



Relationship Between Structural Brain Development and Working Memory in Moderately Preterm Adolescents

Shelby Rentmeester, Amanda S. Hodel, Sara E. Van Den Heuvel, Ruskin H. Hunt, Heather W. Sesma & Kathleen M. Thomas

University of Minnesota, Minneapolis, MN, United States.

Pediatric Academic Society, May 3-6, 2014, Vancouver, Canada



Introduction

Children born very preterm (PT) and/or low-birth weight are at risk for deficits in executive functioning skills, including working memory (e.g., Omizzolo et al., 2013). Recent studies have reported that structural brain differences in frontal and temporal lobe development in children born very PT are related to individual differences in executive function skills. For example, adolescents (age 15) born very PT show thinning of the entorhinal cortex, a hub area at the interface between the hippocampus and temporal cortex association areas. This thinning is correlated with impairments in both perceptual functions and working memory (Skranes et al., 2012).

Children born only moderately PT (32-34 weeks gestation) are also at increased risk for cognitive and neurodevelopmental problems, though less research has focused on this group, particularly in adolescence (Vohr, 2013).

The current study investigated both behavioral indices of working memory development and structural brain development in adolescents with a history of moderately PT birth.

Question

Does moderately preterm birth (32-34 weeks gestation) impact working memory development and related brain circuitry at adolescence?

Participants

Children born moderately PT and full-term (FT) control children were recruited from an existing longitudinal sample (Stolarova et al., 2003) and from a community participant pool.

PT inclusion criteria: born 32-34 weeks gestation, birth weight AGA, 5 minute Apgar score > 7. No history of IVH, limited mechanical ventilation (< 24 hours), and no significant maternal pregnancy complications (including diabetes and alcohol/drug use).

FT inclusion criteria: born 39-41 weeks gestation with no history of major pre- or perinatal complications.

Demographics: Demographics did not differ by group. Children were predominantly white (93%) and came from college-educated (or higher) families (>75%). Median household income for the sample was between \$101-125,000.

Participants: Working Memory Measures

	Preterm Children (n = 17)	Full-Term Children (n = 27)
Age at Test	M = 12.77 years Range = 12.29-13.43 years	M = 12.62 years Range = 12.30-13.02 years
Sex	6 female, 11 male	16 female, 11 male
Gestational Age	M = 33.13 weeks Range = 32-34 weeks	M = 40.25 weeks Range = 39-41 weeks

Participants: Structural MRI Measures

Children were prescreened for contraindications for MRI (including braces, permanent retainer, history of moderate or severe claustrophobia, or implanted metal). The final MRI sample included 13 PT children (6 female, 7 male) and 16 FT children (8 female, 8 male).

Methods

Working Memory Measures

Spatial Working Memory: CANTAB spatial span task was used to estimate forward and backward spatial span length (possible length ranging from 2 to 9 for each task).

Verbal Working Memory: WISC-IV digit span and letter number sequencing subtests were used to generate a composite working memory score.

Behavior Rating Inventory of Executive Function (BRIEF): Parent-report questionnaire designed to measure executive function in children and adolescents within everyday contexts, including a working memory subscale.

Structural MRI Measures

Structural MRI Scan: T1-weighted 3D MPRAGE anatomical series acquired on a Siemens 3T Trio Scanner

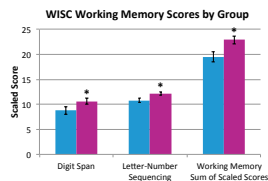
- TR = 2530 ms, TE = 3.56 ms, FOV = 256 mm, flip angle = 7 degrees
- 1 mm iso-voxel, 240 sagittal slices

MRI Analyses: Freesurfer Image Analysis Suite was used to obtain automated, volumetric segmentation data

Group difference analyses included age and sex as covariates. Volumetric analyses also controlled for individual differences in total intracranial volume (ICV).

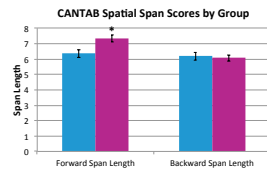
Brain-behavior analyses used linear regression models which included age, sex, and total intracranial volume (when appropriate) as covariates.

Behavioral Results



Adolescents born moderately PT had lower verbal working memory scores.

Neither overall IQ nor parent ratings of global executive function and working memory abilities differed by group.



Adolescents born moderately PT had shorter forward spatial working memory span.

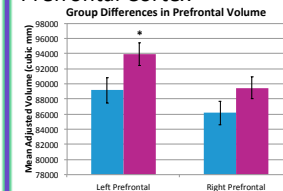


Acknowledgments

This work was supported by the Minnesota Medical Foundation and the Department of Pediatrics (Sesma), Ruth L. Kirschstein National Research Service Awards (T32 HD007151-05; Hodel), and a University of Minnesota Graduate School Fellowship (Hodel). The authors would like to thank Jordan Mathison, Kristen Wilk, and members of the Cognitive Development and Neuroimaging Lab, as well as the children and families who participated in this research.

MRI Results

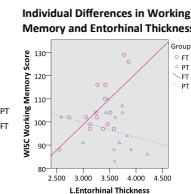
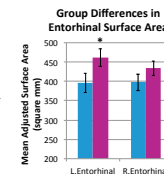
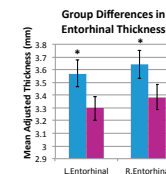
Prefrontal Cortex



Adolescents born moderately PT had reduced left prefrontal gray matter volume (primarily in left inferior and middle frontal subregions).

Within the PT group, individual differences in spatial working memory were predicted by left prefrontal cortex volume.

Temporal Cortex



No group difference in overall temporal lobe volume. Adolescents born moderately PT had thicker bilateral entorhinal cortex but smaller left entorhinal surface area.

Individual differences in entorhinal thickness and surface area predicted verbal working memory and parent reported working memory in FT, but not PT, children.

Discussion

Adolescents born very PT show long-term alterations in structural and functional brain development. The current study suggests that children born in the moderately preterm range (32-34 weeks) show similar group differences in working memory in comparison to full-term children, along with altered frontal lobe and temporal lobe development.

Specifically, we found that adolescents born moderately PT had smaller left frontal lobe volumes at age 12-14 years. Additionally, the association between spatial working memory performance and individual differences in prefrontal volume in moderately PT children suggests that structural differences in brain development are related to meaningful differences in cognitive function.

Moderately PT adolescents also show altered temporal lobe development, including thicker entorhinal cortex with smaller surface area at age 12. Others have shown that children born at very low birth weight have thinner entorhinal cortices by age 15. The time course and extent of normative decreases in cortical thickness over adolescence may be altered in children born moderately PT, along with brain structure-cognitive function relations.

Conclusion

Working memory, frontal and temporal lobe structural development, and brain structure-cognitive function relations are altered following a history of moderately preterm birth.