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Minor neurological dysfunction in five year old very preterm children is associated with lower processing speed

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ABSTRACT

Background: Minor neurological dysfunction (MND) is present in one quarter to one third of children born very preterm (VP). The more severe form, complex (c)-MND has been associated with learning disabilities, behavioural and motor problems.
Objective: To study the association between c-MND and neurocognitive and motor disabilities at age five in VP children without CP.
Methods: Ninety-four children born with gestational age < 30 weeks and/or a birth weight < 1000 g were assessed at five years corrected age. MND was classified according to Touwen. The Wechsler Preschool and Primary School Scale of Intelligence (WPPSI-III-NL) was used to measure intelligence. Simple reaction time, focused attention and visuomotor coordination were measured using the Amsterdam Neuropsychological Tasks, and working memory using a Digit Span Task. For motor skills the Movement Assessment Battery for children (M-ABC2) was used.
Results: Eighty-one percent was classified as 'normal' (no or simple (s-)-MND) and 19% as 'abnormal'(c-MND or mild CP). The abnormal group had a significantly lower processing speed quotient (PSQ), M-ABC percentile score and slower simple Reaction Time than the normal group.
Verbal IQ, Performance IQ, working memory, focused attention and visuomotor coordination did not differ between groups. Exclusion of the mild CP cases (n = 4) led to similar results.
Conclusions: Five year old VP children with c-MND have lower PSQ, slower reaction time, and poorer motor skills, than those without c-MND. Neurological examination should include identification of MND to help identify children at risk for neurocognitive disabilities.

1. Introduction

Minor neurological dysfunction (MND) is defined as the occurrence of neurological symptoms in the absence of evident neurological pathology i.e. cerebral palsy (CP). While the incidence of CP is decreasing in preterm infants [1], MND is still often occurring [2]. Seven to 20% of healthy term born children has a form of MND and prevalence before puberty increases with age [3]. The prevalence of simple (s-) and complex (c-) MND at the age of five in a population of preterm small and appropriate for gestational age neonates is much higher, between 26 and 49% [2,4–6]. The presence of s-MND is considered to reflect the lower end of the normal distribution of physiological brain function [3]. C-MND is strongly related to pre- and perinatal risk factors and is considered as a borderline form of CP [3]. Known risk factors in prematurity (i.e. perinatal infection, intra-ventricular haemorrhage (IVH), chronic lung disease etc.) increase the risk of MND [3,6]. These risk factors also lead to diffuse white matter damage or localised damage in cerebellum and/or basal ganglia [3]. MRI studies have demonstrated that mild to moderate basal ganglia lesions and/or marked white matter damage are associated with MND [7].

Basal ganglia and cerebellum have thalamo-cortical connections to the pre-motor cortex as well as to prefrontal areas. Damage to these circuitries therefore may not only become apparent in slow processing speed but also in motor and learning difficulties that are characteristic in children with MND.

Abbreviations: MND, minor neurological dysfunction; c-MND, complex-minor neurological dysfunction; s-MND, simple minor neurological dysfunction; WPSSI-III-NL, Wechsler Preschool and Primary Scale of Intelligence third edition, Dutch version; IQ, intelligence quotient; PSQ, processing speed quotient; M-ABC-2, Movement Assessment Battery for children-2; VP, very preterm; SES, socio-economic status; ANT, Amsterdam Neuropsychological Tasks; RT, Reaction Time; NICU, neonatal intensive care unit.

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In previous studies in a preterm population and also in a population of female healthy term born children, the presence of c-MND was indeed found to increase the risk of concurrent learning disabilities and behavioural problems [6,8,9]. Within the spectrum of MND, especially fine manipulative and coordination problems were associated with lower IQ [10].

Also, the development of autism spectrum and other psychiatric disorders in children born before 32 weeks gestational age was found to be related to MND [11,12]. Moreover, in previous papers we have demonstrated that abnormal motor scores were associated with c-MND [13].

Thus, in literature c-MND is a risk factor for a broad array of developmental problems. To get further insight in the association between c-MND and its associated developmental problems, we set out to study, in a cohort of very preterm born children, the relationship between MND, neurocognitive measures and motor function with special attention to speed measures. We expected to find worse neurocognitive and motor skills in children with c-MND but not with s-MND.

2. Methods

2.1. Patients

The present study is a single centre prospective cohort study as part of the follow-up program of the Neonatal Intensive Care Unit (NICU) from Emma's Children's Hospital in the Academic medical Centre, Amsterdam, the Netherlands. The study population consisted of children born at gestational age of <30 weeks or with a birth weight of <1000 g. Exclusion criteria were severe handicaps, as a result of which an age appropriate IQ test was not feasible, a genetic syndrome, participation in other studies that required a different study protocol or no previous follow-up visits to our clinic. Moreover, for the current study, the presence of CP > GMFSC > 1 was an exclusion criterion (see Fig. 1 for details of patient flow). For detailed description of the protocol see Potharst et al. [2]. At the corrected age of five years old, children were invited at our outpatient clinic for long term follow-up assessments between December 2007 and June 2009.

2.2. Assessment schedule

For every participant two separate visits were planned shortly after the child reached the corrected age of five years. During the first appointment one of three trained child psychologists assessed intelligence, inhibition, sustained attention and visual-motor coordination. In the second session within three months of the first visit, the psychologist assessed working memory, focused attention and processing speed, while one of three trained paediatricians assessed motor and neurological status.

Perinatal and socio-economic characteristics were taken from the ongoing NICU database. A combined measure of parental education level was used as a proxy of socio-economic status (SES) [2]. Standard scores of the outcome measures were calculated from raw scores based on the corrected age at testing.

2.3. Outcome measures

2.3.1. Neurological development

Neurological development was assessed using the standardised and age specific neurological examination according to Touwen [14]. Eight different domains were tested: posture, reflexes, fine manipulation, involuntary and associated movements, coordination, sensory deficits and cranial nerve dysfunction. According to the classification of Hadders-Algra [3], children were classified as neurologically normal if having no abnormal domains. If 1 or 2 domains were scored abnormally this was classified as s-MND and 3 or more abnormal domains as c-MND. CP was diagnosed when definite abnormalities in posture, tone and reflexes were found. Classification of CP was done according to Gross Motor Function Classification Scale (GMFSC) [15]. We divided the patients into two groups. The first ('neuro-normal') group consisted of

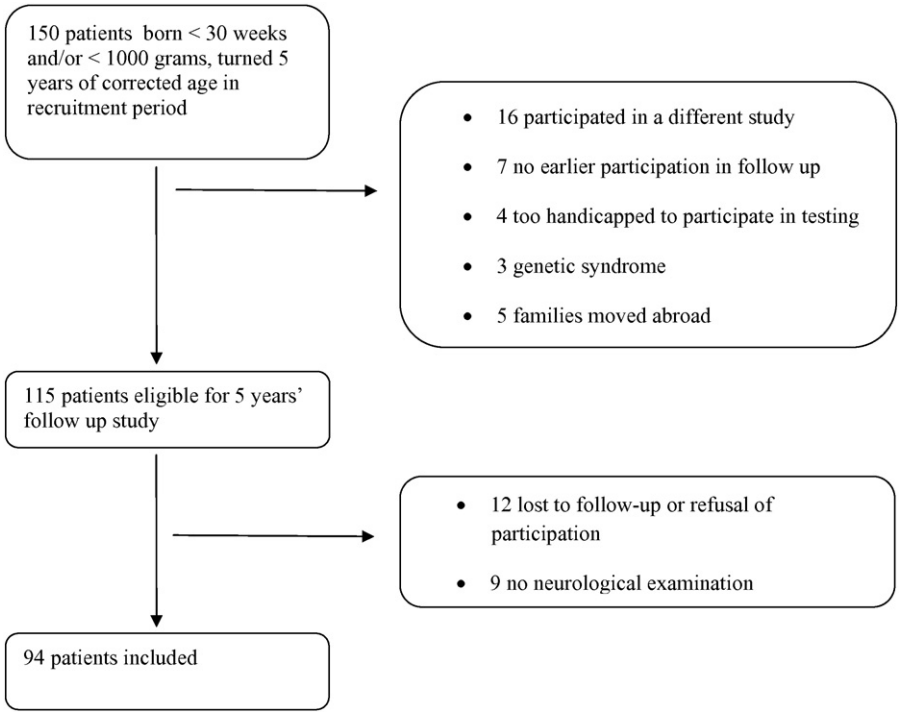

Fig. 1. Patient flow of inclusion.