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Relationship between white matter pathology and performance on the General Movement Assessment and the Test of Infant Motor Performance in very preterm infants

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ABSTRACT

Background: Cerebral Magnetic Resonance Imaging, the General Movement Assessment, and the Test of Infant Motor Performance are all tools that can predict neurodevelopmental outcome in preterm infants. However, how these tests relate to each other is unclear.
Aims: To examine the relationship between cerebral Magnetic Resonance Imaging measured at term age, and the General Movement Assessment and Test of Infant Motor Performance measured at 10–15 weeks post-term age.
Study design: Prospectively collected data in a sample of very preterm infants.
Subjects: Fifty-three infants (23 female, 30 male) with a median gestational age of 28 weeks (range: 23–30 weeks) and a median birth weight of 1000 g (range: 515–1465 g).
Outcome measures: Test of Infant Motor Performance, General Movement Assessment.
Results: Infants with abnormal white matter were significantly more likely to have both abnormal general movements ($p = 0.01$) and abnormal Test of Infant Motor Performance scores ($p = 0.001$). Infants with abnormal general movements were significantly more likely to have lower Test of Infant Motor Performance Scores ($p = 0.01$).
Conclusions: Abnormal white matter is related to motor deviations as measured by the General Movement Assessment and the Test of Infant Motor Performance as early as 3 months post-term age in a cohort of preterm infants.

1. Introduction

Over the past four decades there have been dramatic improvements in survival of preterm infants across late, very, and extremely preterm epochs [1]. As a result there are increasing numbers of survivors at risk for neuromotor and neurodevelopmental impairments. There continues to be a graded response of risk across all preterm gestational ages with those infants at 22–26 weeks gestation at highest risk of death and neurodevelopmental disability [2]. Clinicians assessing high-risk preterm infants have a variety of assessments to choose from when examining neurological and neuromotor development; however clinical assessment and correlation with brain pathology are not clear.

Magnetic Resonance Imaging (MRI) brain scans have significantly increased our ability to examine brain structure in the neonate. Abnormalities identified on cerebral MRI at term-equivalent age in preterm infants have been found to predict later neurodevelopmental outcomes [3]. Furthermore, moderate to severe white matter injury has been associated with neurosensory impairment, severe cognitive delay, and cerebral palsy [4].

Cerebral MRI has significantly enhanced our understanding of the preterm brain; however early neuroimaging does not replace the need for bedside clinical assessment. MRIs are not always available or used with preterm infants. As a result, it is important for clinicians who use clinical neurodevelopmental tests to understand the neurological

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implications of those tests and to document early signs of neurological dysfunction in order to identify children who need close monitoring and follow-up, and to direct and guide appropriate early habilitative interventions.

Traditional infant neurological assessments identify behavioral and neurodevelopmental repertoires, control of posture and movement, and other observable responses to external stimuli. These tools are based on responses to elicited stimuli, such as reflexes, and assessment of passive and active muscle tone; however clinical use can be limited by the infant's behavioral state and physiological status. The General Movement Assessment (GMA) is distinguished from traditional evaluations because the infant's spontaneous, endogenously generated movements are analyzed and used to identify neuromotor impairment [5]. The quality of general movements (GM) is thought to be modulated by cerebral functioning and is considered a reflection of neurological status [6]. Abnormal GMs have been associated with neuropathologies of the white matter [7], basal ganglia, thalamic [8], and cerebellar [9] brain regions.

The GMA [10] identifies a developmentally regulated pattern of spontaneous movements that emerge at 9–12 weeks post-conceptional age in the embryo and regress around 20 weeks post-term. At 10–15 weeks post-term, the predominant GMs are an identifiable pattern of continuous, small amplitude movements of the neck, trunk and limbs during wakefulness that disappear with agitation, termed fidgety movements. Absence of these fidgety movements at 10–15 weeks predicts the development of cerebral palsy with a high degree of accuracy [11]. Abnormal quality of the concurrent motor repertoire has been associated with minor neurologic dysfunction [12], intelligence at school age [13] and adaptive behavior in 10–11 year old children born preterm with a very low birth weight [14].

The Test of Infant Motor Performance (TIMP) has also been shown to be predictive of developmental delay in the infant tested at 12 weeks post-term age [15]. The TIMP is a norm-referenced measure designed to evaluate motor control and organization of posture and movement for functional activities in infants 32 weeks gestational age to 4 months post-term age and measures both spontaneous behaviors and elicited items [16]. While both the TIMP and the GMA tested at 12 weeks post-term age are predictive of future outcome, Snider et al. [17] found no concurrent validity between the two tests.

This study describes the relationship between the GMA, the TIMP, and neuropathologies detected on brain MRI scan at term age in a cohort of high-risk preterm infants. The aims of our study were (1) to elaborate on the relationship between the GMA and the TIMP at 3 months post-term age; (2) analyze the extent to which term-age MRI was related to performance on the GMA at 10–15 weeks post-term age; and (3) to analyze the relationship between term-age MRI and the TIMP scores at 10–15 weeks post-term age.

2. Methods

2.1. Participants

Infants born at ≤31 weeks gestational age, and a birth weight of ≤1500 g, who required oxygen at birth, were recruited prospectively between July 2011 and March 2013 from the XXXX Children's Hospital neonatal intensive care unit. Infants with congenital malformations, genetic syndromes, or who had respiratory distress that was severe enough that they were not expected to live (oxygenation index ≥20) were excluded from the study. Informed parental consent was obtained from each infant and ethical approval for the study was granted by the University's institutional review board.

2.2. MR image and data acquisition

MRI scans were performed at term equivalent age. Infants were fed an hour prior to the scan and gently restrained, without sedation, using a MedVac immobilization bag (CFI Medical Solutions Inc., Fenton, MI, USA) [18]. Pulse oximetry was used to monitor heart rate and oxygenation throughout the study. Standard hearing protection was applied. MR imaging was performed on a 3 T Philips MRI scanner (Achieva, Best, the Netherlands) using a standard head 8-channel SENSE MRI coil array, designed for adult head imaging with high signal-to-noise ratio and optimum uniformity. Acquisition schema was as follows:

i. 3D *T1-weighted TFE*: 1-mm isotropic spatial resolution, TI = 1100 ms, TR/TE = 8.0/2.9 ms, TFE factor 144.
ii. 3D T2-*weighted*, *turbo spin echo*: 1-mm isotropic spatial resolution, matrix 192 × 132 TR/TE = 2500/264 ms, TSE factor 100.

2.3. Assessments

2.3.1. General Movement Assessment

Fidgety movements were assessed according to the Prechtl method [6]. In this study, fidgety movements were classified as normal if present (intermittent or continual), and as aberrant if abnormal (exaggerated with respect to speed and amplitude), sporadic (interspersed with long pauses) or absent.

Video recordings were made using a standardized observation system, with the baby in a state of active wakefulness. The recordings were made at 10–15 weeks post term age. Two raters who are general movement assessment certified and blinded to the imaging and outcome data classified the video recordings according to the Prechtl methodology [10]. An additional GMA certified rater from a second institution also rated the cases using the same method (Kappa = .21). If there was a discrepancy between assessments, the videos were sent to a third (tie-breaking) reader who was blind to what the previous readers reported. There were 16 cases of discrepancy. The tie-breaking reader agreed with the first raters in 4 cases and with the second rater in 12 cases. The consensus or the tie-breaking reader's scores were used for analysis.

2.4. TIMP

The TIMP consists of 42 test items: 13 observed items and 29 elicited items, which test the infant's postural and motor control. Each item has its own scale; the number of points varies from 0 to 6. A total raw score is summed from item scores (maximum 142) and results of scores are categorized as “average” (within −0.5 to +1.0 standard deviations (SD) of age mean), “low average” (−0.5 to −1.0 SD below age mean), “below average” (−1.0 to −2.0 SD below age mean), and “far below average” (>−2.0 below age mean).

Infants were assessed with the TIMP at 10–15 weeks post-term age. The TIMP was performed by an experienced and reliable tester blinded to imaging data.

2.5. MRI qualitative scoring

A pediatric neuroradiologist independently scored the scans and was blinded to neonatal morbidities and scores on other assessments. A standardized scoring system [4] was used to grade gray and white matter (WM) pathology. The WM was scored on a scale from 1 to 3 for the following five areas: nature and extent of WM signal abnormality, periventricular white matter volume loss, thinning of the corpus callosum, ventricular dilation, and presence of any cystic abnormalities.

The WM pathology scores for the individual items were totaled and classified into four groups: normal (score: 5–6), mild (score: 7–9), moderate (score: 10–12), and severe (score: 13–15). Gray matter was scored similarly with a scale from 1 to 3 for the following: size of the subarachnoid space, gyral maturation, and cortical gray matter signal abnormality. The gray matter pathology scores for the individual items