Brain Morphometry and Executive Function in Children Born High Birth Weight

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Introduction

Our previous research suggests that diabetes during pregnancy may impact infant recognition and explicit memory performance early in life (see Nelson 2007 for review), potentially due to the effects of iron deficiency on the hippocampus and other brain regions (Rao & Georgieff, 2007; Riggins et al., 2009). Additionally, children with severe iron deficiency show poorer cognitive and behavioral outcomes (Lozoff et al., 2000). Reduced cognitive performance has also been reported for children born high birth weight, or large for gestational age, a correlate of diabetic pregnancy and fetal iron deficiency (Sorensen et al., 1998; Seidman et al., 1992). While several studies have reported reductions in regional brain volume as a consequence of preterm birth and/or low birth weight, less is known regarding brain growth in children born high birth weight. This study examined the relation between high birth weight, behavioral performance on a task of executive function, parent reports of externalizing behavior, and quantitative brain morphometry in nine- and ten-year-old children.

Average Birth Weight (ABW)
Up to74%ile
n=23 (7 female)

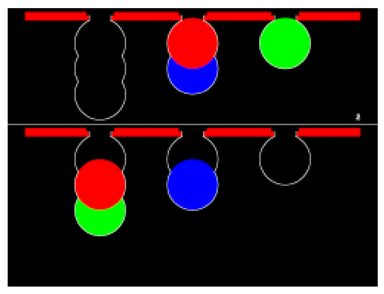
Participants

35 Children
Age range:
9.2-10.4 years

High Birth Weight (HBW)
75%ile and above
n=11 (5 female)

Methods: Stockings of Cambridge

- CANTAB Stockings of Cambridge task
- Specified arrangement of three colored balls on top portion of screen
- Participant required to match arrangement by moving colored balls on lower portion of screen
- Varying degrees of difficulty (2, 3, 4, 5 moves required for successful completion)
- Planning ability assessed by tracking number of moves required to replicate arrangement

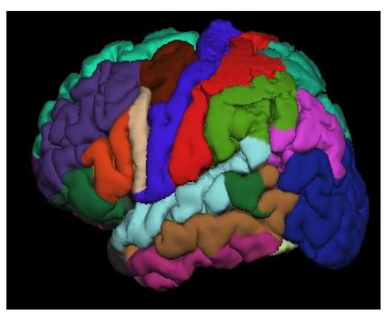


Methods: Child Behavior Checklist (CBCL)

- Parent-report questionnaire assessing child's problem behaviors
- Externalizing behavior subscore measures aggressive and destructive behaviors

Methods: Ferritin

- Newborn ferritin levels were obtained from cord blood samples at time of delivery for 20 participants
- Nine participants had low ferritin levels (<76 mg/L)



Methods: Structural Imaging

- T1-weighted anatomical 3-D FLASH images collected on a Siemens 3T Trio scanner
  - TR = 20, TE = 4.7, 256 x 256, FOV = 256, 1 mm slice thickness, slices = 176 sagittal
- Freesurfer software used to obtain automated segmentation of cortical and subcortical regions (Fischel et al., 2002)
- Measurements of individual subcortical regions regressed on intracranial volume (ICV)
- Measurements of cortical volumes regressed on the overall cerebral cortex volume (CCV) for corresponding hemisphere
- Standardized residuals used in analyses (Fjell et al., 2005)

Results: Regression

(HBW only, N=11) — *Problems solved in the minimum number of moves*

	r	*B*	*SE B*	ß	R^2	ΔR^2
Step 1					.01	.01
Constant	-.93	19.45				
Age	.14	.07	.17	.31		
Step 2					.08	.06
Constant		-.25	19.91			
Age	.14	.07	.17	.15		
CBCL Externalizing	-.25	-.03	.04	-.26		
Step 3					.68	.59*
Constant		7.49	12.77			
Age	.14	.03	.10	-.07		
CBCL Externalizing	-.25	-.01	.04	-.74*		
Lh Prefrontal vol	-.53*	-1.12	.31	-.91**		

** p < .01, * p < .05

- Corrected left prefrontal volume negatively predicts the number of problems solved in the minimum number of moves in the HBW group
- Smaller left prefrontal volume is related to better overall performance on the Stockings of Cambridge task in the HBW group
- These effects were not observed in the average birth weight group
- CBCL Externalizing scores predict problems solved in minimum number of moves only when left prefrontal volume is added into the model

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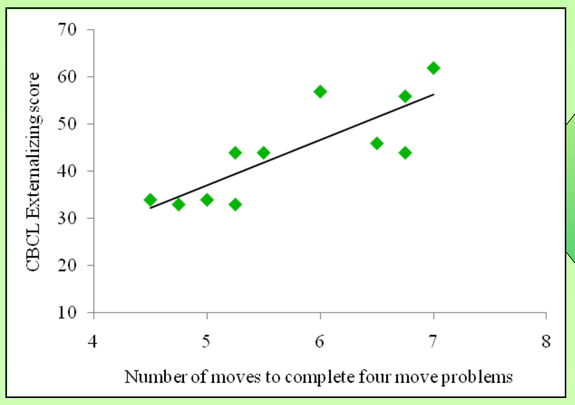
Results: Correlations

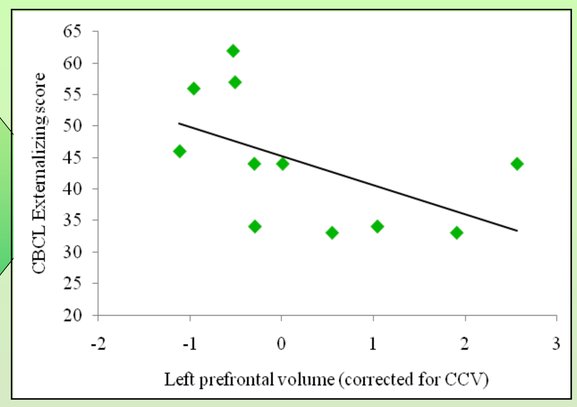


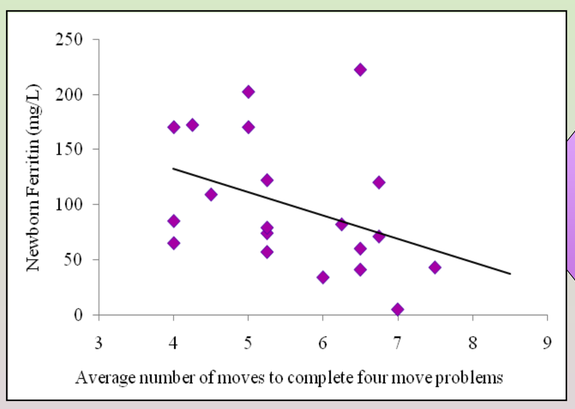
High Birth Weight

- Number of moves required to solve a four move problem is positively correlated with CBCL externalizing scores (r= .817)
- Children scoring higher on externalizing behaviors exhibit greater difficulty in solving four move problems

High Birth Weight

- CBCL externalizing scores are negatively correlated with corrected left prefrontal volumes (r= -.733)
- Children who have larger corrected prefrontal volumes have lower externalizing behavior scores



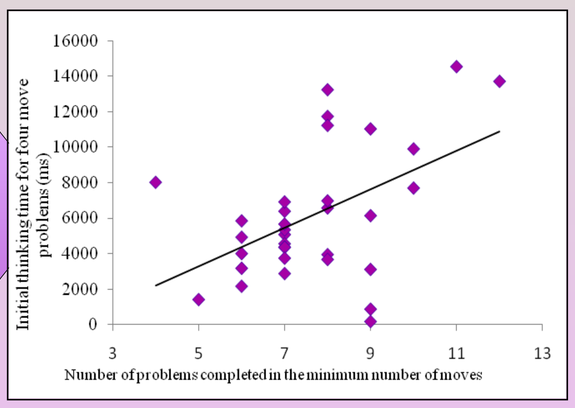


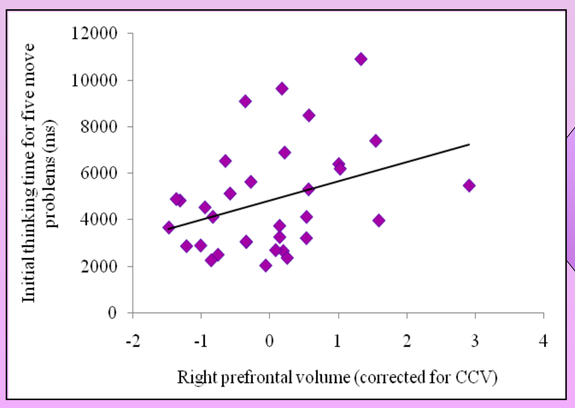
Whole Group

- Newborn ferritin scores are negatively correlated with the number of moves required to solve four move problems (r= -.470)
- Children with lower newborn ferritin levels require a greater number of excess moves to solve four move problems

Whole Group

- Average time spent thinking prior to beginning a trial for four move problems is positively correlated with the number of problems completed in the minimum number of moves (r= .375)





Whole Group

- Average initial thinking time on five move problems is positively correlated with corrected right prefrontal volume (r= .361)
- Children with larger corrected prefrontal volumes exhibited more overall initial thinking time on five move problems

Conclusions

Our findings indicate a link between prefrontal volume, measures of executive function, and parental reports of externalizing behaviors. Although in general larger prefrontal volumes were associated with better performance and lower ratings of externalizing behaviors, smaller left prefrontal volume in the high birth weight group predicted more problems solved in the minimum number of moves. Little is known about the way that the volume of brain structures may impact cognitive function, especially in the case of high birth weight. Additionally, newborn ferritin is negatively correlated with behavioral performance on the Stockings of Cambridge planning task suggesting that prenatal iron deficiency may have an impact on executive functions in middle childhood.

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