Direct Brain Recordings in Craniosynostosis Can Predict Future Language Development

**Presenter:** Robin T. Wu, BS

**Co-Authors:** Paul Abraham, BS; James Nie, BS; Alexander H. Sun, BS; Jenny F. Yang, MD, MHS; Carolyn Chuang, MD, MHS; Taylor Halligan, BS; Connor J. Peck, BS; James C. McPartland, PhD; Rajendra Sawh-Martinez, MD, MHS; Derek M. Steinbacher, MD DDS; Michael Alperovich, MD, MSc; John A. Persing, MD

**Affiliation:** Yale School of Medicine, New Haven, CT

**PURPOSE:** Non-syndromic craniosynostosis is associated with a multitude of language deficits. Early detection and prevention is essential for language remediation in these cohorts. The current standard assessment, the Bayley Scales of Infant Development (BSID), provides little predictive value for long-term development. Auditory event-related potentials (ERPs), in particular the mismatch negativity (MMN), measure passive neurological responses to speech sounds and suggest a promising avenue for analyzing infant speech development, particularly in craniosynostosis. We now provide long-term follow up neurocognitive assessment of patients with midline synostosis (sagittal and metopic) in comparison to BSID and ERP testing in infancy.

**METHODS:** Non-syndromic craniosynostosis infants who received surgical correction for craniosynostosis were recruited one month post-operatively from the institutional Craniofacial Clinic. Participants were given the BSID by a licensed child psychologist. Immediately following, participants were presented with a non-native phoneme discrimination paradigm involving the Hindi retroflex phoneme /\da/ and the dental phoneme /\da/ in random order. Auditory stimuli were set at 80 dB, and EEG was recorded at 250 Hz with a 128-channel HydroCel Geodesic Sensor Net. Analysis focused on four electrode clusters: left and right frontal electrodes and left and right central electrodes. The MMN component was calculated as the largest negative amplitude in the difference wave between 80-300ms after stimulus presentation. Once patients reached ≥6 years of age, they completed a battery of neurodevelopmental tests (Wechsler Abbreviated Scale of Intelligence and Wechsler Fundamentals) with 6 sub-assessments that measure language-related functional domains. Statistical comparisons were performed with univariate regressions.

**RESULTS:** Of twenty non-syndromic sagittal and metopic craniosynostosis patients who received BSID/ERP testing post-operatively and are currently eligible for long-term neurocognitive follow-up, data is currently available for nine (average age 8.1 years; 22% female; 55% sagittal, 33% metopic, 11% metopic and sagittal; all patients received whole vault cranioplasties). Univariate regression analyses showed that left frontal cluster MMN positively predicted word reading scores ($\beta$ 3.00, $R^2$ 0.48), reading comprehension scores ($\beta$ 3.57, $R^2$ 0.54), and reading composite scores ($\beta$ 3.33, $R^2$ 0.57). Right frontal and bilateral central clusters did not significantly predict scores. In comparison, BSID receptive language scores negatively predicted word reading ($\beta$ -27.48, $R^2$ 0.67) and reading comprehension ($\beta$ -17.41, $R^2$ 0.86), while BSID cognitive, expressive language, and language composite scores had no predictive value for future neurocognitive language scores.

**CONCLUSION:** Our prospective longitudinal assessment shows that ERP assessment in patients with sagittal and metopic synostosis has significantly better predictive value for future neurocognitive assessment than the current gold standard BSID test. Left frontal measurements approximate the location of language associated brain centers. This suggests that high fidelity ERP testing should be performed following surgical correction of craniosynostosis. This may help tailor treatment for possible language deficits in future development.

A Comparison of Intracranial Volumes in Normal Children and Patients with Metopic Craniosynostosis

**Presenter:** Brendan J. Cronin, BA

**Co-Authors:** Michael G. Brandel, BA; Taylor M. Buckstaff, BA; Gabrielle M. Cahill, BS; Emily Mannix, BS; Ryan McKee, BS; Parisa Oviedo, BS; Asra
Hashmi, MD; Christopher M. Reid, MD; Samuel Lance, MD; Hal Meltzer, MD; Amanda A. Gosman, MD

Affiliation: University of California San Diego, La Jolla, CA

PURPOSE: Previous investigations of intracranial volume (ICV) in patients with metopic craniosynostosis have yielded mixed results and are limited by the number of patients included in the study sample. Additionally, no studies have characterized the impact of metopic synostosis on intracranial volume change accompanying growth. In this study, we sought to determine if metopic patients had significantly different intracranial volumes than normal, healthy children. We also compare standardized growth curves of intracranial volume change in normal patients and patients with metopic craniosynostosis.

METHODS: An IRB-approved retrospective review was performed of patients with metopic craniosynostosis at our institution. Intracranial volumes were calculated from manually segmented preoperative CT scans. Structural MRI data for normal children were acquired from the NIH Pediatric MRI Data Repository. Intracranial volumes were calculated in FreeSurfer.

Multivariate linear regression including age, gender and diagnosis (i.e. metopic and normal) was performed to determine the impact of metopic craniosynostosis on intracranial volume.

To compare intracranial volume growth in normal patients and patients with metopic craniosynostosis, a term defining the interaction between age, diagnosis and their effect on intracranial volume was added to the linear regression model. A best fit logarithmic curve of intracranial volume growth was generated for metopic patients and compared to a best fit logarithmic curve for normal patients.

RESULTS: Data were available for 73 metopic craniosynostosis patients (52 males, 21 females; age 1–21 months). 270 MRIs of normal, healthy children were available (141 males, 129 females, age 1–24 months).

Mean metopic ICV was lower than normal ICV within the first 3–6 months (14 metopic patients, mean ICV 646.59cc vs 28 normal patients, mean ICV 903.91cc, p=0.002), 6–9 months (26 metopic patients, mean ICV 737.92cc vs 33 normal patients, mean ICV 868.81cc, p=0.005) and 9–12 months (19 metopic patients, mean ICV 848.01cc vs 29 normal patients, mean ICV 956.62cc, p=0.038). When controlling for age and gender, the difference in intracranial volume associated with metopic synostosis ranged from 112.67cc (13%) to 304.37cc (32%), with the most significant effect from age 3–6 months (304.4cm3, 32%). There was no difference in intracranial volume after 12 months of age (8 metopic patients, mean ICV 997.65cc vs 96 normal patients, mean ICV 1000.11cc, p=0.916).

Intracranial volume growth in patients with metopic synostosis was defined by a significantly different growth equation than normal patients (metopic: $y=230.61\ln(x)+323.0$, normal: $y=103.89\ln(x)+390.4$; $p=0.005$). Compared to normal patients, metopic patients demonstrated more rapid growth velocity from 1–3 months (126.7 vs 57.1cm$^3$/month), 3–6 months (53.3 vs 24.0cm$^3$/month), 6–9 months (31.2 vs 14.1cm$^3$/month) and 9–12 months (22.1 vs 9.9cm$^3$/month).

CONCLUSION: In the first year of life, patients with metopic synostosis have significantly reduced intracranial volumes, yet greater than normal intracranial volume growth velocity. It appears the restrictive effect of metopic synostosis relative to normal patients originates, in part, from disparities of intracranial volume at birth, rather than restricted calvarial growth in early life. As a result, cranial vault reconstruction targeting volume expansion should be performed in early life to more rapidly achieve normal volumes in these patients.

Distraction Osteogenesis for Unicoronal Craniosynostosis Results in Decreased Rates of Postoperative Strabismus

Presenter: Ian C. Hoppe, MD

Co-Authors: Rosaline S. Zhang, BA; Lawrence O. Lin, BS; Greg Heuer, MD, PhD; Jordan W. Swanson, MD, MS; Jesse A. Taylor, MD

Affiliation: Children’s Hospital of Philadelphia, Philadelphia, PA

BACKGROUND: Traditional fronto-orbital advancement (FOA) is the standard of care for patients with isolated unicoronal craniosynostosis (UCS), however it is associated with significant intraoperative blood loss and high rates of