Memory Ability and Hippocampal Volume in Adolescents with Prenatal Poly-Drug Exposure

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Introduction

•Drug abuse among women of childbearing age is a serious public health problem[1,2].
- •The National Survey on Drug Use and Health indicates 9.3% of pregnant women age 18 to 44 are current illicit drug users[3].

• Prenatal drug exposure (PDE) to cocaine, heroin, methamphetamine, or multiple illicit substances has been shown to alter the course of development and adversely impact physical, cognitive, and socio-emotional development.
- • Longitudinal studies have reported that effects tend to be small and attenuated by child or environmental variables [4].
- • In spite of this variability, evidence suggests that subtle effects of PDE in certain domains persist into middle childhood even after rigorous control of confounding variables [4].

• Given the changes that take place throughout the adolescent years, it is reasonable to expect that the effects of PDE may also change over time.
- • Although memory impairment is not seen in childhood, differences in memory performance are apparent in adolescence [5].

•Previous research has shown hippocampal volume to be related to memory performance in typically developing groups.
- • Smaller volumes are associated with better memory [6,7].

Based on previous literature, we hypothesized that PDE adolescents would have worse memory performance than community controls (CC) and that differences at the neural level would be apparent in hippocampal volumes.

Goals

•Compare memory performance between PDE and CC adolescents

•Compare hippocampal volumes between PDE and CC adolescents

•Correlate memory performance with hippocampal volumes

Methods

Participants

Participants were part of a longitudinal follow-up of drug-using women and their infants. Recruitment at hospital of birth, at age 5, and age 14. Eligibility for PDE group included prenatal cocaine and/or heroin exposure, gestational age > 32 weeks, no ICU admission. CC group matched on age, race, and socioeconomic status.
- •28 PDE, 24 CC : Demographically similar on all variables except number of caregivers
- •Age: 14.42 years +/- 14 months
- •Gender: 29 (56%) female, 23 (44%) male
- •PDE: 60.7% of mothers used 3-5 drugs at least 1x/month during pregnancy,

Drug	Cigaret.	Alcohol	Cocaine	Heroin	Mariju.	Barbit.	Tranq.	Amphet.	Halluc.	Methad.
Any Use	85.7%	82.1%	96.4%	60.7%	82.1%	14.3%	3.6%	3.6%	3.6%	14.3%
>1/Month	67.9%	46.4%	89.3%	46.4%	17.9%	14.3%	0%	0%	0%	10.7%

Memory Task and Analysis

California Verbal Learning Test – Child Version (CVLT-C)
- • List A: "shopping list" of 15 items; List B: new "shopping list" of 15 items
- • Hear/recall list A (x5), hear/recall list B, recall list A
- • Dependent measure: number of items recalled for List A and List B

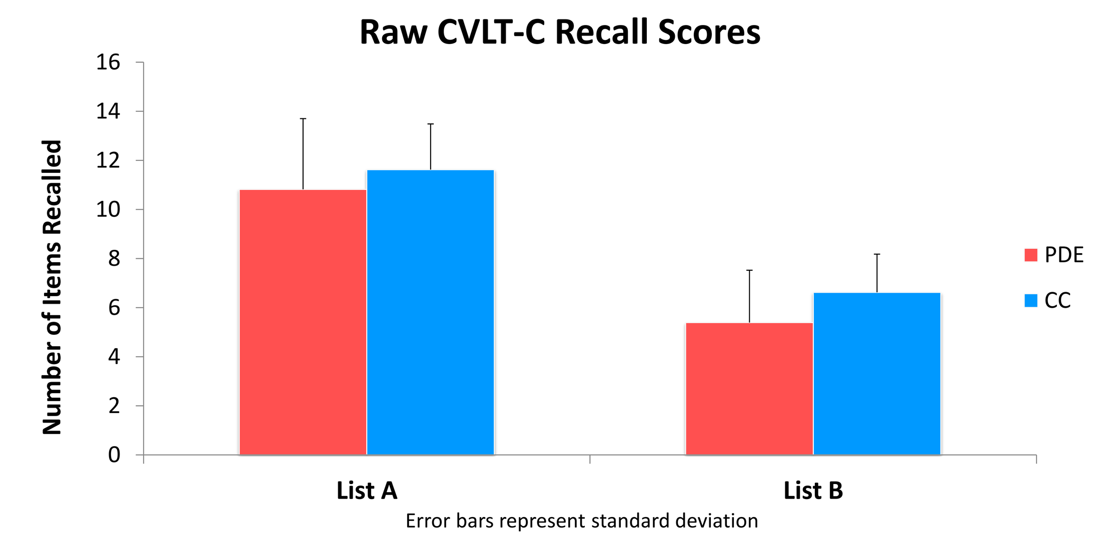
Anatomical Data Acquisition and Analysis

- • 3-T Siemens Allegra
- • Whole-brain oblique axial T1-weighted images (TR = 2.5 s, TE = 4.38 ms, FA = 80)
- • Cortical reconstruction and volumetric segmentation in Freesurfer

Analysis Models

1. No behavioral covariates (only total cortical gray matter [GM])
2. Covary age, gender, IQ (+ total cortical GM)
3. Covary frequent gestational exposure to tobacco and alcohol (+ total cortical GM)
4. Covary CES-D and number of caregiver changes (+ total cortical GM)

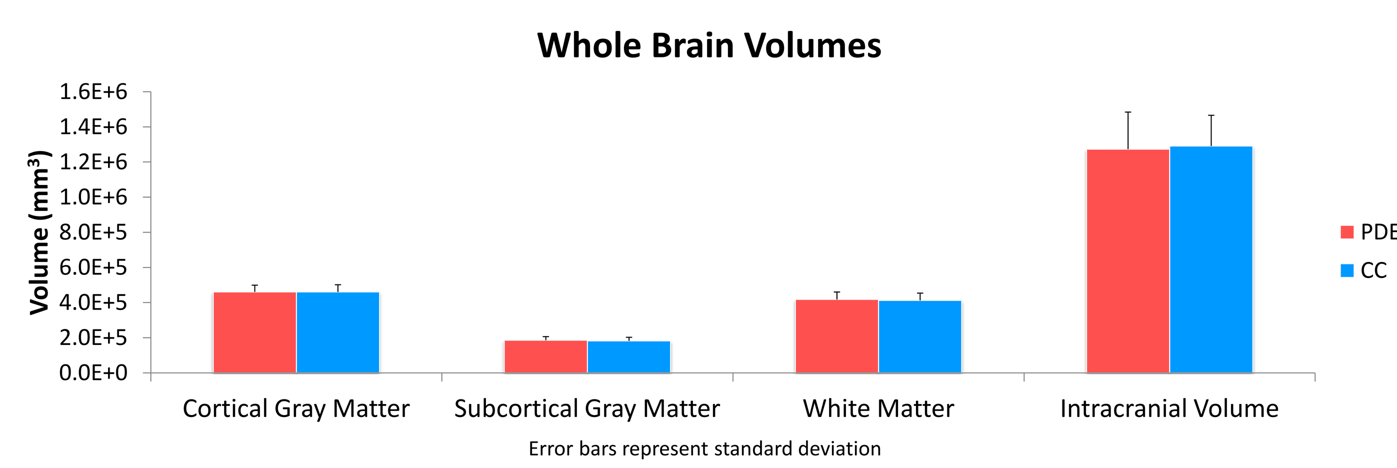
Memory Tasks



Group Difference on CVLT-C List B		
Model	F(df)	Significance
1	F(1,50)=3.80	p=0.023
2	F(1,47)=4.97	p=0.031
3	F(1,48)=2.01	p=0.163
4	F(1,41)=2.51	p=0.121

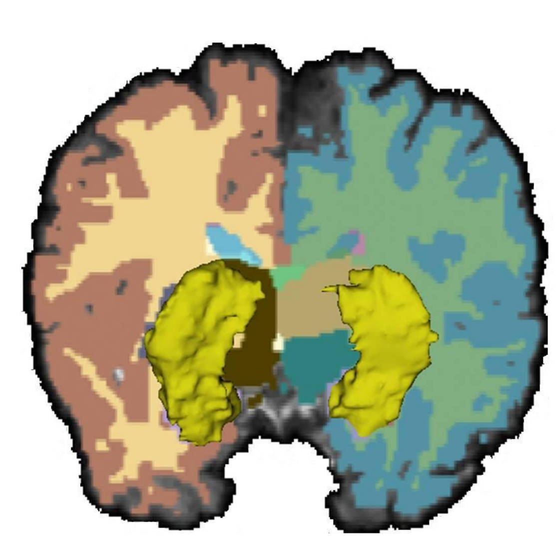
No group differences were apparent between PDE and CC on List A-Trial 5. Group differences were significant for performance on List B as CC adolescents recalled more items than PDE adolescents. This group difference was significant with model 1 and 2.

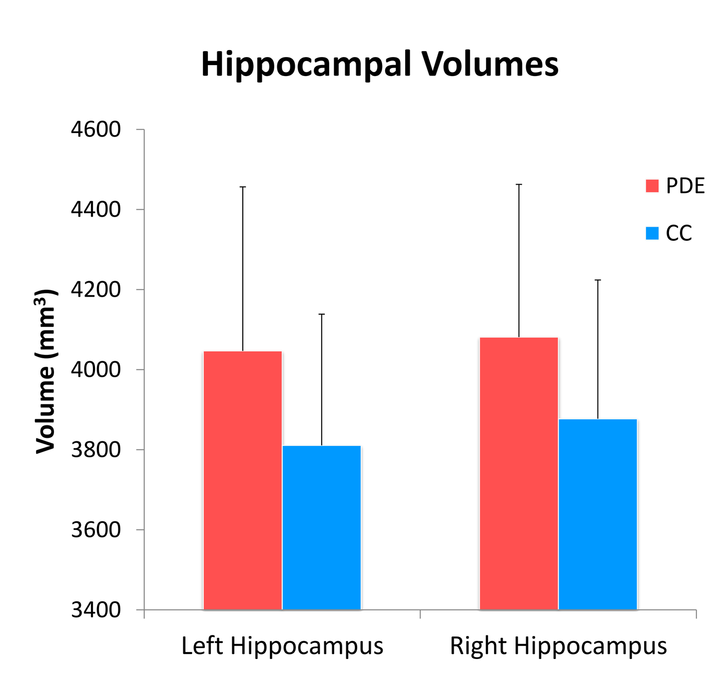
Volume Segmentation



None of the models (1-4) found any significant differences between PDE and CC total cortical gray matter, total white matter, total subcortical gray matter or total intracranial volume.

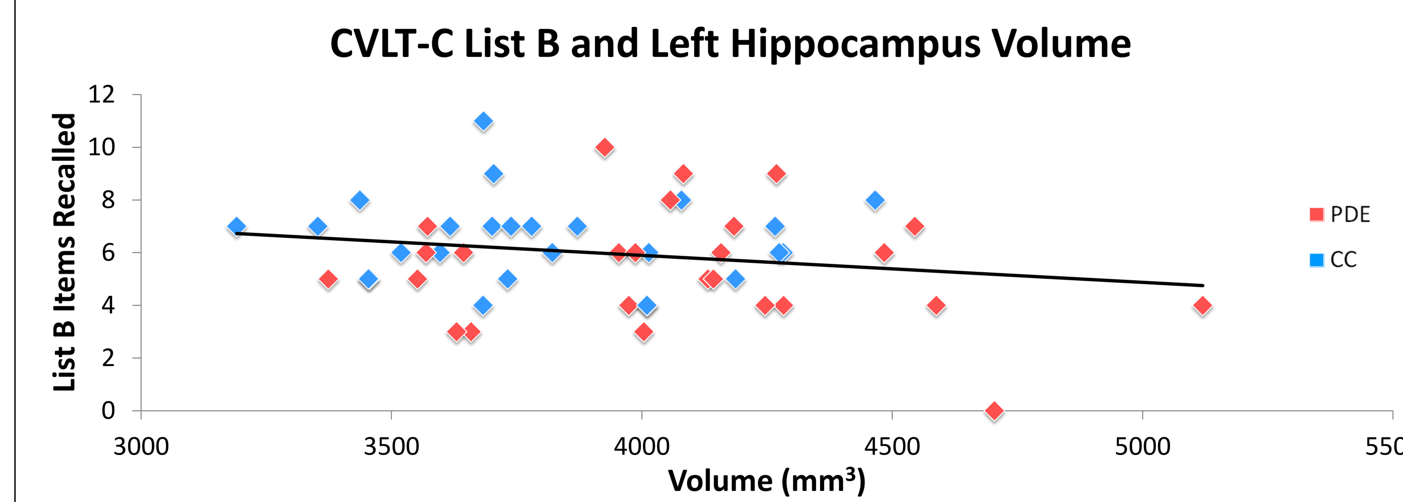
Model	Left Hippocampus	Right Hippocampus
1	p=0.00	p=0.02
2	p=0.00	p=0.02
3	p=0.01	p=0.01
4	p=0.01	p=0.175





Models 1-3 found significant differences between PDE and CC hippocampii bilaterally. Model 4 found significant differences only in the left hippocampus.

Correlations



CVLT-C List B and Left Hippocampus Volume		
Model	Correlation	Significance
1	-0.305	p=0.030
2	-0.316	p=0.029
3	-0.269	p=0.062
4	-0.201	p=0.201

Correlations between CVLT-C List B and left hippocampus volume across collapsed group (n=52).

Discussion

Conclusions

Memory Task
- • Memory differences were not found on CVLT-C List A but there was a significant difference between groups on the subsequent list CVLT-C List B.
  - • This pattern of performance may reflect proactive interference.
  - • Memory impairment may emerge under increased demands.
- •The differences on List B diminished with exposure and quality of care covariates.
  - • Direct and indirect effects through characteristics commonly associated with PDE.

Volume Segmentation
- • No significant differences were found in cortical gray matter, subcortical gray matter, white matter, or intracranial volume with any model.
- •Differences between groups became apparent in the bilateral hippocampii.
  - • Larger hippocampus volumes found in the PDE group.
  - • Significant for all models in the left hippocampus.
  - • Significant for models 1-3 in the right hippocampus.

Correlation
- • Hippocampus size was negatively correlated with CVLT-C List B memory performance.
  - •This finding is consistent with previous research [8].
  - •Collapsed across groups, hippocampal volume was significantly correlated with memory performance in models 1-2 and at trend level significance in model 3.

Future Directions:
- • Re-test memory performance at late adolescence (age 16-20)
- • Perform volume segmentation on late adolescence anatomical (age 16-20)
  - •Analyze differences between subject at late adolescence and across time with-in subject

Synopsis

Goal

Compare and correlate memory performance and hippocampal volume in adolescents prenatally exposed to drugs and their community comparisons.

Conclusion

Prenatal drug exposure relates to worse memory performance and larger hippocampal volumes; memory performance is negatively correlated with hippocampus size.

References

1. Lester BM, Tronick EX. The effects or prenatal cocaine exposure and child outcome. *Infant Mental Health Journal.* 1994; 15(2):107-120.
2. Lester BM, LaGasse LL, Seifer R. Cocaine Exposure and Children: The Meaning of Subtle Effects. *Science.* 1998; 282(5389):633-634.
3. Anon. Results from the 2010 NSDUH: Summary of National Findings, SAMHAS, CBHSQ. Available at: http://oas.samhsa.gov/NSDUH/2k10NSDUH/2k10Results.htm. Accessed March 20, 2012.
4. Ackerman JP, Riggins T, Black MM. A Review of the Effects of Prenatal Cocaine Exposure Among School-Aged Children. *Pediatrics*. 2010, 125(3): 554-565.
5. Betancourt LM, Yand W, Brodsky NL, et al. Adolescents with and without gestational cocaine exposure: Longitudinal analysis of inhibitory control, memory and receptive language. *Neurotoxicology Teratol.* 2011; 33(1):36-46
6. Gogtay N, Nugent III TF, Herman DH, et al. Dynamic mapping of normal human hippocampal development. *Hippocampus.* 2006; 16(8):664-672.
7. Rao H, Betancourt L, Giannetta J, et al. Early parental care is important for hippocampal maturation: Evidence from brain morphology in humans. *Neuroethics Publications.* 2009. Available at: http://repository,upenn,edu/neuroethics_pubs/68.
8. Van Petten C. Relationship between hippocampal volume and memory ability in healthy individuals across the lifespan: review and meta-analysis. *Neuropsychologia.* 2004; 42(10):1394-1413.

Supported by IRP NIDA/NIH, R01 DA07432 (Nair), R01 DA021059 (Black), and R03 DA029113 (Riggins)