

Developmental Coordination Disorder: Is Clumsy Motor Behavior Caused By a Lesion of the Brain At Early Age?

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SUMMARY

Children presenting with Developmental Coordination Disorder or clumsiness often exhibit signs of minor neurological dysfunction (MND). The data of the Groningen Perinatal Project, a long-term follow-up project on the relations between prenatal and perinatal adversities and neurological, behavioral, and cognitive development revealed that two basic forms of MND can be distinguished: simple and complex MND. During school age children with *simple MND* are characterized by the presence of one or two dysfunctional clusters of MND, in adolescence by the presence of choreiform dyskinesia or hypotonia. Probably the major sources of origin of simple MND are genetic constitution and stress during early life. Simple MND might reflect the lower tail of the normal distribution of the quality of non-pathological brain function. In line with this hypothesis is the finding that simple MND is associated with only a moderately increased risk for learning- and behavioral problems. Children with *complex MND* present at school age with at least three dysfunctional clusters of MND, in adolescence with problems in fine manipulation or coordination. Perinatal adversities play an

evident etiological role in the development of complex MND, suggesting that it might be attributed to a lesion of the brain at early age. In line with this idea is the finding that complex MND shows a strong correlation with attention and learning problems.

KEYWORDS

minor neurological dysfunction, soft neurological signs, prenatal stress, preterm birth, intrauterine growth retardation

INTRODUCTION

During the last century many terms, such as *dyspraxia*, *minimal brain dysfunction*, *sensory integrative dysfunction*, and *developmental coordination disorder* have been used to describe children with clumsy motor behavior (Geuze et al., 2001; Henderson & Henderson, 2003). But gradually it was realized that the heterogeneity in labels was confusing and counterproductive. Participants at an international, multidisciplinary consensus meeting in 1994 agreed to use the DSM-IV term Developmental Coordination Disorder or DCD (American Psychiatric Association, 1994; Polatajko et al., 1995). The term DCD in general refers to children with normal intelligence who have poor motor coordination without evidence of frank neurological pathology, such as cerebral

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palsy or muscular dystrophy.¹ The motor problems of children with DCD are so serious that they affect daily activities at home and at school.

The heterogeneity in terminology has hampered research, such as the search for etiological factors and the understanding of pathogenetic mechanisms of clumsy motor behavior or DCD. What percentage of DCD cases can be attributed to damage of the nervous system remains to be determined, and for those cases in which this attribution can be made, whether the damage occurred in prenatal, perinatal, or early postnatal development. At present these questions can not be answered. But, recent research allows for the answering of a relatively close question: what part of minor neurological dysfunction in childhood is caused by a lesion of the brain at early age? The aim of the present paper is to discuss the latter question.

MINOR NEUROLOGICAL DYSFUNCTION

Minor neurological dysfunctions can be detected during a standardized and age-specific neurological examination. These dysfunctions are also known as *soft neurological signs*. But the term MND is preferable to the expression soft neurological signs as the word soft has the fallacious connotation of ambiguity (Touwen, 1987). Examples of assessment techniques for the detection of MND are the assessments according to Touwen (1979) or Herzig (1987) for school age children or the technique of Hempel (1993) for children at pre-school age. The assessments require a thorough knowledge of the age-specific properties of the child's neuromotor performance. Essential to the diagnosis of MND is the presence of a *cluster* of signs of dysfunction. This means that the presence of a single sign of dysfunction,

such as the isolated presence of a Babinski sign, does not allow for the label MND. The clusters are organized according to the functional, neuro-behavioral subsystems of the nervous system used in clinical practice (Touwen, 1979; Hadders-Algra et al., 1988a). The inter-observer agreement on the presence or absence of a cluster of dysfunctions is high (Hadders-Algra & Groothuis, 1999). Descriptions of the clusters at pre-school age and beyond are presented in Tables 1 and 2.

The data of the Groningen Perinatal Project (GPP), a long-term follow-up project on relations between prenatal and perinatal adversities and neurological, behavioral and cognitive development indicated that basically two distinct forms of MND can be distinguished: simple MND and complex MND (Hadders-Algra, 2002). In the following paragraphs the clinical relevance will be explained, especially that of the complex form of MND.

The criteria for simple and complex MND are age specific. This phenomenon is due to the developmental changes in the nervous system, which induce changes in the expression and prevalence of MND. Extrapolations of the data of the Groningen Perinatal Project (GPP) to the general population (see Hadders-Algra & Touwen, 1992) indicate that the rate of MND at pre-school age is relatively low (5% to 7%). During the following years, the frequency of MND shows a steady increase, reaching its peak of about 25% shortly before the emergence of puberty. The age-dependent increase in the prevalence of MND runs parallel to—and is presumably related to—the age-dependent increase in the complexity of brain function. The onset of puberty induces a substantial decline in the number of dysfunctional clusters of MND, so that at the age of 14 years only 7% to 8% of children exhibit MND. In addition, most adolescent children with MND present with only one dysfunctional cluster. Possibly the decline in MND around puberty is

¹ The diagnosis DCD can also be given to children with mental retardation, in case the motor difficulties are in excess of those usually associated with mental retardation (DSM-IV).

TABLE 1

Functional, i.e. neurobehavioral clusters of MND, based on the neurological examination of Hempel (1993) for children aged 1½ - 4 years, adapted from Hadders-Algra et al. (2003)

Cluster of dysfunction	Signs	Criteria for dysfunctional cluster
Dysfunctional muscle tone regulation	Abnormalities in muscle tone Abnormal posture during sitting, crawling, standing and walking	One or two of the following: - consistent mild deviations in muscle tone - consistent mild deviations in posture
Reflex abnormalities	Abnormal intensity and/or threshold or asymmetry in: - biceps reflex - knee jerk - ankle jerk Footsole response: uni- or bilateral Babinski sign	Presence of at least two signs
Gross motor dysfunction	Dyscoordination of arm and leg movements during crawling Block-like movements of trunk during crawling, standing and walking Age-inadequate balance Age- inadequate manoeuvrability during walking Age-inadequate ability to avoid objects during walking	Presence of at least two signs
Fine motor dysfunction	Absent pincergrasp in 1 or 2 hands Exclusive hand preference Abnormal quality of arm movements Poor adjustment of handopening Abnormal quality of hand movements	Presence of at least two signs
Rarely occurring miscellaneous disorders	Motor behavior of face, eyes, pharynx, tongue Involuntary movements, such as tremor	Evidence of at least one of the following: Mild cranial nerve palsy Consistent presence of tremor

TABLE 2

Functional, i.e., neurobehavioral clusters of MND, based on the neurological examination of Touwen (1979) for children aged 4 years and older, adapted from Hadders-Algra et al. (1988a).

Cluster of dysfunction	Based on	Criteria for dysfunctional cluster
Dysfunctional muscle tone regulation	Muscle tone Posture during sitting, crawling, standing and walking	One or more of the following: - consistent mild deviations in muscle tone - consistent mild deviations in posture
Reflex abnormalities	Abnormal intensity and/or threshold or asymmetry in: - biceps reflex - knee jerk - ankle jerk Footsole response: uni- or bilateral Babinski sign	Presence of at least two signs
Choreiform dyskinesia	Spontaneous motor behavior Test with extended arms Movements of face, eyes, tongue	Presence of at least one of the following - Marked choreiform movements of distal and facial muscles - Slight or marked choreiform movements of proximal muscles, eyes or tongue
Coordination problems	Finger-nose test Fingertip-touching test Diadochokinesis Kicking Knee-heel test Reaction to push (sitting, standing) Romberg Tandem gait Standing on one leg	Presence of age-inadequate performance of at least two tests
Fine manipulative ability	Finger-opposition test: - smoothness - transition Follow-a-finger test Circle test	Presence of age-inadequate performance of at least two tests
Rarely occurring miscellaneous disorders	Motor behavior of face, eyes, pharynx, tongue Associated movements during diadochokinesis, finger-opposition test, walking on toes or heels	Evidence of at least one of the following: - Mild cranial nerve palsy - Excessive amount of associated movements for age

TABLE 3

Age specific criteria for simple and complex MND (see Hadders-Algra 2002; Hadders-Algra et al., 2003)

AGE	METHOD	SIMPLE MND	COMPLEX MND
1½ to 4 yr	Hempel, 1993	1 MND cluster of dysfunction	> 1 MND cluster of dysfunction
4 yr to onset of puberty	Touwen, 1979	1-2 MND clusters of dysfunction	> 2 MND clusters of dysfunction
After onset of puberty	Touwen, 1979	<ul style="list-style-type: none"> • mild hypotonia • choreiform dyskinesia 	<ul style="list-style-type: none"> • mild coordination problems • mild fine manipulative disability

mediated by the hormonal changes occurring during this phase of life (Lunsing et al. 1992; Soorani-Lunsing et al. 1993). Candidate hormones are thyroxine and estrogen. Thyroxine utilization increases during puberty, and this might affect myelination, which could result in an improvement of the neurological condition (Timiras, 1972). The onset of puberty is also accompanied by a rise in gonadal hormones, such as estrogens in girls and androgens in boys. In the brain, the androgens are metabolized into estrogens (Jacobson, 1991; Martini & Melcangi, 1991). Recently, evidence has been accumulating that estrogens might play a positive role in response to brain injury, for instance by inducing axonal sprouting and enhancing synaptic transmission (Garcia-Segura et al. 2001). In addition, Hampson (1990) demonstrated that an increase in estrogen level can result in an improvement of motor performance. Thus, one could speculate that an increase in estrogen-level might induce a decline in MND.

Because of the developmental changes in MND, the criteria for simple and complex MND are age-specific. Before the onset of puberty the distinction is based on the number of clusters of dysfunction that the child exhibits; after the onset of puberty—when most children with MND present with a single

cluster of MND—discrimination is based on the type of dysfunction present (Table 3). Seemingly the process of puberty converts the nonspecific, quantitative expression of dysfunction of the pre-pubertal nervous system into a specific, qualitative, and possibly more adult-like display of brain dysfunction.

SIMPLE MND

The data of the GPP indicated that the estimated prevalence of simple MND in the general population is 15% at 9 years and 3% to 4% at 14 years (Hadders-Algra, 2002). The project revealed that only few perinatal risk-factors were associated with the development of simple MND. Simple MND turned out to be related to some extent to severe intrauterine growth retardation, namely, being born with a birthweight below the 2.3 percentile of the growth curve, an Apgar score at 3 minutes < 7, diseases like frequent colds between the age of 9 and 12 years, a family history of neuropsychiatric disorders, and male gender (Hadders-Algra et al., 1988a; Soorani-Lunsing et al., 1993). The presence of simple MND was associated with a moderately increased risk for learning and

behavioral problems, such as Attention Deficit Hyperactivity Disorder (ADHD; Hadders-Algra et al. 1988b; Soorani-Luning et al., 1994).

The GPP-findings make plausible the notion that simple MND has two major sources of origin. First, simple MND could, just like ADHD, have a substantial genetic component (cf., Faraone & Biederman, 1998). This hypothesis might imply that simple MND represents the lower tail of the normal distribution of the quality of non-pathological brain function. The other source of origin of simple MND could be stress during early life, such as stress associated with preterm birth (see for example, Hellerud & Storm, 2002), severe intrauterine growth retardation, mild to moderate degrees of perinatal asphyxia, or prenatal stress resulting from psychological stress of the mother.

Animal research indicates that prenatal stress can induce permanent alterations in the structure and function of the central nervous system (Weinstock, 2001). Studies in rats showed that prenatal stress induced by psychological stress of the mother does results not only in a long-term dysregulation of the hypothalamic-pituitary-adrenal axis, such as hyperreactivity to stress, but also in changes in serotonergic and noradrenergic activity in the cerebral cortex and alterations in dopaminergic activity in the striatum and prefrontal cortex (Peters, 1982; 1983; 1990; Weinstock, 2001). The results of other studies indicate that alterations in the development of the early arising monoaminergic systems (Lagercrantz & Ringstedt, 2001) can result in permanent changes of behavior and mild balance problems (Cases et al., 1995). Prenatal stress also can induce an impaired development of the maps of body representation in the primary somatosensory cortex (Cases et al. 1998) and inappropriately developed ocular dominance columns in the visual cortex (Gu & Singer, 1995). Schneider and coworkers (1992a, 1992b; 1992c; 1993; 1998), who addressed the sequelae of prenatal stress in rhesus and squirrel

monkeys, demonstrated that also in primates prenatal stress causes long-term alterations in the neurochemical make-up of the brain. The changes were accompanied by minor neuromotor dysfunctions such as balance problems, a delay in cognitive development, and behavioral abnormalities such as sleeping problems and decreased levels of explorative behavior, locomotion and social play, as well as sleeping problems.

In humans the evidence of the effect of maternal psychological stress on brain development of her offspring is as yet inconclusive (Mulder et al., 2002). The prospective studies of Zuckerman et al. (1990) and Lou et al. (1994) indicate that prenatal stressors of human life have a moderately negative effect on the neurobehavioral condition of the newborn infant. Whether this negative effect persists during further development is unclear. Retrospective studies suggest that prenatal psychological stress might have long-term consequences for brain development as they pointed to a relation between prenatal stress and an increased risk for psychiatric morbidity such as schizophrenia and depression (Huttunen & Niskanen, 1978; Watson et al. 1999). In contrast to the equivocal effect of psychological forms of prenatal stress, multiple studies have shown that non-psychological stress during early human life has a long lasting adverse effect on the child's neuromotor condition. For instance, severe intrauterine growth retardation, which is not accompanied by abnormalities in blood flow velocity profiles in the fetal aorta, is associated with an increased risk of simple MND (Hadders-Algra et al. 1988a; Ley et al., 1996). Likewise, preterm birth and low birthweight are related to less adequate motor control and DCD, irrespective of the presence of minor abnormalities on the neonatal ultrasound scans of the brain (Hadders-Algra et al. 1999; Holsti et al. 2002; Fallang et al. 2003).

In conclusion, simple MND might be considered to reflect a normal (non-pathological)

but non-optimal form of brain function. For example, the front-striatal dopaminergic system may operate in a non-optimal manner. A non-optimal brain wiring can be due to genetic constitution (e.g., Faraone & Biederman, 1998) or to aberrant 'fetal programming' resulting from stress in early life (Kajantie et al., 2002).

COMPLEX MND

The data of the GPP indicate that the estimated prevalence of complex MND at 9 years is 6% and that at 14 years 3% to 4% (Hadders-Algra, 2002). The project revealed that complex MND has strong prenatal and perinatal roots. Complex MND is associated in particular with neonatal neurological deviancy, birth before 33 weeks gestation, and a low obstetrical optimality score (Hadders-Algra et al., 1988a; Soorani-Lunsing et al., 1993). Ley et al. (1996), who studied MND at school age in growth retarded infants, showed that the development of complex MND was associated with an absent or reversed end-diastolic blood flow velocity in the fetal aorta. Their data and those of the GPP suggest that complex MND might be the result of a lesion of the brain at early age. The association between the low obstetrical optimality score and complex MND indicates that the lesion of the brain might be the consequence of a chain of obstetrical adversities.

Similar chains of prenatal and perinatal adversities are known to play a role in the etiology of cerebral palsy (Stanley et al., 2000), which might imply that complex MND could be regarded as a borderline form of cerebral palsy. Certain perinatal adversities occur during the part of life that corresponds to the last trimester of pregnancy. In this period especially the cerebellum and periventricular regions show a high developmental activity, which is associated with an increased vulnerability to harmful conditions. A site of

predilection for lesions is the central white matter (Volpe, 1995). Thus it could be surmised that at least part of complex MND might be due to an interruption of connecting fibre systems, such as the corpus callosum (Mercuri et al., 1996) or the descending systems in the internal capsule. Interestingly, a recent study indicated that lesions of the periventricular white matter in preterm infants are associated with a significant reduction of the cerebral cortical gray matter at term age (Inder et al. 1999). Also the type of dysfunctions that play a prominent role in complex MND, namely, the dysfunctions in fine manipulation and coordination (Table 3), point into a similar direction as they may reflect dysfunction of the cortico-striato-thalamo-cortical and cerebello-thalamo-cortical pathways. These circuitries play a role not only in sensorimotor aspects of motor programming, movement planning, program selection, and motor memory but also in cognitive tasks involved in learning and in regulating attention (Alexander & Crutcher, 1990; Leiner et al., 1993; Diamond, 2000). This could explain the strong association of complex MND with cognitive and attentional difficulties (Hadders-Algra et al. 1988b; Soorani-Lunsing et al., 1994).

DCD, CLUMSINESS, AND MND

Few studies have investigated the relation between clumsiness or DCD and MND. The data of the GPP indicated that teachers' reports of clumsiness are related more strongly to the child's neurological condition than are parents' reports of clumsiness (Fig. 1). Teachers considered 55% of the children with complex MND as clumsy against 13% of children with a normal neurological condition and 28% of children with simple MND. Similar relationships between DCD and MND were reported by Jongmans et al. (1997). This group studied preterm children at the age of 6 years both

by means of the Movement ABC (Henderson & Sugden, 1992) and the Touwen (1979) neurological examination. On the basis of the Touwen assessment, a neurological optimality score was computed. On the basis of this optimality score, children were classified as neurologically normal (score > 15th percentile), borderline (score between 5th and 15th percentile) and abnormal (score < 5th percentile). The border-line scores could be interpreted as the presence of simple MND, whereas the abnormally low scores probably represented complex MND. The large majority (92%) of children with 'complex MND' had a Movement ABC score below the 15th percentile, which in general is taken as the cut-off point for DCD (see Henderson & Henderson, 2003; Fig. 2). Their data underline that especially the children with complex

MND frequently suffer from motor problems interfering with activities of daily life.

CONCLUDING REMARKS

In children presenting with clumsiness or DCD, the distinction into two types of MND has considerable clinical relevance. Simple MND, which at school-age is the most frequently encountered form of MND, has limited clinical significance (Table 4). Simple MND reflects the presence of a normal, but non-optimally wired brain, which either has a genetic origin or can be attributed to stressful events during early life. Complex MND, on the other hand, can be considered a distinct form of perinatally acquired and more

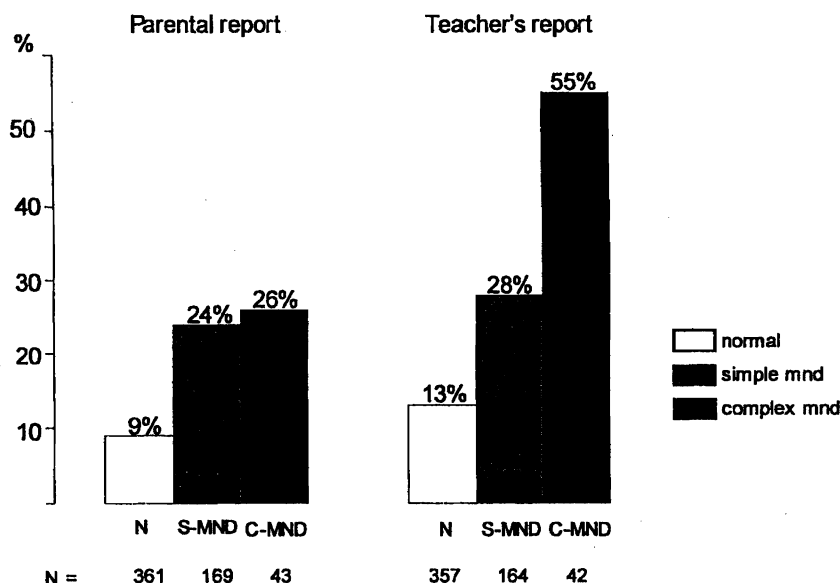


Fig. 1. Data of the Groningen Perinatal Project: relationship between neurological condition and clumsiness reported by parents (left panel) and teachers (right panel) in a group of nine-year-old children (see Hadders-Algra et al. 1988b).

TABLE 4

Relation between MND and clumsiness, behavioral and learning problems

	SIMPLE MND	COMPLEX MND
Relation with pre- and perinatal adversities	±	+++
Relation with clumsy motor behavior	++	+++
Relation with behavioral problems (especially ADHD)	+	+++
Relation with learning problems	+	+++

± = very weak relation, + = weak relation, ++ = clear relation, +++ very strong relation

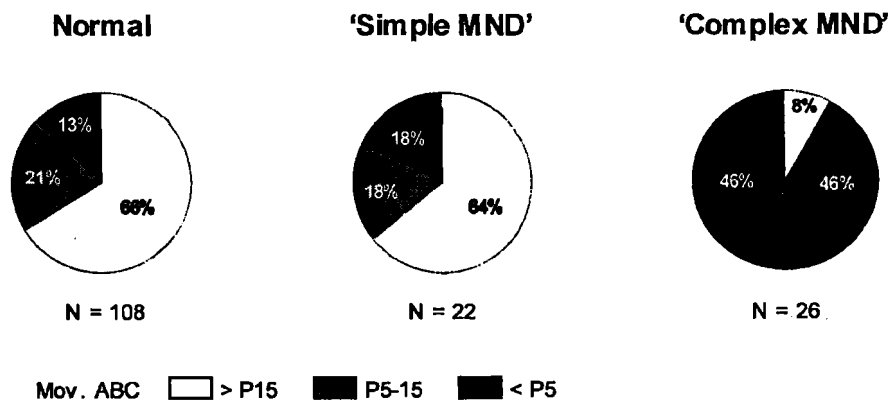


Fig. 2: Neurological condition and performance on the Movement ABC in 6-year-old preterms (Adapted from Jongmans et al. 1997.) The neurological classification is based on the neurological optimality score of the Touwen assessment. Neurologically normal represents an optimality score > 15th percentile, 'simple MND' denotes an optimality score between the 5th and 15th percentile and 'complex MND' indicates the presence of an optimality score < 5th percentile.

extensive form of brain dysfunction. It has been hypothesized that this form of brain dysfunction might be due to an early lesion in one or more of the connecting fiber systems in the nervous system. The presence of substantial neural dysfunction in children with complex MND is associated with a high chance of the development of motor problems interfering with the activities of daily life and it induces a pronounced vulnerability for the development of other problems, such as specific learning disorders or attention problems (Table 4). Thus it seems that especially children with complex MND deserve our clinical support and attention.

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