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Cognition and behaviour in children with congenital abdominal wall defects

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ABSTRACT

Aim: To characterise neurodevelopment at age two years and cognition and behaviour at age five years in children born with abdominal wall defects (gastroschisis or exomphalos).

Study design: Participants were treated as neonates for gastroschisis or exomphalos and invited for routine clinical follow-up at ages two and five years. Thirty-nine two year-olds and 20 five year-olds with gastroschisis and 20 two year-olds and 10 five year-olds with exomphalos returned for age-appropriate assessments of development (two years) and intellectual functioning (IQ), executive function, and behavioural problems. Results were compared with normative data from the tests and published data from local term-born children.

Results: For both gastroschisis and exomphalos two year-olds, neurodevelopment was in line with the test normative data, but below the level of local normative data for all domains (effect sizes from −0.4 to −1.4 standard deviations). At five years, children with gastroschisis performed similarly to the normative mean for IQ but had high rates of various executive functioning problems on parent report (18–41% compared with 7% expected from norms). There was also a tendency for increased frequency of internalising problems (33% compared with normative expectation of 16%). Five year-olds with exomphalos also performed similarly to the normative mean for IQ and had low rates of executive and behavioural problems.

Conclusions: Survivors of gastroschisis and exomphalos may be at risk of poor neurodevelopment in toddlerhood, depending on the reference group, and children with gastroschisis may be particularly at risk for executive functioning difficulties despite an IQ within normal limits.

1. Introduction

Anterior abdominal wall defects such as gastroschisis and exomphalos (omphalocele) are significant congenital malformations requiring surgical repair and intensive care in the newborn period (1,2). They occur in 1.6–4.9 (gastroschisis) and 1.3–1.9 (exomphalos) per 1000 live births (3–5). Survival rates in these conditions are high, but these infants are at risk of compromised foetal development and medical complications (6). Despite this, long-term neurodevelopmental outcome data are lacking for these populations.

Studies of neurodevelopmental outcomes have often combined gastroschisis and exomphalos samples to maximise power (7). However, there are important medical and demographic differences between these conditions (8). Gastroschisis is increasing in incidence, with known risk factors including young maternal age and prenatal substance exposure (9). Infants with gastroschisis are frequently born preterm and small for their gestational age (SGA) (10,11), which are also risk factors for poor neurodevelopmental outcomes. While some reported neurodevelopmental outcomes have been encouraging (10), recent reports have highlighted intellectual ability, (12) attention, (12,13) and behaviour (13) as areas of risk for school-aged children treated for gastroschisis. A distinctly different condition, exomphalos

Abbreviations: ADHD, attention deficit hyperactivity disorder; BASC-2, Behaviour Assessment System for Children – Second Edition; BRIEF-P, Behaviour Rating Inventory of Executive Function-Preschool version; IRSAD, Index of Relative Social Advantage and Disadvantage; SES, Socioeconomic status; SGA, (small for gestational age); WPPSI-III, Wechsler Preschool and Primary Scale of Intelligence-3rd edition, Australian standardisation

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can be isolated or occur in the context of other congenital anomalies or syndromes, such as Beckwith-Wiedemann syndrome (2). Poorer cognitive, language, and motor development and increased autism spectrum disorder (ASD) symptoms have been reported in two year-old children with giant exomphalos (14), but data further into childhood are lacking, as are those for children with exomphalos minor.

To address these gaps in the literature, we aimed to characterise neurodevelopment at age two years, and cognitive development and behaviour at age five years, in children born with gastroschisis or exomphalos. It was hypothesised that, consistent with their early biological risks, these children would perform below normative expectations on gold-standard measures of developmental and cognitive outcomes.

2. Method

2.1. Participants

Participants were children treated under general anaesthesia for gastroschisis or exomphalos as newborn infants at The Royal Children's Hospital, Melbourne Australia. Surviving infants were invited for routine clinical follow-up at ages two and five years. Two year-old participants were born from 2009 to 2014 (assessed 2011–16) and five year-olds were born between 2006 and 2010 (assessed 2012–15). Of children with gastroschisis, the two year-old cohort comprised 63 children, and the five year-old cohort comprised 37 children, including 12 children in both cohorts. Of children with exomphalos, the two year-old cohort comprised 31 children, and the five year-old cohort comprised 16 children, with seven in both cohorts. The Royal Children's Hospital Human Research Ethics Committee approved this study based on a parental opt-out process for data collected clinically to be used for research purposes.

2.2. Measures

2.2.1. Background variables

Medical and psychosocial characteristics that may be associated with neurodevelopment were described for all cohorts. Background medical variables were collected from medical records, including sex, gestational age, birthweight, SGA status (< 10th percentile), age at first surgery in days, intestinal atresia (gastroschisis only), presence of chromosomal abnormality (exomphalos only) and length of first hospital stay in days. Larger defect size was defined as delayed repair due to a need for silo formation (gastroschisis) or a diagnosis of giant exomphalos. Socioeconomic status (SES) was approximated using the Index of Relative Social Advantage and Disadvantage (IRSAD), derived from 2011 Australian Census data for the mother's postcode area at the time of birth. IRSAD scores were analysed as deciles; lower deciles reflect greater disadvantage (15). At five years, psychosocial data were collected, including maternal age at birth, maternal education level (lower: ≤ 12 years; higher: > 12 years), presence of two caregivers in the home, whether the family received government financial assistance, primary language spoken in the home, and the child's level of education. Additional medical data were collected, including parent reported diagnoses of developmental disorders (attention deficit hyperactivity disorder (ADHD), ASD, and/or other), and engagement with early intervention or allied health services.

2.2.2. Neurodevelopmental assessment

Development was assessed at age two years using the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) (16). This widely-used tool includes cognitive, receptive language, expressive language, fine motor, and gross motor scales. Receptive and expressive language scales combine to form a language composite, and fine and gross motor scales form a motor composite. Assessments were administered by experienced allied health clinicians aware of participants' clinical histories. Performances on age-standardised measures were interpreted based on term-corrected age to avoid a known bias in test scores from prematurity (17). At age five years, neuropsychologists assessed intellectual abilities with the Wechsler Preschool and Primary Scale of Intelligence-3rd edition, Australian standardisation (WPPSI-III) (18). Age-standardised scores were again based on term-corrected age. Parents rated executive functioning in everyday life via the Behaviour Rating Inventory of Executive Function-Preschool version (BRIEF-P), and behaviour was assessed by the Behaviour Assessment System for Children – Second Edition (BASC-2; preschool parent report version) (19). The outcomes of interest were the frequency of elevated scores according to the questionnaire manuals (BRIEF > 93rd percentile, BASC-2 > 84th percentile).

2.3. Analysis

Age-standardised outcomes at ages two and five years were compared to normative data using one-sample *t*-tests (continuous variables) and binomial tests (categorical variables). Rates of mild delay were examined (scores > –1SD below the normative mean, i.e., scores below the 16th percentile). The Bayley-III remains the gold-standard early development assessment, but it was standardised on North American children and concerns have been raised that it overestimates children's development elsewhere (20). As we did not have a control group, mean Bayley-III scores were also compared via measures of effect size to previously published local data from a large term-born, normal birthweight group (n = 202; mean age = 2.0 years, SD = 0.1) (21). Effect sizes relative to the test norms and local comparison data were calculated using Glass's delta, which uses the normative standard deviation to determine the magnitude of effect. Effect sizes were interpreted according to Cohen's conventions (0.2 = small, 0.5 = medium, 0.8 = large).

3. Results

3.1. Participant characteristics and loss to follow-up

Table 1 shows the participant characteristics for both diagnoses. All children underwent a single operation during their neonatal admission.

3.1.1. Gastroschisis

Three children in the two year-old cohort and two in the five year-old cohort died during the neonatal period, leaving 63 and 35 eligible survivors respectively. Children assessed were broadly similar in their neonatal characteristics to those not assessed, although five year-olds with gastroschisis were more often preterm than those not assessed (supplementary Table). In both age groups, between a quarter and a third of children underwent silo closure. At age five years, 13 children (65%) were at kindergarten, with the remainder in their first primary school year. Parents reported that over 40% of five year-olds had received allied health or early intervention services. Two (10%) children had an ASD diagnosis, and one of these children had a comorbid diagnosis of learning difficulty. No children had a reported diagnosis of ADHD.

3.1.2. Exomphalos

All children in the two year-old exomphalos cohort survived to age two years, but four children in the five year-old cohort died in the neonatal period. Neonatal factors were similar between survivors assessed and not assessed. Amongst five year-olds, two (33%) had a diagnosis of Beckwith-Wiedemann syndrome, and five (50%) children were attending kindergarten with the remainder in their first primary school year. Parents reported that 60% had received allied health or early intervention services. Parents reported ASD in two (10%) children, while no children had a reported ADHD diagnosis.