



## Minor neurological dysfunction and cognition in 9-year-olds born at term



Hedwig K. Kikkert, Corina de Jong, Mijna Hadders-Algra\*

Department of Paediatrics – Developmental Neurology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

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### ABSTRACT

**Background:** In children with developmental disorders, motor problems often co-occur with cognitive difficulties. Associations between specific cognitive deficits underlying learning problems and minor neurological dysfunction (MND) are still unknown.

**Aims:** To assess associations between specific types of MND as clinical markers of non-optimal brain function and performance in specific cognitive domains.

**Study design:** Part of a randomized controlled trial.

**Subjects:** Three hundred and forty one 9-year-old children born at term (177 boys, 164 girls).

**Outcome measures:** Children were neurologically assessed to detect eight types of MND: mild dysfunction in posture and muscle tone, reflexes, coordination, fine manipulative ability, sensory function, cranial nerve function, choreiform dyskinesia and excessive associated movements. Cognitive function in the domains of attention, memory and language was evaluated using the Test of Everyday Attention for Children (TEA-Ch), a developmental neuropsychological assessment (NEPSY) and the Children's Memory Scale.

**Results:** Fine manipulative disability and coordination problems were associated with lower scores on attention, memory and learning and language, other types of MND were not. Girls with coordination problems performed significantly worse on attention/executive function than those without this dysfunction; however, in boys, such association was absent.

**Conclusion:** Particularly, fine manipulative disability and coordination problems were associated with worse cognitive function in the domains of attention, learning and memory and language. Previous and present data suggest a minor sex difference in neurocognitive associations: in girls dysfunction of the cerebello-thalamo-cortical pathways may be associated with cognitive deficits, while in boys cognitive impairment may be associated with dysfunction of cortico-striato-thalamo-cortical pathways.

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### 1. Introduction

Children with developmental disorders frequently exhibit both motor problems and cognitive difficulties. For instance, developmental coordination disorder (DCD) has been associated with attention deficit/hyperactivity disorder (ADHD) and cognitive deficits in the domains of working memory, language and executive functions [1]. Children with ADHD often have additional problems with balance, coordination and fine motor skills [1]. Also dyslexia has been associated with minor neurological dysfunction (MND), in particular fine manipulative disability [2]. In addition, MND has been associated with

learning problems, such as problems with reading, spelling and arithmetic [3–5].

MND refers to findings during a standardized and age-specific neurological examination. It denotes the occurrence of minor neurological dysfunction in absence of evident neurological pathology. MND has been associated with perinatal adversities, such as preterm birth [5] and maternal drug or alcohol use during pregnancy [6,7] and can be expressed in severity of MND and in type of MND. The severity of MND is based on a distinction between simple MND and complex MND. Complex MND reflects the clinically relevant form of brain dysfunction on account of its strong associations with a) prenatal and perinatal risk factors, such as gestational age [5], – resembling the etiology of cerebral palsy – and b) learning and behavioral problems. Conversely, simple MND, the more prevalent form of MND, has weak relationships with perinatal adversities and with learning and behavioral problems. Simple MND may be seen as a typical, but non-optimal form of brain development and may in fact be regarded as a minor neurological *difference*.

The different types of MND include dysfunctional posture and muscle tone, fine manipulative disability and dyscoordination. Specifically, the latter two types of MND have been related to learning

**Abbreviations:** MND, minor neurological dysfunction; TEA-CH, Test of Everyday Attention for Children; NEPSY, a developmental neuropsychological assessment; CMS, Children's Memory Scale; DCD, developmental coordination disorder; ADHD, attention deficit/hyperactivity disorder; LCPUFA, long chain polyunsaturated fatty acids; OOS, obstetric optimality score; HOME, Home Observation for Measurement of the Environment; WAIS III, Wechsler Adult Intelligence Scale III; BMI, body mass index.

\* Corresponding author at: University Medical Center Groningen, Developmental Neurology, Hanzeplein 1, 9713 GZ Groningen, The Netherlands. Tel.: +31 50 3614247; fax: +31 50 3619158.

E-mail address: [m.hadders-algra@umcg.nl](mailto:m.hadders-algra@umcg.nl) (M. Hadders-Algra).

problems [4,8] and to lower IQ scores [9]. However, the nature of the cognitive deficits underlying these learning difficulties is still unknown. The Groningen LCPUFA (long chain polyunsaturated fatty acids) project offered the possibility to study relationships between MND and specific cognitive domains in nine-year old children born at term. As mentioned above, deficits in memory, attention, executive functions and language have been associated with DCD; DCD in turn is associated with severity and specific types of MND [10]. Previously, we reported that in children born at term especially type, rather than severity, of MND was associated with lower IQ [9]. Therefore, we aimed to assess relations between specific cognitive domains and type of MND. Based on the above mentioned studies, we expected that specifically fine manipulative disability and coordination problems will be associated with cognitive deficits. In addition, sex differences in the association between MND and cognition were assessed. The rationale for the specific attention to sex was twofold. First, it is well known that sex differences exist in developmental disorders, for example ADHD occurs more often in boys and eating disorders more often in girls [11]. Second, imaging studies have demonstrated differences in the developmental course of the brain [12]. Previously, we demonstrated that in boys fine manipulative disability was associated with lower IQ scores, but in girls no such association was found [9]. Therefore, we hypothesize that in boys, fine manipulative disability in particular will be associated with lower scores on cognitive tests.

## 2. Methods

### 2.1. Participants

Three hundred and forty-one term born children (177 boys, 164 girls) aged from 8 years and 10 months to 9 years and 7 months

(mean 9.0 SD 0.22) participated in the study. The children took part in a double-blind randomized controlled trial on the effects of the supplementation of formula with LCPUFA during the first two months after birth. Children with perinatal risk were excluded from the study. Infants were randomized into two groups: a group receiving formula with LCPUFA (Nutrilon Premium® with 0.45% (by wt) arachidonic acid and 0.30% (by wt) docosahexaenoic acid) (n = 145) and a group receiving control formula without LCPUFA (n = 169). A third group of infants were breastfed after birth (n = 160). Of the 474 infants enrolled at birth, 72% participated in the follow-up assessment at nine years (Fig. 1; for details see [13]).

Extensive information on social background, obstetric conditions and pre- and perinatal circumstances was collected, which enabled us to form an obstetric optimality score (OOS) [14]. The Home Observation for Measurement of the Environment (HOME) was used to evaluate social background at 18 months and an abbreviated version of the Wechsler Adult Intelligence Scale (WAIS III) was applied to estimate maternal verbal IQ.

At nine years, data on current social situation was collected. Characteristics of the participating children and children lost to follow-up can be found in Table 1. The ethics committee of the University Medical Center Groningen approved the study design and all parents provided written informed consent for participation of their child in the study.

### 2.2. Procedures

An age-specific technique designed for the evaluation of minor neurological dysfunction [15] was used to assess neurological condition. The assessment, which takes developmental changes into account, was videotaped. Items of the examination are grouped in eight domains of dysfunction: fine manipulative ability, coordination,

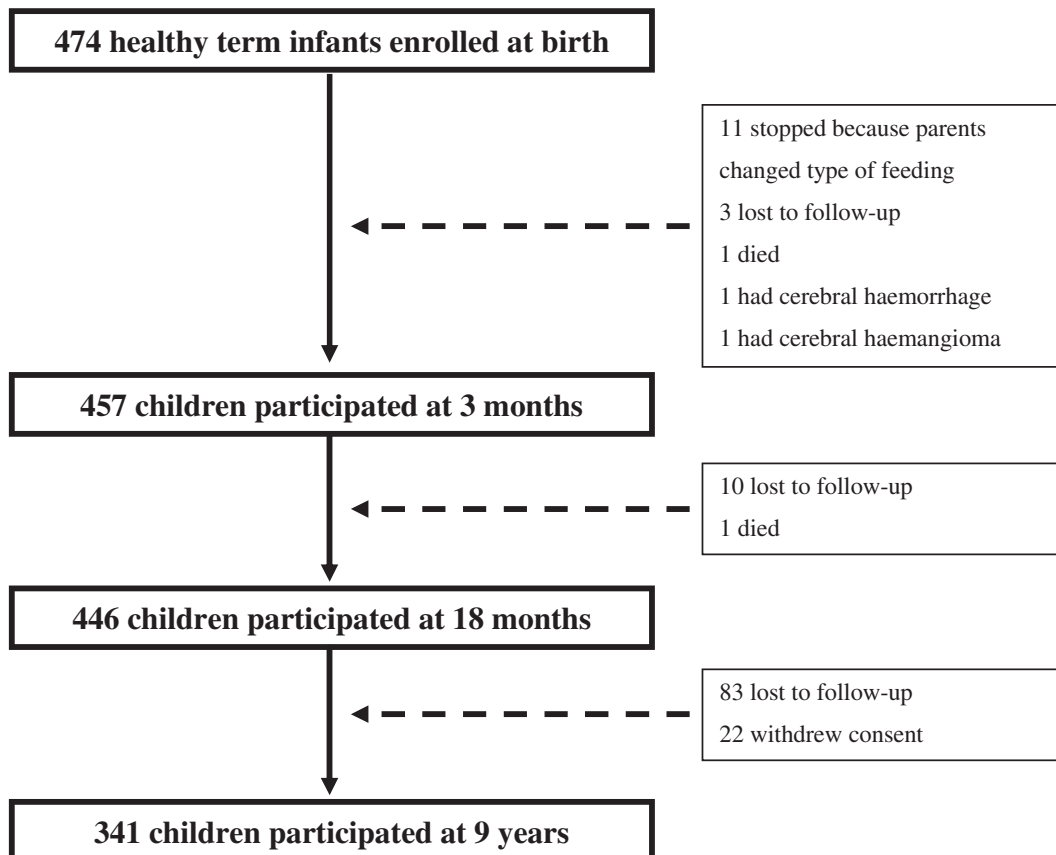


Fig. 1. Flowchart of children from study enrolment until 9 years follow-up.

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