body weight on both sides, torso convex right or left & arm or leg position asymmetric' 29 'arm & leg position asymmetric'
59. Prone position, head raising.	1 'normal' 2 'briefly'

Items	Item Categories
	3 'briefly & other' 4 'absent' 5 'absent & other'
Tactile-kinaesthetic response	
60. Response to touch.	1 'normal (neutral, comfortable)' 2 'slight resistance/scared' 3 'slight resistance/scared & other' 4 'distinct resistance/scared' 5 'no response'
61. Response to position changes on surface.	1 'normal (neutral, adjusted posture)' 2 'limp, passive' 3 'rigid slightly' 4 'rigid distinctly' 5 'falls apart (spontaneous moro response), slightly' 6 'falls apart (spontaneous moro response), distinctly' 7 'limp, passive & rigid distinctly' 8 'limp, passive & falls apart (spontaneous moro response), slightly' 9 'limp, passive & falls apart (spontaneous moro response), distinctly' 10 'rigid & falls apart (spontaneous moro response), slightly' 11 'rigid slightly & falls apart (spontaneous moro response) distinctly' 12 'rigid, slightly & other' 13 'rigid & falls apart (spontaneous moro response), distinctly' 14 'rigid distinctly & falls apart (spontaneous moro response) slightly' 15 'falls apart (spontaneous moro response), slightly & other'
62. Response to position changes in space.	1 'normal (neutral, adjusted posture)' 2 'limp'

Items	Item Categories
	3 'rigid slightly' 4 'rigid distinctly' 5 'signs of fear' 6 'limp & rigid slightly' 7 'limp & rigid distinctly' 8 'limp & signs of fear' 9 'limp & other' 10 'rigid slightly & signs of fear' 11 'rigid distinctly & signs of fear' 12 'signs of fear & other' 13 'limp, rigid slightly & signs of fear' 14 'limp, signs of fear & other' 15 'rigid slightly, signs of fear & other' 16 'rigid distinctly, signs of fear & other'
63. Tactile-kinaesthetic, response while carried on arm.	1 'normal (snuggles up, some posture control)' 2 'limp' 3 'rigid slightly' 4 'rigid distinctly' 5 'signs of fear' 6 'limp & rigid slightly' 7 'limp & rigid distinctly' 8 'limp & signs of fear' 9 'rigid slightly & signs of fear' 10 'rigid distinctly & signs of fear' 11 'signs of fear & other' 12 'limp, rigid slightly & other'

Note. For the computation of the motor functioning score all items were categorised into ‘within’ (=1) and ‘outside the normal range’ (>1).

Appendix C. Motor and Neurological Items at 20 months (All Categories).

Items	Item Categories
Fine motor: oculomotor, orofacial	
1. Face muscles.	1 'normal' 2 'weak paresis right & left' 3 'hypertonic right & left' 4 'hypotonic right & left' 5 'uncoordinated movements' 6 'weak paresis left' 7 'hypotonic right' 8 'hypertonic right & left and uncoordinated movements' 9 'hypotonic right & left and uncoordinated movements' 10 'hypotonic right & left and other' 11 'hypotonic right & left, uncoordinated movements & other' 12 'weak paresis left & uncoordinated movements' 13 'uncoordinated movements & other'
2. Facial expression.	1 'normal, variable, age-appropriate differentiation' 2 'poor facial expression' 3 'poor facial expression and other'
3. Mouth and tongue movement.	1 'normal' 2 'uncoordinated' 3 'uncoordinated & other'
4. Eating procedure	1 'normal' 2 'problems'
5. Eyes, fixation.	1 'normal, immediate, > 5 sec' 2 'unclear'

Items	Item Categories
	3 'absent'
6. Eyes, eye contact.	1 'normal' 2 'short' 3 'unclear' 4 'absent' 5 'short & other'
7. Eyes, eye position at rest.	1 'normal' 2 'strabismus right convergent' 3 'strabismus right divergent' 4 'strabismus left convergent' 5 'strabismus left divergent' 6 'constant' 7 'inconstant' 8 'strabismus right & left convergent' 9 'strabismus right & left divergent' 10 'strabismus right convergent & constant' 11 'strabismus right convergent & inconstant' 12 'strabismus right divergent & constant' 13 'strabismus right divergent & inconstant' 14 'strabismus left convergent & constant' 15 'strabismus left convergent & inconstant' 16 'strabismus left divergent & constant' 17 'strabismus left divergent & inconstant' 18 'strabismus right & left convergent & constant' 19 'strabismus right & left convergent & inconstant' 20 'strabismus right & left divergent & constant'

Items	Item Categories
	21 'strabismus right & left divergent & inconstant' 22 'strabismus right divergent & left convergent & inconstant'
8. Eyes, eye position at fixation.	1 'normal (Hirschberg test), parallel' 2 'right slightly lateral' 3 'right distinctly lateral' 4 'right slightly medial' 5 'right distinctly medial' 6 'left slightly lateral' 7 'left distinctly lateral' 8 'left slightly medial' 9 'left distinctly medial' 10 'right & left slightly lateral' 11 'right & left distinctly lateral' 12 'right & left slightly medial' 13 'right & left distinctly medial' 14 'right slightly & left distinctly lateral' 15 'right distinctly & left slightly lateral' 16 'right slightly lateral & left distinctly medial' 17 'right slightly medial & left slightly lateral'
9. Eyes, pupils (shape)	1 'normal, symmetric, round parallel' 2 'narrow right and left' 3 'wide right and left' 4 'wide right' 5 'narrow left' 6 'wide left and other'

Items	Item Categories
10. Eyes, pupil reaction to light.	1 'normal, symmetric, immediate' 2 'delayed right and left' 3 'delayed right' 4 'delayed left' 5 'absent right and left' 6 'absent right' 7 'absent left' 8 'delayed right & absent left' 9 ' delayed right & other' 10 'delayed left & other' 11 'delayed right and left & other'
11. Eyes, pupil reaction to convergence	1 'normal, symmetric, immediate' 2 'delayed right and left' 3 'delayed right' 4 'delayed left' 5 'absent right and left' 6 'absent right' 7 'absent left' 8 'delayed right & absent left' 9 ' delayed right & other'
12. Eyes, forced/abnormal head posture during fixation.	1 'normal' 2 'abnormal posture'
13. Eyes, following movement to full extent	1 'normal, no eye muscle paresis' 2 'right eye restricted to right' 3 'right eye restricted to left'

Items	Item Categories
	4 'left eye restricted to right' 5 'left eye restricted movement to left' 6 'right eye restricted to right & left' 7 'right eye restricted to right & left eye restricted to left' 8 'right eye restricted & not over middle line to right' 9 'right & left eye restricted to left' 10 'left eye restricted to left & upward' 11 'left eye restricted & not over middle line to left' 12 'right eye restricted to right, up & down' 13 'left eye restricted to left, up & down' 14 'left eye restricted to left, down & not over middle line left' 15 'right eye restricted to right, left, up and down' 16 'right eye restricted to right & up, left eye to left & up' 17 'right eye restricted to right, left eye to left & not over middle line right & left' 18 'left eye restricted to right & left, up & down' 19 'right & left eye restricted to right, left, up and down' 20 'right & left eye restricted to right, left, up and down & not over middle line right & left'
14. Eyes, following movement, smooth.	1 'normal, smooth' 2 'uneven' 3 'slightly uncoordinated' 4 'distinctly uncoordinated' 5 'uneven & slightly uncoordinated' 6 'uneven & distinctly uncoordinated' 7 'slightly uncoordinated & other' 8 'distinctly uncoordinated & other'

Items	Item Categories
15. Eyes, nystagmus.	1 'normal, no nystagmus' 2 'at rest: slightly right' 3 'at rest: distinctly right & left' 4 'at rest: slightly right & left, horizontal' 5 'at rest: distinctly right & left, horizontal' 6 'at rest: slightly right & left, other' 7 'at rest: distinctly right, horizontal & vertical' 8 'whilst fixation: slightly right & left' 9 'whilst fixation: distinctly right & left' 10 'whilst fixation: distinctly right, horizontal' 11 'whilst fixation: distinctly right, other' 12 'whilst fixation: slightly left, horizontal' 13 'whilst fixation: slightly right & left, horizontal' 14 'whilst fixation: distinctly right & left, horizontal' 15 'whilst fixation: distinctly right & left, horizontal, other' 16 'at rest: distinctly right & left, horizontal; whilst fixation: other' 17 'at rest & whilst fixation: distinctly right & left' 18 'at rest & whilst fixation: slightly right & left, horizontal' 19 'at rest: slightly right & left, horizontal; whilst fixation: distinctly right & left, horizontal' 20 'at rest & whilst fixation: distinctly right & left, horizontal'
16. Eyes, eyelid flutter.	1 'normal, no eye lid flutter' 2 'with eye movement' 3 'with noise' 4 'with change of position' 5 'with noise & change of position' 6 'with noise & other'

Items	Item Categories
	7 'with eye movement, noise & change of position' 8 'with noise, change of position & other'
17. Eyes, vision, with orientating assessment.	1 'normal' 2 'unclear impaired right & left' 3 'certain impaired right & left' 4 'unclear absent right & left' 5 'certain absent right & left' 6 'unclear impaired right' 7 'unclear impaired left' 8 'certain impaired right' 9 'certain impaired left' 10 'certain absent right' 11 'certain absent left' 12 'unclear impaired right & certain impaired left' 13 'unclear impaired right & certain absent left' 14 'certain impaired right & unclear impaired left' 15 'certain impaired right & certain absent left' 16 'unclear absent right & certain absent left'
18. Eyes, glare sensitivity, assessed by examiner.	1 'normal, no glare sensitivity' 2 'glare sensitive'
19. Ears, hearing, observed during examination.	1 'normal, can hear moderately loud speech' 2 'unclear' 3 'absent'
Gross motor: sitting	

Items	Item Categories
20. Sitting, posture during independent or supported sitting	1 'normal' 2 'any problems'
21. Sitting, posture retention/balance: head.	1 'yes'
22. Sitting, posture retention/balance: torso.	1 'normal' 2 'poor control' 3 'no control' 4 'poor control & other' 5 'no control & other'
23. Sitting, posture retention/balance: hips.	1 'normal' 2 'poor control' 3 'no control' 4 'poor control & other' 5 'no control & other'
24. Sitting, posture retention/balance: lateral support reaction.	1 'normal' 2 'right poor' 3 'right absent' 4 'left poor' 5 'right hand mostly closed' 6 'left hand mostly closed' 7 'right & left poor' 8 'right & left absent' 9 'right absent & left poor' 10 'right poor & left absent' 11 'right poor & other' 12 'left poor & other'

Items	Item Categories
	13 'right poor & hand mostly closed' 14 'left poor & hand mostly closed' 15 'left absent & hand mostly closed' 16 'left absent & hand always closed' 17 'right & left hand mostly closed' 18 'right & left poor & right hand mostly closed' 19 'right & left poor & left hand mostly closed' 20 'right & left poor & other' 21 'right absent & left poor & right hand mostly closed' 22 'right poor & left absent & left hand mostly closed' 23 'right & left absent & right hand mostly closed' 24 'right & left poor, right & left hand mostly closed' 25 'right & left absent, right & left hand mostly closed' 26 'right & left absent, right mostly & left hand always closed' 27 'right & left absent, right & left hand always closed'
25. Sitting, posture retention/balance: movement transitions (from lying to sitting, from sitting to standing, from supine to prone and in reverse).	1 'normal/fluent' 2 'clumsy' 3 'impaired by hypertonia' 4 'sudden loss of tonus/strength' 5 ' clumsy & impaired by hypertonia' 6 'clumsy & sudden loss of tonus/strength' 7 'clumsy & other' 8 'impaired by hypertonia & sudden loss of tonus/strength' 9 'impaired by hypertonia & other' 10 'sudden loss of tonus/strength & other'

Items	Item Categories
26. Sitting, posture retention/balance: pulling up to sit, head control.	1 'normal/head is stable' 2 'poor head control' 3 'no head control'
Fine motor	
27. Fine motor function, quantity	1 'normal' 2 'increased' 3 'decreased'
28. Fine motor function, variable and economic movements.	1 'normal/yes' 2 'grasping, hand too wide open (right or left)' 3 'fingers/hands not adjusted to object (right or left)' 4 'monoformous movements' 5 'mostly synchronous movements' 6 'mostly palmar grasping (right or left)' 7 'no grasping (right or left)' 8 'hands too wide open & not adjusted to object' 9 'hands too wide open & monoformous movements' 10 'hands too wide open & mostly synchronous movements' 11 'hands too wide open & palmar grasping' 12 'hands too wide open & no grasping' 13 'hand too wide open & other' 14 'not adjusted to object & monoformous movements' 15 'not adjusted to object & palmar grasping' 16 'not adjusted to object & other' 17 'monoformous & mostly synchronous movements' 18 'monoformous movements & mostly palmar grasping' 19 'monoformous movements & no grasping'

Items	Item Categories
	20 'monoformous movements & other' 21 'mostly synchronous movements & no grasping' 22 'palmar grasping & no grasping' 23 'palmar grasping & other' 24 'no grasping & other' 25 'hands too wide open, not adjusted to object & monoformous movements' 26 'hands too wide open, not adjusted to object & palmar grasping' 27 'hands too wide open, not adjusted to object & no grasping' 28 'hands too wide open, not adjusted to object & other' 29 'hands too wide open, monoformous movements & palmar grasping' 30 'hands too wide open, mostly synchronous movements & palmar grasping' 31 'not adjusted to object, monoformous movements & palmar grasping' 32 'not adjusted to object, monoformous & mostly synchronous movements' 33 'not adjusted to object & palmar grasping & other' 34 'not adjusted to object, monoformous movements & other' 35 'not adjusted to object, no grasping right & other' 36 'monoformous, mostly synchronous movements & palmar grasping' 37 'monoformous, palmar grasping & other' 38 'hands too wide open, not adjusted to object, monoformous & mostly synchronous movements' 39 'hands too wide open, not adjusted to object, monoformous movements & palmar grasping' 40 'hands too wide open, not adjusted to object, monoformous movements & no grasping' 41 'hands too wide open, not adjusted to object, mostly synchronous movements & palmar grasping' 42 'hands too wide open, not adjusted to object, palmar grasping & other' 43 'hands too wide open, monoformous movements, palmar grasping & other'

Items	Item Categories
	44 'not adjusted to object, monoformous movements, palmar grasping & other' 45 'not adjusted to object, monoformous, mostly synchronous movements & palmar grasping' 46 'hands too wide open, not adjusted to object, monoformous, mostly synchronous movements & palmar grasping' 47 'hands too wide open, not adjusted to object, monoformous movements, palmar grasping & other' 48 'hands too wide open, not adjusted to object, monoformous movements, palmar and no grasping & other' 49 'not adjusted to object, monoformous movements, palmar and no grasping & other'
29. Fine motor function, movements symmetric, fluent etc.	1 'normal, fluent, adjusted' 2 'abrupt movements right or left (slightly/distinctly)' 3 'inadequate strength right or left (increased/decreased)' 4 'inadequate speed right or left (increased/decreased)' 5 'hypertonia right or left (slightly/distinctly)' 6 'dystonia right or left (slightly/distinctly)' 7 'intention tremor right or left (slightly/distinctly)' 8 'contralateral hypertonic fisting right or left (slightly/distinctly)' 9 'abrupt movements & inadequate strength' 10 'abrupt movements & inadequate speed' 11 'abrupt movements & contralateral hypertonic fisting' 12 'abrupt movements & other' 13 'inadequate strength & speed' 14 'inadequate strength & hypertonia' 15 'inadequate strength & intention tremor' 16 'inadequate strength & contralateral hypertonic fisting' 17 'inadequate strength & other'

Items	Item Categories
	18 'inadequate speed & hypertonia'
	19 'inadequate speed & dystonia'
	20 'inadequate speed & intention tremor'
	21 'inadequate speed & other'
	22 'hypertonia & dystonia'
	23 'hypertonia & intention tremor'
	24 'hypertonia & contralateral hypertonic fisting'
	25 'hypertonia & other'
	26 'dystonia & contralateral hypertonic fisting'
	27 'contralateral hypertonic fisting & other'
	28 'abrupt movements & inadequate strength & speed'
	29 'inadequate strength & speed, hypertonia'
	30 'inadequate strength & speed & other'
	31 'inadequate speed, hypertonia & other'
	32 'inadequate speed, hypertonia & dystonia'
	33 'inadequate strength, intention tremor & other'
	34 'inadequate strength, hypertonia & intention tremor'
	35 'inadequate speed, hypertonia & contralateral hypertonic fisting'
	36 'inadequate strength, hypertonia & contralateral hypertonic fisting'
	37 'inadequate strength, intention tremor & contralateral hypertonic fisting'
	38 'inadequate strength, contralateral hypertonic fisting & other'
	39 'inadequate strength & speed & contralateral hypertonic fisting'
	40 'hypertonia, contralateral hypertonic fisting & other'
	41 'hypertonia, dystonia & contralateral hypertonic fisting'
	42 'abrupt movements, inadequate speed & other'
	43 'abrupt movements, inadequate strength & hypertonia'

Items	Item Categories
	44 'abrupt movements, inadequate speed & hypertonia' 45 'abrupt movements, inadequate strength & intention tremor' 46 'abrupt movements, hypertonia & contralateral hypertonic fisting' 47 'abrupt movements, inadequate strength & contralateral hypertonic fisting' 48 'abrupt movements, inadequate strength & speed, hypertonia' 49 'inadequate strength & speed, hypertonia, contralateral hypertonic fisting' 50 'inadequate strength, hypertonia, contralateral hypertonic fisting & other' 51 'abrupt movements, inadequate speed, hypertonia & contralateral hypertonic fisting' 52 'abrupt movements, inadequate speed, hypertonia & other' 53 'abrupt movements, inadequate strength, hypertonia & intention tremor' 54 'abrupt movements, inadequate strength & speed & intention tremor' 55 'abrupt movements, inadequate strength & speed & contralateral hypertonic fisting' 56 'abrupt movements, inadequate strength, hypertonia & contralateral hypertonic fisting' 57 'abrupt movements, inadequate strength & speed, hypertonia & contralateral hypertonic fisting' 58 'abrupt movements, inadequate strength & speed, hypertonia & other' 59 'abrupt movements, inadequate strength & speed, hypertonia & intention tremor' 60 'abrupt movements, inadequate strength, hypertonia, dystonia & contralateral hypertonic fisting' 61 'abrupt movements, inadequate strength & speed, dystonia & other' 62 'abrupt movements, inadequate strength & speed, dystonia, intention tremor & contralateral hypertonic fisting'
30. Fine motor function, co-movements.	1 'normal/no co-movements' 2 'contralateral mirror movements: slightly/distinctly right' 3 'contralateral mirror movements: slightly/distinctly left' 4 'contralateral close of hand: slightly/distinctly right'

Items	Item Categories
	5 'contralateral close of hand: slightly/distinctly left' 6 'contralateral mirror movements: right & left' 7 'contralateral close of hand: right & left' 8 'contralateral mirror movements right & close of hand right' 9 'contralateral mirror movements right & close of hand left' 10 'contralateral mirror movements right & other' 11 'contralateral mirror movements left & close of hand left' 12 'contralateral close of hand left & other' 13 'contralateral mirror movements right and left & close of hand right' 14 'contralateral mirror movements right and left & close of hand left' 15 'contralateral mirror movements right and left & other' 16 'contralateral mirror movements right & close of hand right and left' 17 'contralateral mirror movements left & close of hand right and left' 18 'contralateral mirror movements left, close of hand right & other' 19 'contralateral close of hand right and left & other' 20 'contralateral mirror movements & close of hand: right & left' 21 'contralateral mirror movements right and left, close of hand left & other'
Gross motor: standing	
31. Standing, posture	1 'normal' 2 'any problems'
32. Standing, posture retention	1 'normal/stable balance' 2 'balance slightly decreased' 3 'balance distinctly decreased'
Gross motor: walking	

Items	Item Categories
33. Walking, quality: economic, rhythmic, automated, variable.	1 'yes, normal' 2 'slightly poor' 3 'distinctly poor' 4 'monoformous' 5 'slightly poor & monoformous' 6 'distinctly poor & monoformous'
34. Walking, movements fluent, stable, harmonious.	1 'yes, normal' 2 'clumsy (slightly/distinctly)' 3 'jerkily (slightly/distinctly)' 4 'ataxic (slightly/distinctly)' 5 'hypertonic right (slightly/distinctly)' 6 'hypertonic left (slightly/distinctly)' 7 'clumsy & jerkily' 8 'clumsy & ataxic' 9 'clumsy & hypertonic right' 10 'clumsy & hypertonic left' 11 'clumsy & other' 12 'jerkily & ataxic' 13 'jerkily & hypertonic right' 14 'jerkily & hypertonic left' 15 'jerkily & other' 16 'ataxic & hypertonic right' 17 'ataxic & other' 18 'hypertonic right & left' 19 'hypertonic right & other' 20 'clumsy, jerkily & ataxic'

Items	Item Categories
	21 'clumsy, hypertonic right & left' 22 'jerkily, hypertonic right & left' 23 'clumsy, jerkily & hypertonic right' 24 'clumsy, jerkily & hypertonic left' 25 'clumsy, jerkily & other' 26 'clumsy, ataxic & hypertonic right' 27 'clumsy, ataxic & other' 28 'clumsy, jerkily, hypertonic right & left' 29 'clumsy, jerkily, hypertonic right & other' 30 'jerkily, ataxic, hypertonic right & left' 31 'clumsy, jerkily, ataxic, hypertonic right & left' 32 'clumsy, jerkily, hypertonic right & left & other'
35. Walking, moderate pace, variable	1 'normal (moderate pace, variable)' 2 'slowed' 3 'can only run' 4 'slowed & other' 5 'can only run & other'
36. Walking, posture	1 'normal' 2 'any problems'
37. Walking, posture retention: head.	1 'yes, stable' 2 'slightly poor' 3 'distinctly poor'
38. Walking, posture retention: torso.	1 'yes, stable' 2 'slightly poor' 3 'distinctly poor'

Items	Item Categories
39. Walking, posture retention: pelvis.	1 'yes, stable' 2 'slightly poor' 3 'distinctly poor'
Gross motor: crawling	
40. Crawling, quality: economic, rhythmic, automated, variable.	1 'yes, normal' 2 'slightly poor' 3 'distinctly poor' 4 'monoformous' 5 'slightly poor & monoformous' 6 'distinctly poor & monoformous'
41. Crawling, movements fluent, stable, harmonious.	1 'yes, normal' 2 'jerkily (slightly/distinctly)' 3 'ataxic (slightly/distinctly)' 4 'hypertonic right (slightly/distinctly)' 5 'hypertonic left (slightly/distinctly)' 6 'jerkily & other' 7 'ataxic & other' 8 'hypertonic right & left' 9 ' jerkily & hypertonic right & left' 10 'ataxic & hypertonic right & left' 11 'hypertonic right & left & other'
42. Crawling, posture.	1 'normal, symmetric' 2 'right hand closed (slightly/distinctly)' 3 'left hand closed (slightly/distinctly)' 4 'right arm rotated inward or outward (slightly/distinctly)' 5 ' step length below half torso length'

Items	Item Categories
	6 'right & left hand closed' 7 ' left hand closed & left arm rotated inward or outward' 8 'left hand closed & step length below half torso length' 9 'right & left arm rotated inward or outward' 10 'right arm rotated inward or outward & step length below half torso length' 11 'left arm rotated inward or outward & step length below half torso length' 12 'left arm rotated inward or outward & other.' 13 'step length below half torso length & other' 14 'right and left hand closed & step length below half torso length' 15 'left hand closed & right and left arm rotated inward or outward' 16 'left hand closed, left arm rotated inward or outward & step length below half torso length' 17 'right and left arm rotated inward or outward & step length below half torso length' 18 'right and left arm rotated inward or outward & other' 19 'right and left hand closed & right and left arm rotated inward or outward' 20 'right and left arm rotated inward or outward, step length below half torso length & other' 21 'right and left hand closed, right and left arm rotated inward or outward & step length below half torso length' 22 'right and left hand closed, right and left arm rotated inward or outward & other'
43. Crawling, posture retention: head.	1 'yes, stable above torso axis'
44. Crawling, posture retention: torso.	1 'yes, stable in horizontal axis' 2 'sagging' 3 'sagging & other'
45. Crawling, posture retention: pelvis.	1 'yes, stable in torso axis' 2 'hip of main leg bent >=90 degrees' 3 'pelvis tilts laterally right'

Items	Item Categories
	4 'pelvis tilts laterally left' 5 'hip of main leg bent >=90 degrees & other' 6 'pelvis tilts laterally right & left' 7 'hip of main leg bent >=90 degrees, pelvis tilts laterally right & left' 8 'pelvis tilts laterally right & left & other'
46. Crawling, raising arm to grab an object and not losing balance.	1 'yes, not losing balance while grabbing an object' 2 'difficult due to loss of balance, raising left arm' 3 'difficult due to loss of balance, raising right or left arm' 4 'difficult due to loss of balance, raising right or left arm & other' 5 'difficult due to hypertension, raising right arm' 6 'difficult due to hypertension, raising right or left arm'
Gross motor: movements, muscle tone	
47. Readiness to jump.	1 'normal, immediate, symmetric' 2 'right slow' 3 'right absent' 4 'left slow' 5 'left absent' 6 'right & left slow' 7 'right & left absent' 8 'right slow & left absent' 9 'right absent & left slow' 10 'right slow & other' 11 'left slow & other' 12 'left absent & other' 13 'right & left absent & other'

Items	Item Categories
48. Involuntary movements.	1 'no, normal (during the whole examination)' 2 'fine tremor: during arousal' 3 'fine tremor: constant' 4 'gross tremor: slight' 5 'gross tremor: distinct' 6 'dystonic athetoid movements: partly' 7 'dystonic athetoid movements: always' 8 'choreathetoid movements: partly' 9 'ataxic movements: partly' 10 'cramps' 11 'fine tremor: during arousal & dystonic athetoid movements: partly' 12 'gross tremor: distinct & dystonic athetoid movements: always' 13 'gross tremor: distinct & cramps' 14 'dystonic athetoid movements: partly & ataxic movements: partly' 15 'choreathetoid movements: partly & ataxic movements: partly' 16 'choreathetoid movements: always & cramps' 17 'choreathetoid movements: partly, choreatic movements: always & cramps'
49. Stereotypes.	1 'no, normal' 2 'yes'
50. Muscle tone at rest, obtained from posture.	1 'normal, symmetric, moderate' 2 'slightly decreased' 3 'distinctly decreased' 4 'slightly increased' 5 'distinctly increased'

Items	Item Categories
51. Muscle tone at activity (observed while handling an object, in vertical position and fast running).	1 'normal, moderately strong, adjusted to movement' 2 'right arm increased (slightly/distinctly)' 3 'left arm increased (slightly/distinctly)' 4 'right leg increased (slightly/distinctly)' 5 'left leg increased (slightly/distinctly)' 6 'both arms increased' 7 'both legs increased' 8 'right arm and leg increased' 9 'left arm and leg increased' 10 'right arm increased & spastic' 11 'left arm increased & spastic' 12 'right leg increased & spastic' 13 'left leg increased & spastic' 14 'both legs increased & spastic' 15 'left arm and leg increased & spastic' 16 'right arm and leg increased & spastic' 17 'both arms & right leg increased' 18 'both arms & left leg increased' 19 'right arm & both legs increased' 20 'left arm & both legs increased' 21 'both arms & legs increased' 22 'right arm & both legs increased & spastic' 23 'left arm & both legs increased & spastic' 24 'both legs increased, spastic & dystonic' 25 'both arms & legs increased & spastic' 26 'both arms & legs increased & dystonic'

Items	Item Categories
	27 'both arms & legs increased & spastic & dystonic'
Sensitivity, muscle strength, muscle paresis, joint mobility	
52. Sensitivity (reaction to non-visual contact with a brush on arms, legs, face and tummy).	1 'normal, immediate reaction' 2 'excessive reaction' 3 'delayed reaction' 4 'weak reaction' 5 'no reaction' 6 'abnormal abdominal wall reflex' 7 'delayed & weak reaction' 8 'excessive reaction & abnormal abdominal wall reflex' 9 'delayed reaction & abnormal abdominal wall reflex' 10 'delayed reaction & other' 11 'weak reaction & abnormal abdominal wall reflex' 12 'no reaction & other' 13 'delayed, weak & no reaction' 14 'no reaction, abnormal abdominal wall reflex & other'
53. Muscle strength.	1 'normal' 2 'weakness right leg (slightly/distinctly)' 3 'weakness right arm (slightly/distinctly)' 4 'weakness left arm (slightly/distinctly)' 5 'weakness right torso (slightly/distinctly)' 6 'weakness right neck (slightly/distinctly)' 7 'weakness both legs' 8 'weakness right leg & arm' 9 'weakness right & left torso'

Items	Item Categories
	10 'weakness right & left neck' 11 'weakness right torso & shoulder girdle' 12 'weakness right & left shoulder girdle' 13 'weakness right leg, arm & torso' 14 'weakness both legs & arms' 15 'weakness both legs & right and left torso' 16 'weakness both legs & right and left neck' 17 'weakness both legs & right and left shoulder girdle' 18 'weakness both arms & right and left torso' 19 'weakness right & left torso & shoulder girdle' 20 'weakness right & left neck & shoulder girdle' 21 'weakness right leg, arm, neck & shoulder girdle' 22 'weakness left leg, arm, torso & shoulder girdle' 23 'weakness right leg, arm, torso, neck and shoulder girdle' 24 'weakness left leg, arm, torso, neck & shoulder girdle' 25 'weakness left leg & arm, right & left torso, left shoulder girdle' 26 'weakness both legs, arms & right and left torso' 27 'weakness both legs, right and left torso & shoulder girdle' 28 'weakness both legs, arms & right and left shoulder girdle' 29 'weakness right & left torso, neck & shoulder girdle' 30 'weakness both arms & right and left torso & shoulder gridle' 31 'weakness both legs, arms & right and left torso & shoulder girdle' 32 'weakness right & left leg, torso, neck & shoulder girdle' 33 'weakness both legs, arms, torso, neck and shoulder girdle'
54. Peripheral muscle paresis.	1 'no' 2 'yes'

Items	Item Categories
55. Joint mobility.	1 'normal' 2 'increased' 3 'impaired due to contractures' 4 'increased & contractures' 5 'impaired due to contractures & other'
Reflexes	
56. Knee jerk	1 'immediate, moderate right & left' 2 'decreased right & left' 3 'absent right & left' 4 'increased right & left' 5 'increased with clonus right & left' 6 'reflex zones broadened right & left' 7 'immediate, moderate and reflex zones broadened right & left' 8 'increased and reflex zones broadened right & left' 9 'increased with clonus and reflex zones broadened right & left' 10 'immediate, moderate right & decreased left' 11 'immediate, moderate right & absent left' 12 'immediate, moderate right & increased left' 13 'immediate, moderate right & increased and reflex zones broadened left' 14 'decreased right & immediate, moderate left' 15 'decreased right & absent left' 16 'decreased right & increased left' 17 'absent right & immediate, moderate left' 18 'absent right & decreased left' 19 'absent right & increased left' 20 'increased right & immediate, moderate left'

Items	Item Categories
	21 'increased right & increased with clonus left' 22 'increased right & increased and reflex zones broadened left' 23 'increased right & not testable left' 24 'increased right & missing left' 25 'increased with clonus & increased left' 26 'increased and reflex zones broadened right & immediate, moderate left' 27 'increased and reflex zones broadened right & increased left' 28 'increased and reflex zones broadened right & increased with clonus and reflex zones broadened left' 29 'increased with clonus and reflex zones broadened right & immediate, moderate left' 30 'increased with clonus and reflex zones broadened right & increased left' 31 'immediate, moderate right & not testable left' 32 'decreased right & not testable left' 33 'immediate, moderate right & missing left' 34 'not testable right & increased left' 35 'not testable right & immediate, moderate left' 36 'missing right & immediate, moderate and reflex zones broadened left' 37 'missing right & absent left' 38 'unclear coding right & absent left'
57. Achilles tendon	1 'immediate, moderate right & left' 2 'decreased right & left' 3 'absent right & left' 4 'increased right & left' 5 'increased with clonus right & left' 6 'reflex zones broadened right & left' 7 'immediate, moderate and reflex zones broadened right & left'

Items	Item Categories
	8 'increased and reflex zones broadened right & left' 9 'increased with clonus and reflex zones broadened right & left' 10 'immediate, moderate right & decreased left' 11 'immediate, moderate right & absent left' 12 'immediate, moderate right & increased left' 13 'immediate, moderate right & increased and reflex zones broadened left' 14 'decreased right & immediate, moderate left' 15 'decreased right & absent left' 16 'decreased right & increased left' 17 'absent right & immediate, moderate left' 18 'absent right & decreased left' 19 'absent right & increased left' 20 'increased right & immediate, moderate left' 21 'increased right & increased with clonus left' 22 'increased right & increased and reflex zones broadened left' 23 'increased right & not testable left' 24 'increased right & missing left' 25 'increased with clonus & increased left' 26 'increased and reflex zones broadened right & immediate, moderate left' 27 'increased and reflex zones broadened right & increased left' 28 'increased and reflex zones broadened right & increased with clonus and reflex zones broadened left' 29 'increased with clonus and reflex zones broadened right & immediate, moderate left' 30 'increased with clonus and reflex zones broadened right & increased left' 31 'immediate, moderate right & not testable left' 32 'decreased right & not testable left'

Items	Item Categories
	33 'immediate, moderate right & missing left' 34 'not testable right & increased left' 35 'not testable right & immediate, moderate left' 36 'missing right & immediate, moderate and reflex zones broadened left' 37 'missing right & absent left' 38 'unclear coding right & absent left'
58. Biceps tendon	1 'immediate, moderate right & left' 2 'decreased right & left' 3 'absent right & left' 4 'increased right & left' 5 'increased with clonus right & left' 6 'reflex zones broadened right & left' 7 'immediate, moderate and reflex zones broadened right & left' 8 'increased and reflex zones broadened right & left' 9 'increased with clonus and reflex zones broadened right & left' 10 'immediate, moderate right & decreased left' 11 'immediate, moderate right & absent left' 12 'immediate, moderate right & increased left' 13 'immediate, moderate right & increased and reflex zones broadened left' 14 'decreased right & immediate, moderate left' 15 'decreased right & absent left' 16 'decreased right & increased left' 17 'absent right & immediate, moderate left' 18 'absent right & decreased left' 19 'absent right & increased left' 20 'increased right & immediate, moderate left'

Items	Item Categories
	21 'increased right & increased with clonus left' 22 'increased right & increased and reflex zones broadened left' 23 'increased right & not testable left' 24 'increased right & missing left' 25 'increased with clonus & increased left' 26 'increased and reflex zones broadened right & immediate, moderate left' 27 'increased and reflex zones broadened right & increased left' 28 'increased and reflex zones broadened right & increased with clonus and reflex zones broadened left' 29 'increased with clonus and reflex zones broadened right & immediate, moderate left' 30 'increased with clonus and reflex zones broadened right & increased left' 31 'immediate, moderate right & not testable left' 32 'decreased right & not testable left' 33 'immediate, moderate right & missing left' 34 'not testable right & increased left' 35 'not testable right & immediate, moderate left' 36 'missing right & immediate, moderate and reflex zones broadened left' 37 'missing right & absent left' 38 'unclear coding right & absent left'
Tactile and auditive responses/sensitivity	
59. Reaction to touch.	1 'normal' 2 'slightly decreased sensitivity' 3 'distinctly decreased sensitivity' 4 'slightly increased sensitivity' 5 'distinctly increased sensitivity' 6 "distinct preference for 'firm touch'"

Items	Item Categories
	7 "slightly decreased sensitivity & distinct preference for 'firm touch'" 8 "distinctly decreased sensitivity & distinct preference for 'firm touch'" 9 "distinctly increased sensitivity & distinct preference for 'firm touch'"
60. Pain sensitivity.	1 'normal, yes' 2 'distinctly high' 3 'distinctly low'
61. Response to change of position.	1 'normal, neutral or signs of wellbeing' 2 'slight resistance/startled' 3 'distinct resistance/startled' 4 'hangs limp' 5 'stiffens' 6 'slight resistance/startled & hangs limp' 7 'slight resistance/startled & stiffens' 8 'distinct resistance/startled & hangs limp' 9 'distinct resistance/startled & stiffens' 10 'slight resistance/startled & other' 11 'distinct resistance/startled & other' 12 'distinct resistance/startled, stiffens & other'
62. Quantity of movement (urge to move) during examination.	1 'normal, yes' 2 'increased' 3 'decreased' 4 'increased & other' 5 'decreased & other'
63. Distinct noise sensitivity (according to examiner)	1 'normal, no' 2 'abnormal, yes'

Note. For the computation of the motor functioning score all items were categorised into ‘within’ (=1) and ‘outside the normal range’ (>1).

Appendix D. Motor and Neurological Items at 56 months (All Categories).

Items	Item Categories
Fine motor: oculomotor, orofacial	
1. Face, facial muscles.	1 'normal: symmetric, moderate tone, fluent movement' 2 'paresis right' 3 'paresis left' 4 'hypotonic' 5 'hypertonic' 6 'dyskinesia' 7 'muscle weakness' 8 'paresis right & muscle weakness' 9 'hypotonic & dyskinesia' 10 'hypertonic & dyskinesia' 11'hypotonic & muscle weakness'
2. Face, lips form to whistle.	1 'normal, yes effortlessly' 2 'no'
3. Face, stick out tongue.	1 'normal: holding tongue for 5 sec, calm and symmetric' 2 'cannot hold' 3 'fasciculation' 4 'dyskinesia' 5 'cannot hold & fasciculation' 6 'cannot hold & dyskinesia'
4. Face, tongue movement.	1 'normal, quick, rhythmic and fluent' 2 'with effort, slow' 3 'movement cannot be imitated' 4 'dyskinesia' 5 'dyskinesia & movement cannot be imitated'
5. Face, mouth and tongue motor function.	1 'normal, whilst speaking, chewing, swallowing: harmonic, functional'

Items	Item Categories
	2 'clumsy' 3 'dyskinesia/spasticity' 4 'impossible' 5 'clumsy & dyskinesia/spasticity' 6 'clumsy & impossible' 7 'clumsy, dyskinesia/spasticity & impossible'
6. Eyes, eye position at rest.	1 'normal, parallel' 2 'strabismus right, convergent' 3 'strabismus right, divergent' 4 'strabismus right, inconstant' 5 'strabismus left, convergent' 6 'strabismus left, divergent' 7 'strabismus left, inconstant' 8 'nystagmus at rest' 9 'strabismus right, convergent & constant' 10 'strabismus right, convergent & inconstant' 11 'strabismus right, divergent & constant' 12 'strabismus right, divergent & inconstant' 13 'strabismus left, convergent & constant' 14 'strabismus left, convergent & inconstant' 15 'strabismus left, divergent & constant' 16 'strabismus left, divergent & inconstant' 17 'strabismus right & left, convergent' 18 'strabismus right & left, divergent' 19 'strabismus right & left, inconstant' 20 'strabismus right divergent & left convergent' 21 'strabismus right, convergent & nystagmus' 22 'strabismus left, convergent & nystagmus'

Items	Item Categories
	23 'strabismus right, inconstant & left convergent' 24 'strabismus left, divergent and constant & nystagmus' 25 'strabismus right convergent & left convergent and not constant' 26 'strabismus right convergent and constant & left not constant' 27 'strabismus right, convergent & inconstant & left convergent' 28 'strabismus right & left, convergent & constant' 29 'strabismus right & left, convergent & inconstant' 30 'strabismus right & left, divergent & constant' 31 'strabismus right & left, divergent & inconstant' 32 'strabismus right, convergent and constant & left, convergent and inconstant' 33 'strabismus right, convergent and inconstant & left, convergent and constant' 34 'strabismus right & left, convergent & constant & nystagmus' 35 'strabismus right & left, convergent & inconstant & nystagmus'
7. Eyes, pupils (shape).	1 'normal, yes round and isocorical' 2 'no'
8. Eyes, eye follow movements.	1 'normal, conjugated, fluent, no nystagmus' 2 'nystagmus in final position' 3 'nystagmus' 4 'unconjugated eye movements' 5 'saccades' 6 'nystagmus in final position & unconjugated eye movements' 7 'nystagmus & unconjugated eye movements' 8 'unconjugated eye movements & saccades' 9 'unconjugated eye movements & other'
9. Eyes, extent of eye follow movements.	1 'normal, unrestricted' 2 'eye muscle paresis' 3 'eye muscle paresis & other'

Items	Item Categories
Sensorimotor: sitting, standing, walking, climbing stairs	
10. Sitting, independent sitting > 5 min.	1 'normal, yes' 2 'no'
11. Sitting, posture.	1 'normal: symmetric, variable, hips bent 90 degrees' 2 'kyphotic' 3 'scoliotic' 4 'further asymmetries' 5 'kyphotic & scoliotic' 6 'kyphotic & further asymmetries' 7 'kyphotic & other' 8 'scoliotic & other' 9 'further asymmetries & other' 10 'kyphotic, scoliotic & further asymmetries' 11 'kyphotic, scoliotic & other' 12 'kyphotic, further asymmetries & other'
12. Sitting, joint mobility.	1 'normal' 2 'increased' 3 'impaired due to contractures' 4 'increased & contractures' 5 'contractures & other'
13. Sitting, balance.	1 'normal, yes (symmetric, stable)' 2 'no'
14. Sitting, quantity of moving.	1 'normal, spontaneous movements < 25% of time' 2 'no sitting for 3 min' 3 'movement up to 50% or more than 50% of time: arms' 4 'movement up to 50% or more than 50% of time: hands' 5 'movement up to 50% or more than 50% of time: legs'

Items	Item Categories
	6 'movement up to 50% or more than 50% of time: feet' 7 'movement up to 50% or more than 50% of time: arms & hands' 8 'movement up to 50% or more than 50% of time: arms & legs' 9 'movement up to 50% or more than 50% of time: arms & feet' 10 'movement up to 50% or more than 50% of time: arms & other' 11 'movement up to 50% or more than 50% of time: hands & legs' 12 'movement up to 50% or more than 50% of time: hands & feet' 13 'movement up to 50% or more than 50% of time: hands & other' 14 'movement up to 50% or more than 50% of time: legs & feet' 15 'movement up to 50% or more than 50% of time: legs & other' 16 'movement up to 50% or more than 50% of time: feet & other' 17 'movement up to 50% or more than 50% of time: arms, hands & legs' 18 'movement up to 50% or more than 50% of time: arms, hands & feet' 19 'movement up to 50% or more than 50% of time: arms, hands & other' 20 'movement up to 50% or more than 50% of time: arms, legs & feet' 21 'movement up to 50% or more than 50% of time: arms, legs & other' 22 'movement up to 50% or more than 50% of time: arms, feet & other' 23 'movement up to 50% or more than 50% of time: hands, legs & feet' 24 'movement up to 50% or more than 50% of time: hands, legs & other' 25 'movement up to 50% or more than 50% of time: hand, feet & other' 26 'movement up to 50% or more than 50% of time: legs, feet & other' 27 'movement up to 50% or more than 50% of time: arms, hands, legs & feet' 28 'movement up to 50% or more than 50% of time: arms, hands, legs & other' 29 'movement up to 50% or more than 50% of time: arms, legs, feet & other' 30 'movement up to 50% or more than 50% of time: hands, legs, feet & other' 31 'movement up to 50% or more than 50% of time: arms, hands, legs, feet & other'
15. Sitting, muscle strength.	1 'normal (ankle, elbow, finger, knee joints)' 2 'decreased, doubtful'

Items	Item Categories
	3 'decreased, certain '
16. Standing, independent standing > 5 min.	1 'normal, yes' 2 'no'
17. Standing, posture	1 'normal' 2 'weak posture' 3 'any other posture problem'
18. Standing, arms extended.	1 'normal, arms symmetric' 2 'arm deviation' 3 'ataxia' 4 'balance with low compensating movements' 5 'balance with compensating movements of whole body' 6 'no balance possible' 7 'dyskinesia: tremor' 8 'dyskinesia: athetosis' 9 'arms symmetric & balance with low compensating movements' 10 'arms symmetric & balance with compensating movements of whole body' 11 'arms symmetric & dyskinesia: chorea' 12 'arms symmetric & other' 13 'arm deviation & ataxia' 14 'arm deviation & balance with low compensating movements' 15 'arm deviation & balance with compensating movements of whole body' 16 'arm deviation & dyskinesia: tremor' 17 'arm deviation & other' 18 'ataxia & balance with compensating movements of whole body' 19 'ataxia & dyskinesia: tremor' 20 'ataxia & dyskinesia: athethosis' 21 'balance with low compensating movements & dyskinesia: tremor' 22 'balance with low compensating movements & dyskinesia: tic'

Items	Item Categories
	23 'balance with low compensating movements & other' 24 'balance with compensating movements of whole body & other' 25 'arms symmetric, ataxia & balance with low compensating movements' 26 'arm deviation, balance with low compensating movements & other' 27 'arm deviation, dyskinesia: tremor & other' 28 'arm deviation, balance with compensating movements of whole body, dyskinesia: chorea & athetosis'
19. Standing, arms hanging.	1 'normal, stable balance' 2 'balance with compensating steps' 3 'no balance' 4 'balance with compensating steps & other' 5 'no balance & other'
20. Standing, finger-nose-test.	1 'normal: purposeful 3x right and left' 2 'failed 1-2x right and left' 3 'failed 3x right and left' 4 'constant deviation right and left' 5 'purposeful 3x right & failed 1-2x left' 6 'purposeful 3x right & failed 3x left' 7 'failed 1-2x right & purposeful 3x left' 8 'failed 1-2x right & failed 3x left' 9 'failed 3x right & purposeful 3x left' 10 'failed 3x right & failed 1-2x left' 11 'purposeful 3x & constant deviation right' 12 'failed 1-23x & constant deviation right' 13 'purposeful 3x right & failed 1-2x with constant deviation left' 14 'purposeful 3x right & failed 3x with constant deviation left' 15 'purposeful 3x right & missing left' 16 'failed 1-2x right & missing left'

Items	Item Categories
	17 'missing right & purposeful 3x left' 18 'missing right & failed 1-2x left' 19 'failed 3x right & constant deviation left' 20 'failed 1-2x with constant deviation right & purposeful 3x left' 21 'failed 3x with constant deviation right & purposeful 3x left' 22 'failed 3x with constant deviation right & failed 1-2x left' 23 'failed 3x with constant deviation right & failed 3x left' 24 'failed 1-2x right and failed 1-2x with constant deviation left' 25 'failed 1-2x with constant deviation right and left' 26 'failed 3x with constant deviation right and left'
21. Standing, index finger to examiner's index finger.	1 'normal: purposeful 3x right and left' 2 'failed 1-2x right and left' 3 'failed 3x right and left' 4 'purposeful 3x right & failed 1-2x left' 5 'purposeful 3x right & failed 3x left' 6 'failed 1-2x right & purposeful 3x left' 7 'failed 1-2x right & failed 3x left' 8 'failed 3x right & purposeful 3x left' 9 'failed 3x right & failed 1-2x left' 10 'purposeful 3x & constant deviation right' 11 'purposeful 3x right & failed 1-2x with constant deviation left' 12 'purposeful 3x right & failed 3x with constant deviation left' 13 'purposeful 3x right & missing left' 14 'failed 1-2x right & missing left' 15 'missing right & purposeful 3x left' 16 'missing right & failed 1-2x left' 17 'missing right & failed 3x left' 18 'failed 1-2x with constant deviation right & purposeful 3x left'

Items	Item Categories
	19 'failed 3x with constant deviation right and left'
22. Standing, both tasks: finger-nose-test & index finger to examiner.	1 'normal: linear movements' 2 'slight tremor right' 3 'slight tremor left' 4 'distinct tremor right' 5 'distinct tremor left' 6 'slight tremor right & left' 7 'distinct tremor right & left' 8 'slight tremor right & distinct tremor left' 9 'distinct tremor right & slight tremor left' 10 'slight tremor left & other' 11 'distinct tremor left & other' 12 'slight tremor right & left & other'
23. Walking, independent walking.	1 'normal, yes' 2 'no' 3 'no independent walking: crawling (krabbeln)' 4 'no independent walking: crawling (robben)' 5 'no independent walking: no movement possible'
24. Walking, posture	1 'normal, symmetric, upright, relaxed' 2 'any problem'
25. Walking, movements.	1 'normal, fluent, economical, automated' 2 'clumsy' 3 'shaky-legged' 4 'tense' 5 'extent of movement too large' 6 'not rhythmic, poorly automated' 7 'spastic right' 8 'spastic left'

Items	Item Categories
	9 'ataxia' 10 'asymmetries' 11 'clumsy & shaky-legged' 12 'clumsy & tense' 13 'clumsy & extent of movement too large' 14 'clumsy & not rhythmic' 15 'clumsy & asymmetries' 16 'clumsy & other' 17 'shaky-legged & tense' 18 'shaky-legged & extent of movement too large' 19 'shaky-legged & not rhythmic' 20 'shaky-legged & spastic right' 21 'shaky-legged & spastic left' 22 'shaky-legged & asymmetries' 23 'shaky-legged & other' 24 'tense & not rhythmic' 25 'tense & other' 26 'extent of movement too large & other' 27 'not rhythmic, poorly automated & spastic left' 28 'not rhythmic, poorly automated & dyskinesia' 29 'not rhythmic, poorly automated & asymmetries' 30 'not rhythmic, poorly automated & other' 31 'spastic right & left' 32 'spastic left & asymmetries' 33 'ataxia & other' 34 'asymmetries & other' 35 'clumsy, shaky-legged & tense' 36 'clumsy, shaky-legged & extent of movement too large'

Items	Item Categories
	37 'clumsy, shaky-legged & not rhythmic'
	38 'clumsy, shaky-legged & other'
	39 'clumsy, tense, not rhythmic'
	40 'clumsy, not rhythmic & ataxia'
	41 'clumsy, not rhythmic & asymmetries'
	42 'clumsy & spastic right & left'
	43 'not rhythmic & spastic right & left'
	44 'spastic right & left & asymmetries'
	45 'shaky-legged, tense & extent of movement too large'
	46 'shaky-legged, tense & not rhythmic'
	47 'shaky-legged & spastic right & left'
	48 'spastic right & left & other'
	49 'spastic left, asymmetries & other'
	50 'clumsy, extent of movement too large & other'
	51 'clumsy, not rhythmic & other'
	52 'shaky-legged, tense & other'
	53 'clumsy, shaky-legged, tense & not rhythmic'
	54 'clumsy, tense, not rhythmic & other'
	55 'spastic right & left, asymmetries & other'
	56 'clumsy, not rhythmic, spastic right & asymmetries'
	57 'shaky-legged, not rhythmic, spastic left & other'
	58 'clumsy, shaky-legged, not rhythmic & asymmetries'
	59 'clumsy, shaky-legged, extent of movement too large & not rhythmic'
	60 'shaky-legged, extent of movement too large & spastic right & left'
	61 'shaky-legged, extent of movement too large, not rhythmic & spastic right'
	62 'shaky-legged, extent of movement too large, not rhythmic & spastic left'
	63 'extent of movement too large, not rhythmic & spastic right & left'
	64 'not rhythmic, spastic right & left & asymmetries'

Items	Item Categories
	65 'clumsy, shaky-legged, tense & spastic right & left' 66 'clumsy, shaky-legged, not rhythmic, spastic left & asymmetries' 67 'clumsy, not rhythmic, spastic right & left & asymmetries' 68 'extent of movement too large, not rhythmic, spastic right & left & ataxia' 69 'shaky-legged, extent of movement too large, not rhythmic & spastic right & left' 70 'clumsy, shaky-legged, tense, extent of movement too large & spastic right & left' 71 'clumsy, shaky-legged, not rhythmic, spastic right & left & other' 72 'shaky-legged, tense, not rhythmic, spastic right & left & asymmetries' 73 'shaky-legged, extent of movement too large, not rhythmic, spastic right & left & other'
26. Walking, pressure on feet.	1 'normal, flat' 2 'forefoot right' 3 'forefoot left' 4 'drop foot left' 5 'forefoot right & left' 6 'drop foot right & left' 7 'forefoot right & drop foot right' 8 'forefoot right, often' 9 'forefoot right, constant' 10 'forefoot left, often' 11 'forefoot left, constant' 12 'drop foot right, often' 13 'drop foot right, constant' 14 'drop foot left, often' 15 'drop foot left, constant' 16 'forefoot right & left, often' 17 'forefoot right & left, constant' 18 'drop foot right & left, often' 19 'drop foot right & left, constant'

Items	Item Categories
	20 'forefoot right & drop foot left, often' 21 'forefoot right & drop foot left, constant' 22 'forefoot left & drop foot right, often' 23 'forefoot left & drop foot right, constant' 24 'forefoot left & drop foot left, constant' 25 'forefoot right & left & drop foot left, often' 26 'forefoot right & left & drop foot left, constant' 27 'forefoot right & drop foot right & left, constant' 28 'forefoot and drop foot right & left, often' 29 'forefoot and drop foot right & left, constant'
27. Walking, balance.	1 'normal, stable postural control in all joints' 2 'abnormal'
28. Walking, muscle weakness or paresis.	1 'normal, no muscle weakness or paresis' 2 'difficult walking' 3 'distinctly located' 4 'paresis' 5 'distinctly located & paresis'
29. Walking, step length.	1 'normal, more than one foot length' 2 'no'
30. Walking, walking speed.	1 'normal, moderately fast and deliberately variable' 2 'slow' 3 'can run only' 4 'slow & other'
31. Walking, running.	1 'normal, symmetric, fluent, rhythmic' 2 'too slow' 3 'abnormal quality' 4 'hypertonic reaction arm right' 5 'hypertonic reaction arm left'

Items	Item Categories
	6 'hypertonic reaction leg right'
	7 'too slow & abnormal quality'
	8 'too slow & hypertonic reaction arm right'
	9 'too slow & hypertonic reaction arm left'
	10 'too slow & hypertonic reaction leg left'
	11 'hypertonic reaction arm right & left'
	12 'hypertonic reaction leg right & left'
	13 'abnormal quality & hypertonic reaction arm right'
	14 'abnormal quality & hypertonic reaction arm left'
	15 'abnormal quality & hypertonic reaction leg right'
	16 'abnormal quality & hypertonic reaction leg left'
	17 'hypertonic reaction arm right & leg left'
	18 'hypertonic reaction arm left & leg left'
	19 'too slow, hypertonic reaction arms right & left'
	20 'too slow, hypertonic reaction arm and leg left'
	21 'too slow, hypertonic reaction arm and leg right'
	22 'too slow, hypertonic reaction leg right & left'
	23 'too slow, abnormal quality & hypertonic reaction arm right'
	24 'too slow, abnormal quality & hypertonic reaction arm left'
	25 'abnormal quality, hypertonic reaction legs right & left'
	26 'abnormal quality, hypertonic reaction arms right & left'
	27 'abnormal quality, hypertonic reaction arm left & leg left'
	28 'abnormal quality, hypertonic reaction arm right & leg right'
	29 'abnormal quality, hypertonic reaction arm left & leg right'
	30 'hypertonic reaction arms right & left, leg right'
	31 'hypertonic reaction arms right & left, leg left'
	32 'hypertonic reaction arm right, legs right & left'
	33 'hypertonic reaction arm left, legs right & left'

Items	Item Categories
	34 'too slow, abnormal quality, hypertonic reaction arms right & left' 35 'too slow, abnormal quality, hypertonic reaction arm left & leg left' 36 'too slow, abnormal quality, hypertonic reaction arm right & leg right' 37 'too slow, abnormal quality, hypertonic reaction legs right & left' 38 'too slow, hypertonic reaction arm left, legs right & left' 39 'too slow, hypertonic reaction arm right, legs right & left' 40 'abnormal quality, hypertonic reaction arm left, legs right & left' 41 'abnormal quality, hypertonic reaction arm right, legs right & left' 42 'hypertonic reaction arms and legs right & left' 43 'too slow, hypertonic reaction arms and legs right & left' 44 'abnormal quality, hypertonic reaction arms and legs right & left' 45 'too slow, abnormal quality, hypertonic reaction arms right & left, leg left' 46 'too slow, abnormal quality, hypertonic reaction arm left, legs right & left' 47 'too slow, abnormal quality, hypertonic reaction arms and legs right & left'
32. Climbing stairs (5 steps up and down).	1 'normal, no hands, stable, alternating' 2 'child steps' 3 'with stopping only' 4 'not possible alone' 5 'with stopping only & child steps' 6 'not possible alone & child steps'
33. Climbing stairs (5 steps up and down), posture retention.	1 'normal, stable in all joints' 2 'instable while walking upstairs' 3 'instable while walking downstairs' 4 'instable while walking up- and downstairs'
34. Climbing stairs (5 steps up and down), movement quality	1 'normal, fluent up- and downstairs' 2 'clumsy right' 3 'clumsy left' 4 'slow right'

Items	Item Categories
	5 'slow left' 6 'stiff right' 7 'stiff left' 8 'clumsy right & left' 9 'slow right & left' 10 'stiff right & left' 11 'clumsy & slow right' 12 'clumsy right & slow left' 13 'clumsy & stiff' 14 'clumsy right & other' 15 'clumsy & slow left' 16 'clumsy left & stiff right' 17 'clumsy & stiff left' 18 'slow & stiff right' 19 'slow right & stiff left' 20 'slow right & other' 21 'slow left & stiff right' 22 'slow & stiff left' 23 'stiff right & other' 24 'stiff left & other' 25 'clumsy, slow and stiff left' 26 'slow right & left, stiff right' 27 'slow right & left, stiff left' 28 'slow right & left, other' 29 'stiff right & left, other' 30 'clumsy and slow right & left' 31 'clumsy and stiff right & left' 32 'slow and stiff right & left'

Items	Item Categories
	33 'clumsy and slow right & left, other' 34 'clumsy left, slow and stiff right & left' 35 'slow and stiff right & left, other' 36 'clumsy, slow and stiff right & left'
35. Climbing stairs (5 steps up and down), muscle strength.	1 'normal' 2 'difficulties going upstairs' 3 'arms needed to pull up or for support' 4 'difficulties going upstairs & arms needed to pull up or for support'
Sensorimotor: Balance testing	
36. Walking on toes: movement quality.	1 'normal: fluent' 2 'hesitant' 3 'movement not possible'
37. Walking on toes: compensating movements.	1 'normal: hardly any movements' 2 'moderate movements' 3 'strong movements'
38. Walking on toes: associated muscle tone of arms.	1 'normal, relaxed' 2 'slightly increased' 3 'distinctly increased'
39. Walking heels raised: movement quality.	1 'normal: fluent' 2 'hesitant' 3 'movement not possible'
40. Walking heels raised: compensating movements.	1 'normal: hardly any movements' 2 'moderate movements' 3 'strong movements'
41. Walking heels raised: associated muscle tone of arms.	1 'normal, relaxed' 2 'slightly increased' 3 'distinctly increased'

Items	Item Categories
42. One leg balance: compensating movements, right	1 'normal: hardly any movements' 2 'moderate movements' 3 'strong movements'
43. One leg balance: compensating movements, left	1 'normal: hardly any movements' 2 'moderate movements' 3 'strong movements'
44. One leg balance: associated muscle tone of arms, right	1 'normal, relaxed' 2 'slightly increased' 3 'distinctly increased'
45. One leg balance: associated muscle tone of arms, left	1 'normal, relaxed' 2 'slightly increased' 3 'distinctly increased'
46. One leg balance: time (10 sec), right	1 'normal, 10 sec possible' 2 '5 sec possible' 3 'not possible'
47. One leg balance: time (10 sec), left	1 'normal, 10 sec possible' 2 '5 sec possible' 3 'not possible'
48. Hopping on one leg: movement quality, right.	1 'normal: fluent' 2 'hesitant' 3 'movement not possible'
49. Hopping on one leg: movement quality, left.	1 'normal: fluent' 2 'hesitant' 3 'movement not possible'
50. Hopping on one leg: compensating movements, right.	1 'normal: hardly any movements' 2 'moderate movements' 3 'strong movements'

Items	Item Categories
51. Hopping on one leg: compensating movements, left.	1 'normal: hardly any movements' 2 'moderate movements' 3 'strong movements'
52. Hopping on one leg: associated muscle tone of arms, right.	1 'normal, relaxed' 2 'slightly increased' 3 'distinctly increased'
53. Hopping on one leg: associated muscle tone of arms, left.	1 'normal, relaxed' 2 'slightly increased' 3 'distinctly increased'
54. Hopping on one leg: time (10 sec), right.	1 'normal, 10 sec possible' 2 '5 sec possible' 3 'not possible'
55. Hopping on one leg: time (10 sec), left.	1 'normal, 10 sec possible' 2 '5 sec possible' 3 'not possible'
56. Jump over cord: movement quality.	1 'normal: fluent' 2 'hesitant' 3 'movement not possible'
57. Jump over cord: compensating movements'.	1 'normal: hardly any movements' 2 'moderate movements' 3 'strong movements'
58. Jump over cord: associated muscle tone of arms.	1 'normal, relaxed' 2 'slightly increased' 3 'distinctly increased'
59. Jump over cord: number of jumps (>6).	1 'normal, > 6 jumps' 2 '2-6 jumps' 3 '< 2 jumps'

Items	Item Categories
60. Balance: movement quality, forward.	1 'normal: fluent' 2 'hesitant' 3 'movement not possible'
61. Balance: movement quality, backward.	1 'normal: fluent' 2 'hesitant' 3 'movement not possible'
62. Balance: compensating movements, forward.	1 'normal: hardly any movements' 2 'moderate movements' 3 'strong movements'
63. Balance: compensating movements, backward.	1 'normal: hardly any movements' 2 'moderate movements' 3 'strong movements'
64. Balance: associated muscle tone of arms, forward.	1 'normal, relaxed' 2 'slightly increased' 3 'distinctly increased'
65. Balance: associated muscle tone of arms, backward.	1 'normal, relaxed' 2 'slightly increased' 3 'distinctly increased'
66. Balance: number of errors, forward.	1 'normal, no errors' 2 '1-2 errors' 3 '> 2 errors'
67. Balance: number of errors, backward.	1 'normal, no errors' 2 '1-2 errors' 3 '> 2 errors'
Sensorimotor: supine position	
68. Supine position, posture.	1 'normal, symmetric, stable' 2 'asymmetry' 3 'asymmetry & other'

Items	Item Categories
69. Supine position, joint mobility.	1 'normal, symmetric, loose hip & knee' 2 'increased' 3 'decreased'
70. Supine position, muscle tone	1 'normal, moderate resistance against passive movement' 2 'slightly increased right' 3 'distinctly increased right' 4 'slightly decreased right' 5 'distinctly decreased right' 6 'slightly increased left' 7 'distinctly increased left' 8 'slightly decreased left' 9 'distinctly decreased left' 10 'slightly increased right & left' 11 'distinctly increased right & left' 12 'slightly decreased right & left' 13 'distinctly decreased right & left' 14 'slightly increased right & distinctly increased left' 15 'distinctly increased right & slightly increased left' 16 'slightly decreased right & distinctly decreased left'
71. Supine position, long-sit.	1 'normal, yes, possible' 2 'no, not possible'
Reflexes	
72. Knee jerk.	1 'immediate, moderate right & left' 2 'decreased right & left' 3 'absent right & left' 4 'increased right & left' 5 'increased with clonus right & left' 6 'missing right & immediate, moderate left'

Items	Item Categories
	7 'missing right & decreased left' 8 'missing right & absent left' 9 'missing right & increased left' 10 'missing right & increased with clonus left'
73. Achilles tendon.	1 'immediate, moderate right & left' 2 'decreased right & left' 3 'absent right & left' 4 'increased right & left' 5 'increased with clonus right & left' 6 'immediate, moderate right & decreased left' 7 'immediate, moderate right & absent left' 8 'immediate, moderate right & increased left' 9 'immediate, moderate right & increased with clonus left' 10 'immediate, moderate right & not testable left' 11 'immediate, moderate right & missing left' 12 'decreased right & immediate, moderate left' 13 'absent right & immediate, moderate left' 14 'increased right & immediate, moderate left' 15 'increased with clonus right & immediate, moderate left' 16 'not testable right & immediate, moderate left' 17 'missing right & immediate, moderate left' 18 'increased right & increased with clonus left' 19 'increased right & decreased left' 20 'absent right & decreased left' 21 'increased with clonus right & increased left' 22 'increased right & missing left' 23 'missing right & decreased left' 24 'missing right & increased left'

Items	Item Categories
74. Biceps tendon.	1 'immediate, moderate right & left' 2 'decreased right & left' 3 'absent right & left' 4 'increased right & left' 5 'increased with clonus right & left' 6 'immediate, moderate right & decreased left' 7 'immediate, moderate right & increased left' 8 'immediate, moderate right & increased with clonus left' 9 'immediate, moderate right & not testable left' 10 'immediate, moderate right & missing left' 11 'decreased right & immediate, moderate left' 12 'decreased right & absent left' 13 'decreased right & increased left' 14 'decreased right & increased with clonus left' 15 'absent right & immediate, moderate left' 16 'increased right & immediate, moderate left' 17 'increased with clonus right & immediate, moderate left' 18 'increased right & increased with clonus left' 19 'increased with clonus right & increased left' 20 'not testable right & increased with clonus left'
Sensitivity	
75. Sensitivity, tactile	1 'yes, immediate right & left' 2 '1-2 errors right & left' 3 '>2 errors right & left' 4 'yes, immediate right & 1-2 errors left' 5 '1-2 errors right & yes, immediate left' 6 'yes, immediate right & >2 errors left' 7 '> 2 errors right & 1-2 errors left'

Items	Item Categories
	8 'not testable right & yes, immediate left' 9 'missing right & yes, immediate left' 10 'missing right & 1-2 errors left'
Rapid, rhythmic movements	
76. Hand pro- and supination, rhythm, right.	1 'normal, rhythmic' 2 'error' 3 'no rhythm'
77. Hand pro- and supination, rhythm, left.	1 'normal, rhythmic' 2 'error' 3 'no rhythm'
78. Hand pro- and supination, movement quality, right.	1 'normal, fluent' 2 'halting' 3 'no movement'
79. Hand pro- and supination, movement quality, left.	1 'normal, fluent' 2 'halting' 3 'no movement'
80. Hand pro- and supination, associated tonic reactions, right	1 'normal, no tonic reactions' 2 'contralateral' 3 'generalised'
81. Hand pro- and supination, associated tonic reactions, left	1 'normal, no tonic reactions' 2 'contralateral' 3 'generalised'
82. Hand pro- and supination, contralateral movements, right.	1 'normal, no contralateral movements' 2 'some' 3 'many'
83. Hand pro- and supination, contralateral movements, left.	1 'normal, no contralateral movements' 2 'some' 3 'many'

Items	Item Categories
84. Hand pro- and supination, time (in sec) for 7 cycles, right	(Continuous variable)[a]
85. Hand pro- and supination, time (in sec) for 7 cycles, left	(Continuous variable)[a]
86. Handtapping, rhythm, synchronous	1 'normal, rhythmic' 2 'error' 3 'no rhythm'
87. Handtapping, rhythm, alternating	1 'normal, rhythmic' 2 'error' 3 'no rhythm'
88. Handtapping, movement quality, synchronous	1 'normal, fluent' 2 'halting' 3 'no movement'
89. Handtapping, movement quality, alternating	1 'normal, fluent' 2 'halting' 3 'no movement'
90. Handtapping, associated tonic reactions, synchronous	1 'normal, no tonic reactions' 2 'contralateral' 3 'generalised'
91. Handtapping, associated tonic reactions, alternating	1 'normal, no tonic reactions' 2 'contralateral' 3 'generalised'
92. Handtapping, time (in sec) for 10 movements, synchronous	(Continuous variable)[a]
93. Handtapping, time (in sec) for 10 movements, alternating	(Continuous variable)[a]

Items	Item Categories
94. Finger-thumb opposition, rhythm, right	1 'normal, rhythmic' 2 'error' 3 'no rhythm'
95. Finger-thumb opposition, rhythm, left	1 'normal, rhythmic' 2 'error' 3 'no rhythm'
96. Finger-thumb opposition, movement quality, right.	1 'normal, fluent' 2 'halting' 3 'no movement'
97. Finger-thumb opposition, movement quality, left.	1 'normal, fluent' 2 'halting' 3 'no movement'
98. Finger-thumb opposition, associated tonic reactions, right.	1 'normal, no tonic reactions' 2 'contralateral' 3 'generalised'
99. Finger-thumb opposition, associated tonic reactions, left.	1 'normal, no tonic reactions' 2 'contralateral' 3 'generalised'
100. Finger-thumb opposition, contralateral movements, right.	1 'normal, no contralateral movements' 2 'some' 3 'many'
101. Finger-thumb opposition, contralateral movements, left.	1 'normal, no contralateral movements' 2 'some' 3 'many'
102. Sequential finger-thumb opposition, rhythm, right.	1 'normal, no error' 2 '1-2 errors' 3 '> 2 errors'

Items	Item Categories
103. Sequential finger-thumb opposition, rhythm, left.	1 'normal, no error' 2 '1-2 errors' 3 '> 2 errors'
104. Sequential finger-thumb opposition, movement quality, right.	1 'normal, fluent' 2 'halting' 3 'no movement'
105. Sequential finger-thumb opposition, movement quality, left.	1 'normal, fluent' 2 'halting' 3 'no movement'
106. Sequential finger-thumb opposition, associated tonic reactions, right.	1 'normal, no tonic reactions' 2 'contralateral' 3 'generalised'
107. Sequential finger-thumb opposition, associated tonic reactions, left.	1 'normal, no tonic reactions' 2 'contralateral' 3 'generalised'
108. Sequential finger-thumb opposition, contralateral movements, right.	1 'normal, no contralateral movements' 2 'some' 3 'many'
109. Sequential finger-thumb opposition, contralateral movements, left.	1 'normal, no contralateral movements' 2 'some' 3 'many'
Fine motor skills	
110. Pinboard, time (in sec), right.	(Continuous variable)[a]
111. Pinboard, time (in sec), left.	(Continuous variable)[a]
112. Pinboard, goal-directedness, right.	1 'normal, yes' 2 'missed 3x' 3 'missed >3x'

Items	Item Categories
113. Pinboard, goal-directedness, left.	1 'normal, yes' 2 'missed 3x' 3 'missed >3x'
114. Pinboard, strength.	1 'normal, easy, adjusted' 2 'too strong right' 3 'too weak right' 4 'too strong left' 5 'too weak left' 6 'too strong right & left' 7 'too weak right & left' 8 'too strong right & too weak left' 9 'too weak right & too strong left'
115. Pinboard, movement quality.	1 'normal, fluent' 2 'abnormal right and/or left'
116. Pinboard, finger position, right.	1 'normal, easy, stable finger tip grasp, uses 2 or 3 finger' 2 'uses more than 3 finger, right & left'
117. Pinboard, finger position, left.	1 'normal, easy, stable finger tip grasp, uses 2 or 3 finger' 2 'uses more than 3 finger, right & left'
118. Pinboard, associated tonic reactions	1 'normal, no' 2 'yes'
119. Pinboard, co-movements.	1 'normal, no' 2 'slight' 3 'distinct'
120. Drawing, holding pencil: strength.	1 'normal, relaxed, adjusted' 2 'too strong' 3 'too weak'

Items	Item Categories
121. Drawing, holding pencil: movement quality.	1 'normal, fluent' 2 'clumsy' 3 'hesitant' 4 'shaking' 5 'expansive' 6 'hypertonic' 7 'dyskinesia' 8 'clumsy & hesitant' 9 'clumsy & shaking' 10 'clumsy & expansive' 11 'clumsy & hypertonic' 12 'clumsy & other' 13 'hesitant & shaking' 14 'hesitant & expansive' 15 'hesitant & other' 16 'shaking & expansive' 17 'shaking & hypertonic' 18 'shaking & other' 19 'expansive & hypertonic' 20 'expansive & other' 21 'clumsy, hesitant & shaking' 22 'clumsy, hesitant & expansive' 23 'clumsy, hesitant & hypertonic' 24 'clumsy, shaking & expansive' 25 'clumsy, expansive & hypertonic' 26 'hesitant, shaking & expansive' 27 'hesitant, shaking & hypertonic' 28 'hesitant, shaking & other'

Items	Item Categories
	29 'shaking, expansive & hypertonic' 30 'shaking, hypertonic & dyskinesia' 31 'shaking, hypertonic & other' 32 'expansive, hypertonic & dyskinesia' 33 'clumsy, hesitant, shaking & expansive' 34 'clumsy, hesitant, shaking & other'
122. Drawing, holding a pencil (with 3 fingers).	1 'normal: with 3 fingers' 2 'with fist'
123. Drawing, co-movements.	1 'normal, no' 2 'slightly' 3 'distinctly'
124. Drawing, associated tonic reactions.	1 'normal, no' 2 'yes'
125. Cutting out a circle, fluent movements.	1 'normal, yes' 2 'movements difficult' 3 'cutting not possible'

Note. For the computation of the motor functioning score all items were categorised into ‘within’ (=1) and ‘outside the normal range’ (>1).
[a] Continuous variables were dichotomised using the 85th percentile of the normative group.

Appendix E. Severe neurological impairments at age 56 months and motor problems trajectories.

	BLS				AYLS			
		Motor problems trajectories				Motor problems trajectories		
	Whole Sample	*Low degree*	*High degree*	*p*-value[a]	Whole Sample	*Low degree*	*High degree*	*p*-value[a]
	N=4,741	*N*=4,486	*N*=255		*N*=1,423	*N*=1,391	*N*=32	
Any severe neurological impairments[b]	95 (2.0)	33 (0.7)	62 (24.3)	**<.001**	15 (1.1)	7 (0.5)	8 (25.0)	**<.001**
Cerebral palsy (CP)	62 (1.3)	10 (0.2)	52 (20.4)	**<.001**	10 (0.7)	2 (0.1)	8 (25.0)	**<.001**
CP stages[c]				**<.001**				**<.001**
stage 1	26 (0.5)	8 (0.2)	18 (7.1)		3 (0.2)	2 (0.1)	1 (3.1)	
stage 2	26 (0.5)	2 (0.0)	24 (9.4)		5 (0.4)	0 (0.0)	5 (15.6)	
stage 3	10 (0.2)	0 (0.0)	10 (3.9)		2 (0.1)	0 (0.0)	2 (6.3)	
stage 4	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Blindness	3 (0.1)	1 (0.0)	2 (0.8)	**<.001**	0 (0.0)	0 (0.0)	0 (0.0)	n/a
Deafness[d]	6 (0.1)	4 (0.1)	2 (0.8)	**.002**	0 (0.0)	0 (0.0)	0 (0.0)	n/a
Epilepsy	20 (0.4)	14 (0.3)	6 (2.4)	**<.001**	6 (0.4)	5 (0.4)	1 (3.1)	**.017**
Hydrocephalus	13 (0.3)	4 (0.1)	9 (3.5)	**<.001**	1 (0.1)	1 (0.1)	0 (0.0)	.879

Note. Numbers and percent are shown.

[a] Comparing low with high degree of motor problems trajectory group.

[b] Severe neurological impairments were assessed and determined by specially trained project paediatricians: cerebral palsy (CP), epilepsy, hydrocephalus, blindness, or deafness (not corrected or insufficiently corrected).

[c] CP stages: 1 = more pronounced in fast-paced movement (either with or without impairment of the motor functions of the hand), impairment has a hardly noticeable negative impact (mildest CP); 2 = possible to walk but with noticeable negative impact, additional impairment to the motor function of the hand; 3 = walking is not possible although crawling is; 4= no active movement at all (most severe CP).
[d] Not corrected (1) or insufficiently corrected (2).

Appendix F. Fit statistics for Latent Class Growth Analysis (LCGA) models estimated within BLS and AYLS early childhood motor functioning from birth to 56 months

	BLS			AYLS		
Indicator of model fit	1-class LCGA model	2-class LCGA model	3-class LCGA model	1-class LCGA model	2-class LCGA model	3-class LCGA model
BIC	43870.030	41219.307	40020.175	12821.352	12179.796	11904.356
aBIC	43841.432	41181.175	39972.510	12792.763	12141.676	11856.706
BLRT (k vs. k-1 class)	n/a	$p < 0.001$	$p < 0.001$	n/a	$p < 0.001$	$p < 0.001$
LMR (k vs. k-1 class)	n/a	$p < 0.001$	$p = 0.385$	n/a	$p = 0.027$	$p = 0.171$
VLMR (k vs. k-1 class)	n/a	$p < 0.001$	$p = 0.376$	n/a	$p = 0.024$	$p = 0.162$
Entropy	n/a	0.984	0.978	n/a	0.995	0.944
Participants per class, %						
Class 1	4,741 (100.0)	4,486 (94.6)	4,314 (91.0)	1,423 (100.0)	1,391 (97.8)	1,255 (88.2)
Class 2	n/a	255 (5.4)	338 (7.1)	n/a	32 (2.2)	142 (10.0)
Class 3	n/a	n/a	89 (1.9)	n/a	n/a	26 (1.8)

Abbreviations: aBIC= adjusted BIC; BIC= Bayesian Information Criterion; BLRT=Parametric Bootstrapped Likelihood Ratio Test; LMR=Lo-Mendell-Rubin Test; VLMR=Vuong-Lo-Mendell-Rubin Ratio Test.

Appendix G. Motor problem scores (z-standardized) from birth to 56 months within motor trajectories, BLS and AYLS

	Low degree of motor problems trajectory		High degree of motor problems trajectory			
					p-value	Effect size: Cohen's *d*
BLS	*N*=4,486 (94.6%)		*N*=255 (5.4%)			
At birth	-0.1302	(0.8229)	0.5701	(1.1017)	<**.001**	0.7
5 months	-0.1676	(0.7052)	1.3806	(1.2608)	<**.001**	1.5
20 months	-0.2365	(0.3326)	2.1139	(0.9644)	<**.001**	3.3
56 months	-0.1095	(0.8596)	1.8432	(1.3697)	<**.001**	1.7
AYLS	*N*=1,391 (97.8%)		*N*=32 (2.2%)			
At birth	-0.0886	(0.8381)	1.0010	(1.5194)	<**.001**	0.9
5 months	-0.1353	(0.6576)	1.7058	(1.4000)	<**.001**	1.7
20 months	-0.1464	(0.3916)	2.6429	(0.9311)	<**.001**	3.9
56 months	-0.0622	(0.9220)	2.0693	(1.6435)	<**.001**	1.6

Note. Numbers are reported as means (standard deviation) if not stated otherwise. Effect size Cohen's *d*: small=0.2, medium=0.5, large=0.8

Appendix H. Adjusted estimates[a] of predictors of a high degree of motor problems trajectory in the AYLS (Replication[b])

	High degree of motor problems trajectory Reference: Low degree of motor problems trajectory, OR(95% CI)			
	Model 1	Model 2	Model 3	Model 4
Pre-/pregnancy, perinatal complications				
Pre-pregnancy	**1.60 (1.14, 2.25)**	1.44 (0.99, 2.09)	1.28 (0.84, 1.94)	1.28 (0.84, 1.96)
Pregnancy	1.17 (0.88, 1.56)	0.94 (0.67, 1.32)	0.99 (0.70, 1.42)	1.04 (0.72, 1.51)
Perinatal	1.09 (0.87, 1.37)	0.97 (0.74, 1.28)	0.96 (0.72, 1.27)	0.97 (0.72, 1.29)
Neonatal characteristics and health				
Prematurity (<37 weeks GA)		0.61 (0.16, 2.36)	0.45 (0.12, 1.74)	0.44 (0.11, 1.70)
Low birth weight (<2500g)		1.68 (0.39, 7.16)	1.69 (0.38, 7.42)	1.95 (0.44, 8.68)
Head circumference		0.98 (0.81, 1.18)	0.95 (0.77, 1.17)	0.96 (0.78, 1.19)
SGA		0.68 (0.21, 2.18)	0.62 (0.18, 2.16)	0.64 (0.18, 2.24)
Neonatal complications		**1.29 (1.13, 1.47)**	1.11 (0.90, 1.37)	1.11 (0.90, 1.37)
Neonatal course				
INTI – Clinical course			0.77 (0.54, 1.10)	0.77 (0.54, 1.10)
INTI – Neurological status			**1.82 (1.37, 2.42)**	**1.85 (1.38, 2.48)**

	High degree of motor problems trajectory Reference: Low degree of motor problems trajectory, OR(95% CI)			
	Model 1	Model 2	Model 3	Model 4
Duration in hospital (10 days)			**1.17 (1.00, 1.36)**	**1.19 (1.02, 1.39)**
Early social environment				
Low FAI				2.22 (0.68, 7.26)
High FAI				1.19 (0.47, 2.99)
Poor PIRI				1.13 (0.40, 3.15)
No breastfeeding				0.40 (0.10, 1.62)

Abbreviations: FAI=Family Adversity Index; GA=gestational age; INTI = Intensity of Neonatal Treatment Index; SGA=small for gestational age; PIRI=Parent-Infant Relationship Index.

[a] Adjusted estimates of stepwise multivariate binomial logistic regression analyses (Odds Ratio and 95% Confidence Interval), predictors adjusted for all other variables in the prediction model; [b] The same multivariate regression analyses, established for BLS data was applied to AYLS data.

Appendix I. Sensitivity Analyses

Regression models were repeated excluding children with severe neurological impairments diagnoses at 56 months (BLS: *N*=95; AYLS *N*=15).

BLS. Trajectories of low and high degree of motor problems included *N*=4,453 and *N*=193 children, respectively. All estimates of predictors (Appendix L.1) remained comparable to initial regression models, however some changes in the final adjusted regression model were noted: similar to initial adjusted analyses, unstable or abnormal neonatal neurological status (OR 1.16, CI 1.06-1.26), duration in hospital (OR 1.18, CI 1.11-1.25), and poor parent-infant relationship (OR 1.62, CI 1.17-2.23) uniquely predicted a high degree of motor problems trajectory (Model 4, Appendix L.2). Neonatal complications, however, ceased to be a significant predictor of a high degree of motor problems (OR 1.08, CI 0.99-1.17). All predictors explained 14.8% of the variance in the final model.

AYLS. Both groups of children with low and high degree of motor problems included *N*=1,384 and *N*=24 children, respectively. Regression estimates (Appendices I.1 and I.2) were similar to initial analyses. Similar to initial adjusted analyses, unstable or abnormal neonatal neurological status (OR 1.87, CI 1.35-2.59) and duration in hospital (OR 1.21, CI 1.02-1.44) were associated with a high degree of motor problems trajectory (Model 4, Appendix I.2). All predictors explained 19% of the variance in Model 4.

Appendix I.1. Descriptives and unadjusted estimates[a] of potential predictors of early childhood motor trajectories in the BLS and AYLS (excluding children with severe neurological impairments diagnosed at 56 months)

	BLS				AYLS			
	Low degree of motor problems trajectory	High degree of motor problems trajectory	*Reference: Low degree of motor problems trajectory*		Low degree of motor problems trajectory	High degree of motor problems trajectory	*Reference: Low degree of motor problems trajectory*	
	N=4,453	*N*=193			*N*=1,384	*N*=24		
			OR (95% CI)	*p*-value			OR (95% CI)	*p*-value
Pre-/pregnancy and perinatal complications								
Pre-pregnancy, mean (SD)	1.10(0.78)	1.25(0.99)	**1.26 (1.07, 1.50)**	**.007**	1.24(0.88)	1.71(1.04)	**1.66 (1.12, 2.44)**	**.011**
Pregnancy, mean (SD)	1.34(1.22)	1.63(1.26)	**1.19 (1.07, 1.33)**	**.002**	1.22(1.16)	1.54(1.14)	1.24 (0.91, 1.70)	.177
Perinatal, mean (SD)	3.06(1.74)	3.74(1.68)	**1.24 (1.14, 1.34)**	**<.001**	2.84(1.51)	3.21(1.50)	1.16 (0.90, 1.48)	.256
Neonatal characteristics and health								
Prematurity (<37 weeks GA), n (%)	1,418(31.8)	103(53.4)	**2.45 (1.83, 3.27)**	**<.001**	279(20.2)	7(29.2)	1.63 (0.67, 3.97)	.281
Low birth weight (<2500g), n (%)	1,483(33.3)	116(60.1)	**3.02 (2.25, 4.05)**	**<.001**	218(15.8)	6(25.0)	1.78 (0.70, 4.54)	.226

	BLS				AYLS			
	Low degree of motor problems trajectory *N*=4,453	High degree of motor problems trajectory *N*=193	*Reference: Low degree of motor problems trajectory* OR (95% CI)	*p*-value	Low degree of motor problems trajectory *N*=1,384	High degree of motor problems trajectory *N*=24	*Reference: Low degree of motor problems trajectory* OR (95% CI)	*p*-value
Head circumference, mean (SD)	33.32(2.41)	31.65(3.46)	**0.80 (0.77, 0.84)**	**<.001**	34.56(2.23)	33.02(3.98)	**0.82 (0.72, 0.93)**	**.002**
Male sex, n (%)	2,324(52.2)	109(56.5)	1.19 (0.89, 1.59)	.244	741(53.5)	13(54.2)	1.03 (0.46, 2.31)	.951
SGA, n (%)	1,049(23.6)	73(37.8)	**1.97 (1.46, 2.66)**	**<.001**	184(13.3)	3(12.5)	0.92 (0.28, 3.16)	.909
Neonatal complications, mean (SD)	3.83(2.85)	6.12(3.73)	**1.25 (1.20, 1.31)**	**<.001**	2.10(2.39)	4.29(4.36)	**1.25 (1.12, 1.39)**	**<.001**
Neonatal course								
INTI - Clinical course, mean (SD)	2.26(2.14)	3.66(2.84)	**1.27 (1.20, 1.34)**	**<.001**	1.66(1.93)	3.15(2.39)	**1.37 (1.15, 1.62)**	**<.001**
INTI - Neurological status, mean (SD)	2.30(2.27)	4.04(2.60)	**1.34 (1.27, 1.43)**	**<.001**	1.16(1.56)	3.07(2.18)	**1.70 (1.39, 2.08)**	**<.001**
Duration in hospital (10 days), mean (SD)	1.99(2.02)	4.57(4.70)	**1.29 (1.24, 1.34)**	**<.001**	0.82(1.48)	2.71(4.46)	**1.24 (1.12, 1.36)**	**<.001**

	BLS				AYLS			
	Low degree of motor problems trajectory	High degree of motor problems trajectory	*Reference: Low degree of motor problems trajectory*		Low degree of motor problems trajectory	High degree of motor problems trajectory	*Reference: Low degree of motor problems trajectory*	
	N=4,453	*N*=193			*N*=1,384	*N*=24		
			OR (95% CI)	*p*-value			OR (95% CI)	*p*-value
Early social environment								
Low SES, n (%)	1,674(37.6)	93(48.2)	1.34 (0.98, 1.83)	.061	279(20.4)	5(22.7)	1.42 (0.46, 4.39)	.540
High SES, n (%)	993(22.3)	26(13.5)	**0.63 (0.40, 0.99)**	**.046**	455(33.2)	9(40.9)	1.57 (0.60, 4.10)	.357
Low FAI, n (%)	1,333(30.1)	36(18.7)	0.66 (0.44, 1.00)	.050	173(12.5)	4(16.7)	1.30 (0.40, 4.27)	.668
High FAI, n (%)	1,470(33.2)	91(47.2)	**1.52 (1.10, 2.10)**	**.012**	706(51.0)	11(45.8)	0.87 (0.36, 2.13)	.767
Poor PIRI, n (%)	1,409(33.5)	99(53.2)	**2.26 (1.68, 3.03)**	**<.001**	165(12.0)	6(26.1)	**2.59 (1.01, 6.67)**	**.048**
High PSI, n (%)	1,222(27.9)	50(26.7)	0.94 (0.68, 1.31)	.726	404(29.3)	12(52.2)	**2.63 (1.15, 6.02)**	**.022**
No breastfeeding, n (%)	1,965(45.8)	132(70.6)	**2.84 (2.06, 3.91)**	**<.001**	98(7.3)	4(17.4)	2.68 (0.89, 8.02)	.079

Abbreviations: FAI=Family Adversity Index; GA=gestational age; INTI = Intensity of Neonatal Treatment Index; PIRI=Parent-Infant Relationship Index; PSI=Psychosocial Stress Index; SES=socioeconomic status SGA=small for gestational age.

[a] Unadjusted estimates of univariate binomial logistic regression analyses.

Appendix I.2. Adjusted estimates[a] of significant predictors of a high degree of motor problems trajectory in the BLS and AYLS[b] (excluding children with severe neurological impairments diagnosed at 56 months)

	BLS				AYLS			
	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2	Model 3	Model 4
Pre-/pregnancy, perinatal complications								
Pre-pregnancy	1.18 (0.99, 1.41)	1.14 (0.96, 1.36)	1.17 (0.98, 1.41)	1.20 (0.96, 1.45)	**1.60 (1.08, 2.36)**	**1.59 (1.04, 1.42)**	1.39 (0.87, 2.22)	1.36 (0.82, 2.23)
Pregnancy	1.10 (0.98, 1.23)	0.93 (0.82, 1.07)	0.93 (0.81, 1.06)	0.88 (0.76, 1.02)	1.19 (0.86, 1.65)	1.08 (0.75, 1.56)	1.17 (0.80, 1.72)	1.19 (0.78, 1.81)
Perinatal	**1.20 (1.11, 1.31)**	1.06 (0.96, 1.17)	1.06 (0.96, 1.18)	1.05 (0.95, 1.17)	1.07 (0.83, 1.39)	0.99 (0.73, 1.35)	0.98 (0.71, 1.35)	1.04 (0.75, 1.45)
Neonatal characteristics and health								
Prematurity (<37 weeks GA)		0.92 (0.58, 1.45)	0.90 (0.56, 1.45)	0.94 (0.57, 1.56)		0.54 (0.12, 2.49)	0.36 (0.08, 1.64)	0.37 (0.08, 1.76)
Low birth weight (<2500g)		1.38 (0.84, 2.24)	1.35 (0.81, 2.25)	1.22 (0.72, 2.08)		0.55 (0.09, 3.39)	0.55 (0.09, 3.55)	0.57 (0.08, 3.86)
Head circumference		0.94 (0.87, 1.02)	1.01 (0.93, 1.10)	0.96 (0.91, 1.08)		0.89 (0.71, 1.11)	0.88 (0.69, 1.12)	0.87 (0.67, 1.12)

	BLS				AYLS			
	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2	Model 3	Model 4
SGA		1.21 (0.85, 1.74)	1.22 (0.84, 1.76)	1.16 (0.79, 1.70)		0.62 (0.15, 2.48)	0.61 (0.14, 2.67)	0.64 (0.14, 2.89)
Neonatal complications		**1.18 (1.12, 1.25)**	1.08 (1.00, 1.17)	1.08 (0.99, 1.17)		**1.26 (1.08, 1.47)**	1.01 (0.78, 1.31)	0.96 (0.73 1.26)
Neonatal course								
INTI – Clinical course			**0.88 (0.79, 0.98)**	0.91 (0.81, 1.01)			0.83 (0.55, 1.26)	0.86 (0.56, 1.31)
INTI – Neurological status			**1.20 (1.11, 1.30)**	**1.16 (1.06, 1.26)**			**1.92 (1.41, 2.63)**	**1.87 (1.35, 2.59)**
Duration in hospital (10 days)			**1.20 (1.13, 1.28)**	**1.18 (1.11, 1.25)**			**1.20 (1.01, 1.42)**	**1.21 (1.02, 1.44)**
Early social environment								
Low SES				1.05 (0.74, 1.50)				1.26 (0.33, 4.82)
High SES				0.72 (0.43, 1.19)				1.64 (0.57, 4.75)
Low FAI				0.82 (0.52, 1.29)				2.06 (0.55, 7.67)

	BLS				AYLS			
	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2	Model 3	Model 4
High FAI				1.36 (0.95, 1.95)				0.72 (0.24, 2.13)
Poor PIRI				**1.62 (1.17, 1.23)**				1.71 (0.56, 5.28)
No breastfeeding				1.38 (0.96, 2.00)				0.87 (0.20, 3.77)

Abbreviations: GA=gestational age; INTI = Intensity of Neonatal Treatment Index; PIRI=Parent-Infant Relationship Index; SGA=small for gestational age.

[a] Adjusted estimates of multivariate binomial logistic regression analyses (Odds Ratio and 95% Confidence Interval), predictors adjusted for all other variables in the prediction model; [b] Replication: The same multivariate regression analysis (Model 4) established for BLS data was applied to AYLS data.

Appendix J. Attention regulation, indicators and factor loadings

Indicators	Age	Factor loading
CBCL attention score (parent report)	6 years	0.420
CBCL attention score (parent report)	8 years	0.401
TRCB task orientation (observer report)	6 years	0.795
TRCB task orientation (observer report)	8 years	0.801
TRCB team rating attention span (observer report)	6 years	0.809
TRCB team rating attention span (observer report)	8 years	0.828

Appendix K. 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 'Cognitive function at 6 and 8 years'

	Physiotherapy unmatched: *n*=314 matched: *n*=283	No Physiotherapy unmatched: *n*=862 matched: *n*=828	Standardized bias (%)
Initial motor problem scores			
Motor problems at birth (z-score), mean			
Unmatched	0.39	-0.22	63.5
Matched	0.25	0.27	-1.7
Motor problems at 5 months (z-score), mean			
Unmatched	0.57	-0.21	79.8
Matched	0.37	0.39	-1.9
Child biological characteristics			
Gestational age (weeks), mean			
Unmatched	34.12	37.73	-89.9
Matched	34.56	34.97	-10.3
Birthweight (g), mean			
Unmatched	2128	2892	-82.9
Matched	2209	2220	-1.2
Small for gestational age, %			
Unmatched	33.4	21.3	27.3
Matched	32.9	37.0	-9.4
Head circumference (cm), mean			
Unmatched	30.56	33.33	-81.2
Matched	30.95	30.99	-1.2
Male sex, %			
Unmatched	55.7	48.1	15.2

	Physiotherapy unmatched: *n*=314 matched: *n*=283	No Physiotherapy unmatched: *n*=862 matched: *n*=828	Standardized bias (%)
Matched	54.8	58.6	-7.7
Multiples, %			
Unmatched	13.7	5.5	28.3
Matched	13.8	11.7	7.1
Peri- and neonatal health and medical factors			
Pre-pregnancy complications			
Unmatched	1.22	1.19	3.9
Matched	1.18	1.24	-7.3
Complications during pregnancy			
Unmatched	1.67	1.24	34.1
Matched	1.63	1.71	-6.3
Complications during birth			
Unmatched	3.86	2.95	52.2
Matched	3.81	3.82	-0.7
Neonatal complications			
Unmatched	6.83	3.41	92.6
Matched	6.33	6.06	7.1
Neonatal neurological problems, mean			
Unmatched	8.83	3.93	88.9
Matched	7.78	7.13	12.8
Duration in hospital (days), mean			
Unmatched	52.11	20.65	73.7
Matched	47.20	51.59	-10.3
Early socio-environmental factors			
Socioeconomic status, %			

	Physiotherapy unmatched: *n*=314 matched: *n*=283	No Physiotherapy unmatched: *n*=862 matched: *n*=828	Standardized bias (%)
Middle			
Unmatched	35.0	37.5	-5.1
Matched	34.3	34.3	-0.1
Low			
Unmatched	35.7	30.2	11.7
Matched	36.4	35.0	2.9
No breastfeeding, %			
Unmatched	54.1	40.0	28.5
Matched	52.3	54.9	-5.2
Neurological impairments diagnosed in early childhood			
Severe neurological impairments at 56 months, %			
Unmatched	10.2	0.8	42.0
Matched	4.9	2.7	10.1

Note. Mean bias (%): unmatched=50.0, matched=5.7; 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 12, Chapter 2.

Appendix L. 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 'Attention regulation at 6 and 8 years'

	Physiotherapy unmatched: *n*=346 matched: *n*=312	No Physiotherapy unmatched: *n*=948 matched: *n*=911	Standardized bias (%)
Initial motor problem scores			
Motor problems at birth (z-score), mean			
Unmatched	0.38	-0.21	62.1
Matched	0.25	0.23	1.8
Motor problems at 5 months (z-score), mean			
Unmatched	0.57	-0.20	78.6
Matched	0.37	0.37	-1.0
Child biological characteristics			
Gestational age (weeks), mean			
Unmatched	34.15	37.64	-87.3
Matched	34.59	34.91	-8.0
Birthweight (g), mean			
Unmatched	2129	2867	-79.4
Matched	2219	2230	-1.3
Small for gestational age, %			
Unmatched	35.0	21.7	29.7
Matched	33.7	35.9	-5.1
Head circumference (cm), mean			
Unmatched	30.60	33.25	-77.7
Matched	31.02	31.05	-0.8
Male sex, %			
Unmatched	56.4	48.3	16.1

	Physiotherapy unmatched: *n*=346 matched: *n*=312	No Physiotherapy unmatched: *n*=948 matched: *n*=911	Standardized bias (%)
Matched	55.1	58.7	-7.1
Multiples, %			
Unmatched	13.0	6.2	23.1
Matched	13.5	11.6	6.4
Peri- and neonatal health and medical factors			
Pre-pregnancy complications			
Unmatched	1.24	1.19	5.4
Matched	1.20	1.22	-2.8
Complications during pregnancy			
Unmatched	1.67	1.27	31.9
Matched	1.62	1.69	-5.7
Complications during birth			
Unmatched	3.86	2.97	51.2
Matched	3.80	3.78	1.6
Neonatal complications			
Unmatched	6.81	3.52	89.1
Matched	6.36	6.07	7.8
Neonatal neurological problems, mean			
Unmatched	8.39	4.03	86.9
Matched	7.79	7.18	12.2
Duration in hospital (days), mean			
Unmatched	51.35	21.30	70.0
Matched	46.53	51.64	-12.3
Early socio-environmental factors			
Socioeconomic status, %			

	Physiotherapy unmatched: *n*=346 matched: *n*=312	No Physiotherapy unmatched: *n*=948 matched: *n*=911	Standardized bias (%)
Middle			
Unmatched	34.7	38.2	-7.3
Matched	34.9	34.5	0.8
Low			
Unmatched	35.8	31.5	9.1
Matched	36.9	36.0	1.9
No breastfeeding, %			
Unmatched	55.5	41.5	28.3
Matched	53.5	56.3	-5.6
Neurological impairments diagnosed in early childhood			
Severe neurological impairments at 56 months, %			
Unmatched	9.8	0.9	40.0
Matched	4.8	3.2	7.4

Note. Mean bias (%): unmatched=48.6, matched=5.0; 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 12, Chapter 2.