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Kinematic measurement of 12-week head control correlates with 12-month neurodevelopment in preterm infants

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ABSTRACT

Background: Although new interventions treating neonatal brain injury show great promise, our current ability to predict clinical functional outcomes is poor. Quantitative biomarkers of long-term neurodevelopmental outcome are critically needed to gauge treatment efficacy. Kinematic measures derived from commonly used developmental tasks may serve as early objective markers of future motor outcomes.
Aim: To develop reliable kinematic markers of head control at 12 week corrected gestational age (CGA) from two motor tasks: head lifting in prone and pull-to-sit.
Study design and subjects: Prospective observational study of 22 preterm infants born between 24 and 34 weeks of gestation.
Outcome measures: Bayley Scales of Infant Development III (Bayley) motor scores.
Results: Intrarater and interrater reliability of prone head lift angles and pull-to-sit head angles were excellent. Prone head lift angles at 12 week CGA correlated with white matter NAA/Cho, concurrent Test of Infant Motor Performance (TIMP) scores, and 12-month Bayley motor scores. Head angles during pull-to-sit at 12-week CGA correlated with TIMP scores.
Conclusions: Poor ability to lift the head in prone and an inability to align the head with the trunk during the pull-to-sit task were associated with poorer future motor outcome scores. Kinematic measurements of head control in early infancy may serve as reliable objective quantitative markers of future motor impairment and neurodevelopmental outcome.

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1. Introduction

Neonatal acute brain injury and specific sequelae of prematurity are known causes of childhood developmental disability [1–3]. Although new interventions treating various etiologies of neonatal brain injury show great promise [4–7], our current ability to predict long-term clinical outcomes following administration of these agents is poor. In neonatal therapeutic clinical trials, the gold standard for motor outcome is neurodevelopmental testing at 18–24 months, which is significantly delayed compared to outcome assessments for adults and older children performed within days of injury. Additionally, early phase therapeutic trials for neonates may be drawn out to 2–3 years and offer no immediate efficacy measures reflecting functional outcomes. Thus, it is critical that we identify surrogate functional biomarkers of long-term neurodevelopmental outcome to gauge the efficacy of current therapeutic interventions used for neonatal acute brain injury [8].

An acceptable biomarker for infant neurodevelopmental outcome would be a test that could be conducted quickly and easily, implemented at most nurseries or pediatric clinics, and able to predict outcome early in the neonatal course [9]. Neurodevelopmental tests such as the Test of Infant Motor Performance (TIMP), Alberta Infant Motor Scale (AIMS), and Bayley Scale of Infant Development III (Bayley) are used in many developmental clinics and specific tasks evaluating postural control, head control, and upper extremity movements are beginning to be examined as potential markers of developmental delay [10,11]. Poor postural control, defined as head lag at 6 months during a pull-to-sit (PTS) task, was recently shown to differentiate low-risk controls from infants with autistic siblings and was predictive of social and

Abbreviations: CGA, corrected gestational age; IVH, interventricular hemorrhage; PVL, periventricular leukomalacia; MRS, magnetic resonance spectroscopy; mI, myoinositol; NAA, N-acetylaspartate; Cr, Creatine; Cho, choline; Glx, glutamine + glutamate.

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communication delays at 36 months, including autism spectrum disorder [10,12,13]. Upper extremity, trunk, and head control determines a young infant's ability to explore his environment and thus promote normal patterns of motor and cognitive development [14, 15]; consequently, quantification of head control in early infancy may characterize an essential milestone and serve as a marker of developmental trajectory.

The goal of this study was to develop reliable kinematic markers of head control in early infancy derived from two commonly used motor development tasks, head lifting in prone and pull-to-sit. Kinematic markers were defined as prone head lift angle and head angle during pull-to-sit (PTS). We hypothesized these two kinematic measures of early head control would correlate with magnetic resonance spectroscopy (MRS) performed near term age, concurrent Test of Infant Motor Performance (TIMP) scores at 12 week corrected gestational age (CGA), and later neurodevelopmental scores on the Bayley Scales of Neurodevelopment III (Bayley) at 12 months CGA.

2. Methods

2.1. Participants

This was a prospective study of 22 preterm infants born between 24 and 34 completed weeks of gestation (GA) from November 2010 to January 2012. The Institutional Review Board approved this pilot study and consent was obtained prior to enrollment. Exclusion criteria were GA < 24 weeks or major congenital abnormality.

2.2. Procedures

The infants were seen for testing at term (TIMP and neuroimaging), 12 week CGA (TIMP and kinematic assessment), and 12 months CGA (Bayley). Motor tasks for kinematic assessment were performed at 12 week CGA, as development of head control at this age may differentiate infants at high and low risks for delays [11,16]. Neuroimaging data collection was performed at the MUSC Center for Biomedical Imaging. All other assessments were completed at the MUSC Neuromuscular Research Laboratory (MUSC NRL). An experienced pediatric occupational therapist (PCB) with TIMP certification performed TIMP testing and motor tasks for kinematic assessment for all the infants to minimize external variability. The prone head lift and PTS tasks used for kinematic analysis occurred over 5–10 min while the infants were in a calm and alert state. The same pediatric therapist (PCB), a pediatrician with 30 years experience, and trained research assistants assessed the infants using Bayley III at 12 months CGA (mean: 12.4; range: 11.1–13.9) at the MUSC NRL. Bayley assessors were aware of prior TIMP scores when talking with parents about Bayley results, as unblinding of development scores was an Institutional Review Board requirement. However, the same research assistants were blinded to kinematic measures and MR results at developmental testing.

2.3. Kinematic testing and data acquisition

Infant participants were placed on a 34″ × 18.5″ × 2.5″ foam mat on a large mat table 18″ in height to obtain all measurements related to head control. The mat was labeled with a cross to ensure consistent shoulder and trunk placement in sagittal and coronal planes with the cameras. Colored Duoderm® 1 cm^2 markers were placed over specific anatomical landmarks on the infants, including the right and left temporal window, mastoid process, acromion, iliac crest, and lateral condyles of the femur and ankle. The markers provided visual contrast at the desired landmark to measure angles during the subsequent kinematic data analysis.

Two HDR-HC9 Sony® cameras on tripods were used for video recording and were positioned 36″ lateral to the mat (sagittal plane), and 48″ from the front of the mat (coronal plane). Dartfish InTheAction® software was used to stream and record each infant's 2 consecutive 20 s prone head lift tasks and 4 consecutive PTS trials. Because prior experience, mood, and fatigue likely influenced the motor tasks assessed, repeated trials on both left and right sides were performed and all trials were used in statistical analyses. All recordings were captured under participant study numbers and downloaded to a firewall-protected server.

2.4. Kinematic data analysis

Dartfish® Analyzer software was used for 2D kinematic analysis of recorded movements during prone head lifting and PTS. An infant's prone head lift angle reflected the angle the infant lifted his head and trunk in midline above the mat in prone (Fig. 1A). At the start of a 20 s prone video recording, an angle was drawn with one fixed ray parallel to the mat and the second variable ray drawn to the tragus of

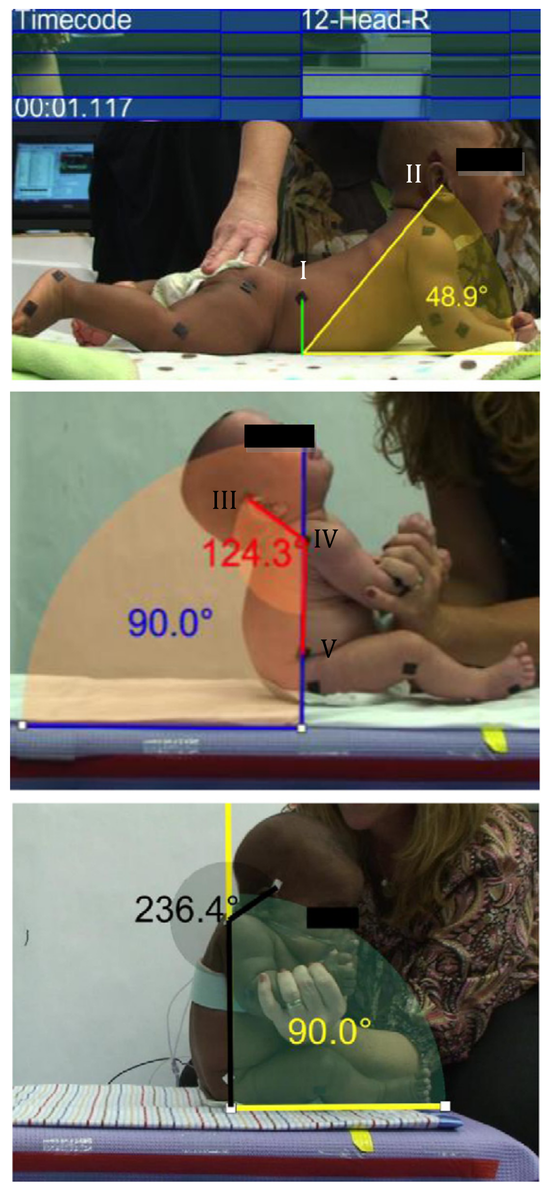

Fig. 1. Kinematic analysis of prone head lift and pull-to-sit tasks using Dartfish®. Anatomical markers: I = posterior iliac crest, II = tragus, III = temporal window, IV = acromion process, V = anterior superior iliac crest. 1A. Maximum prone head lift angle measured with Dartfish® Analyzer tracking tool. An embedded Dartfish® Analyzer data table is shown. 1B. Head angle at a 90° trunk angle during pull-to-sit measured with Dartfish® Analyzer tracking tool. 1C. Head angle at a 90° trunk angle during pull-to-sit measured with Dartfish® Analyzer tracking tool.