Title: Very low birth weight infant growth trajectory is associated with term equivalent age language center maturation

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Background: Very low birth weight infant (VLBWI) in-hospital growth is associated with higher cognitive scores at 18-60 months. Using resting state functional connectivity (rs-FC) MRI, we explored the association between growth trajectory and language center cross-hemispheric intrinsic connectivity distribution (ch-ICD), a marker of brain maturation.

Methods: VLBWI, without severe intraventricular (IVH) (III/IV) or cerebellar hemorrhage, had rs-FC MRI performed 2013 to 2018. Using calculated change in z-score from birth to term equivalent age (TEA), a median change in z-score was identified and used to define two groups: higher weight gain group and a lower weight gain group. Sex, race/ethnicity, insurance status, postmenstrual age (PMA) at birth and MRI, duration of mother’s milk and parenteral nutrition, and neonatal morbidities were compared between groups. Standard rs-FC preprocessing was performed with comparison for differences in ch-ICD for regions responsible for language development, Broca’s area (BA45) and Wernicke’s (BA22). Unadjusted comparisons were performed with Wilcoxon Rank Sum test. Adjusted analyses included multiple linear regression, with effect differences summarized as mean with 95% confidence interval (95%CI). Statistical significance was established at alpha of 0.05.

Results: 87 VLBWI were included in the analysis, 43 (49.4%) in the higher weight gain group and 44 (50.6%) in the lower weight gain group based on a -1.46 median change in weight z-score. Compared to the group with lower weight gain, more infants with higher weight gain had higher PMA at MRI (p=0.04), more were African American and fewer were Hispanic (p=0.03). Adjusted analysis revealed that higher growth rate (mean difference=0.076, 95%CI 0.009, 0.143) and male sex (mean difference=0.067, 95%CI 0.003, 0.132) were significantly associated with greater ch-ICD in Broca’s region. Only absence of IVH grades I/II (mean difference=0.175, 95%CI 0.058, 0.293) and higher PMA at MRI (p=0.04) were significantly associated with greater ch-ICD in Wernicke’s region.

Conclusion: VLBWI in-hospital growth was positively associated with ch-ICD in Broca’s region, a critical region for language in the developing brain.

Word Count: 318