



# Motor and cognitive outcome at school age of children with surgically treated intestinal obstructions in the neonatal period

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## ABSTRACT

**Background:** The motor and cognitive outcome at school age of newborn children with surgically treated intestinal obstructions is unknown. Physiological stress and anesthesia may potentially be harmful in the period of early brain development in newborn infants.

**Objective:** To determine motor and cognitive outcome at school age in children with surgically treated intestinal obstructions as newborns, and to identify clinical risk factors for adverse outcome.

**Study design:** Cohort study of infants born between 1995 and 2002 with atresia, stenosis, or intestinal malrotation. At 6 to 13 years we assessed their motor functions, intelligence, attention, visual perception, visuomotor integration, and verbal memory.

**Results:** Of 44 children three (7%) died. Twenty-seven survivors (66%) were included for follow-up (median gestational age 36.7 weeks, birth weight 3000 g). Motor outcome was abnormal (<5th percentile) in 22% of the children, which was significantly more than in the norm population ( $P < 0.01$ ). Scores on selective attention were abnormal in 15% of the children ( $P < 0.01$ ). Other cognitive functions were not affected. Lower birth weight and intestinal perforation were risk factors for poorer motor outcome ( $R^2 = 53.0\%$ ), intrauterine growth restriction was a risk factor for poorer selective attention ( $R^2 = 36.6\%$ ).

**Conclusions:** Children treated surgically for intestinal obstructions in the neonatal period had an increased risk for poor motor functioning and selective attention at school age. Low birth weight, intrauterine growth restriction and intestinal perforation were risk factors for adverse outcome. We recommend to closely follow the motor and attentional development of these children.

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## 1. Introduction

An intestinal obstruction is a gastrointestinal complication that leads to impaired bowel passage. It occurs in approximately 9 out of every 10,000 newborn infants [1,2]. It can be caused by congenital malformations of the intestine such as an intestinal atresia or stenosis, or by a malrotation of the intestine. Infants who present with such an obstruction often require surgery in the neonatal period to remove the obstruction, promote normal bowel function and allow oral feeding.

During the neonatal period, a period of rapid cerebral growth, major surgery and anesthesia is associated with developmental delay at 1 to 2 years [3]. Specific groups at risk are preterm infants [4,5], infants undergoing cardiac surgery [6], and term infants undergoing noncardiac surgery for a variety of congenital anomalies such as intestinal atresias, esophageal atresia, congenital diaphragmatic hernia, and hypertrophic pyloric stenosis [6]. Potentially harmful factors include physiological stress occurring during surgery [7], anesthesia-induced apoptosis of developing neurons [8], the nature of the underlying congenital anomaly [3,6], and the surgical procedure in itself, whether it consists for example of resection of the ileocecal valve or the creation of an ostomy [9].

Although these factors are recognized risk factors for adverse neurodevelopmental outcome, the motor and cognitive outcome at school age of newborn infants with surgically treated intestinal obstructions is unknown. Our main aim was therefore to determine the outcome of such infants by assessing their motor and cognitive performance at school age. Motor and cognitive outcomes measured at school age are known to be more robust and predictive for later life than outcomes measured at pre-school age. Our secondary aim was to explore which clinical factors were associated with adverse outcome.

**Abbreviations:** AVLT, Auditory Verbal Learning Test; BMI, body mass index; IQ, intelligence quotient; IUGR, intrauterine growth restriction; Movement ABC, Movement Assessment Battery for Children; NEC, necrotizing enterocolitis; NEPSY-II, neuropsychological assessment; OR, odds ratio; SD, standard deviation; SDS, standard deviation score; TEA-Ch, Test of Everyday Attention for Children; WISC-III-NL, Wechsler Intelligence Scale for Children.

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## 2. Methods

### 2.1. Patients

We selected all infants who had been admitted to the Neonatal Intensive Care Unit of the University Medical Center Groningen between 1995 and 2002, and who were diagnosed by laparotomy with duodenal, jejunal, ileal or colon atresia, intestinal stenosis, or a malrotation of the intestine. We excluded patients with major chromosomal and congenital anomalies other than single atresias or stenoses.

### 2.2. Follow-up

The children were invited prospectively to participate in this follow-up study, which was an extension of the regular follow-up program. It entailed the assessment of motor performance and cognition at the age of 6 to 13 years. Parents gave their informed consent for their children to participate in the follow-up program. The study was approved by the Medical Ethical Committee of the University Medical Center Groningen.

### 2.3. Motor outcome

First, we assessed growth at follow-up (height, weight, and BMI). Next, to determine the children's motor outcome, we administered the Movement Assessment Battery for Children (Movement ABC), a standardized test of motor skills for children aged 4 to 12 years [10]. This test yields a score for total movement performance based on subscales for fine motor skills, ball skills, and balance. The tasks composing the Movement ABC are representative of the motor skills that are required of children attending elementary school in The Netherlands and are adapted to the individual child's age.

### 2.4. Cognitive outcome

We assessed total, verbal, and performance intelligence using a shortened version of the Wechsler Intelligence Scale for Children, third edition, Dutch version (WISC-III-NL) [11,12].

In addition, we assessed several neuropsychological functions which are crucial for keeping up at school and participating in everyday life. To assess attention we administered two subtests of the Test of Everyday Attention for Children (TEA-Ch) [13]. For selective attention we used the subtest "map mission". Selective attention refers to a child's ability to select target information from an array of distracters. We measured attentional control with the subtest "opposite worlds". Attentional control refers to the child's ability to change attentional focus flexibly and adaptively.

We assessed visual perception with the subtest "geometric puzzles" and visuomotor integration with the subtest "design copying" of the "Developmental NEuroPSYchological Assessment – version II" (NEPSY-II) [14]. Visual perception refers to the child's ability to perform mental rotations and visuospatial analyses. Visuomotor integration involves integrating visual information with finger-hand movements.

We assessed verbal memory with a standardized Dutch version of Rey's Auditory Verbal Learning Test (AVLT) [15]. This test consists of five learning trials of fifteen words each followed by an immediate recall trial, a delayed recall trial, and a delayed recognition trial. The delayed recall and recognition trials followed after approximately 20 min.

### 2.5. Statistical analysis

Standard deviation scores of height, weight and BMI at follow up were calculated by comparing the scores from our study group to a large Dutch population based growth study, the fifth national growth study [16]. The scores are age adjusted.

We classified the scores of the Movement ABC, TEA-Ch, and NEPSY-II into normal ( $\geq$  15th percentile), borderline (5th to 15th percentile), and abnormal ( $<$  5th percentile), in accordance with the manual based on a Dutch norm population. To classify the scores of the WISC-III-NL and AVLT we used the norm scores, means, and standard deviations of the norm population. A normal score was defined as a score  $\geq -1$  standard deviation (SD) of the mean, borderline as  $-1$  to  $-2$  SDs, abnormal as  $< -2$  SDs. In addition, we calculated the z scores based on the norm scores and percentiles given in the test manuals. We used the norm scores of the various tests, based on Dutch norms, adjusted for age, and acquired in recent years.

To compare the outcome of the study group with the norm scores of the general population, we used the one-sample Student t test in case of normality and the Wilcoxon signed rank test in case of non-normality.

To determine whether clinical characteristics were related to adverse outcome, we calculated odds ratios (ORs) by univariate logistic regression. Adverse outcome was defined as an abnormal score ( $<$  5th percentile). We subsequently used backward multivariate logistic regression to determine which risk factors detected by the univariate analysis ( $P < 0.10$ ) had independent prognostic value for outcome.

Throughout the analyses,  $P < 0.05$  was considered statistically significant. We used SPSS 16.0 software for Windows (SPSS Inc., Chicago, IL) for all the analyses.

## 3. Results

### 3.1. Patient characteristics

A database search resulted in 44 children who met our inclusion criteria, three (7%) of them had died in the neonatal period. Twenty-seven (66%) out of the 41 survivors were included in the follow-up study. The parents of seven children declined the invitation to participate; the parents of all of these children reported that their child attended formal education and did not encounter any neurological or behavioral problems. Seven other children could not be traced. Table 1 shows the patient demographics of the infants who were included in the follow-up. Two infants were born preterm ( $< 32$  weeks) and had an extremely low birth weight ( $< 1000$  g), both were also intrauterinely growth restricted. The gestational age of the surviving infants who did not participate in this study, was comparable to that of the study group (median 37.4 weeks, range 30.7–42.1). The birth weight of the survivors who did not participate was slightly lower (median 2298 g, range 1120–3700) compared to the median of 3000 g in the study group. The number of infants with intrauterine growth restriction (IUGR) was comparable ( $n = 3$ , 21%).

The most common type of obstruction was atresia ( $n = 16$ ). One child had an ileal stenosis. In eight infants the obstruction was caused by a malrotation, in four of whom the malrotation was complicated by a volvulus, while two infants suffered from a volvulus without a malrotation. The median age at surgery was 3 days (range 1–22). All infants received parenteral nutrition for at least one week. Enteral feeding was introduced 2 to 3 days after surgery and, depending on the clinical course, gradually increased in volume. Parenteral feeding was accordingly reduced. We also checked whether post surgery catabolic state was present in our cohort. All children except three were on full enteral feeds within 3 weeks after surgery. Of those three children in whom full postoperative enteral feeding was not reached within 3 weeks, one child had short bowel syndrome, one child was born preterm with birth weight 930 g, and one child required 2 reoperations during the first 2 weeks post surgery. In one child, the one with the short bowel syndrome, insufficient growth after surgery was present, suggesting catabolic state. Six infants required at least one more operation under general anesthesia during their first year, four of these infants required more than one subsequent surgical

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