Brain Volume Differences in Adolescents with Prenatal Poly-Drug Exposure

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Synopsis

Goal

Compare brain volumes involved in cognitive and affective processes in adolescents with prenatal drug exposure to their community comparisons.

Conclusions

Volume differences were found in right Brodmann Area 45, left lateral orbitofrontal, left rostral middle frontal, and bilateral hippocampii. Right BA 45 volume correlates to more cautious Go/No-Go performance and left hippocampal volume correlates to worse memory task performance.

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 use illicit drug[3].
- Prenatal drug exposure (PDE) to illicit drugs has been shown to adversely impact physical, cognitive, and socio-emotional growth.
  - 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 some effects of PDE in certain domains persist.
- Recent neuroimaging studies show that PDE impacts neural development
  - PDE Children and adolescents show differences in brain structure and function, including lower mean cortical gray matter[5]and small volumes of subcortical structures[6] versus comparison groups

Based on previous literature, we hypothesized that PDE adolescents would have volumetric differences from community controls in frontal and subcortical brain regions involved in cognitive and affective process.

Methods

Participants

- Recruited at birth, age 5 and age 14 at hospital or primary care clinics
  - Eligibility for PDE group included: prenatal cocaine/heroin exposure, no ICU
  - PDE: 60.7% of mothers used 3-5 drugs at least 1x/month during pregnancy
- 28 PDE, 24 CC: matched on age, race, socioeconomic status, and maternal age
  - Age: 14.42 +/- 14 months; Gender: 22 (42%) male, 29 (57%) female
  - Unmatched on: number in maternal care, prenatal cigarette/alcohol exposure

Go/No-Go Task

- Press spacebar as quickly as possible for all stimuli except "X"
- Dependant measures: errors of commission, errors of omission, response style

CVLT-C Memory Task

- Recall list of 15 items (List A, List B) immediately after presentation of list
- Dependant measures: List A recall, List B recall, percent change List A to List B recall

Anatomical Data Acquisition and Analysis

- 3-T Siemens Allegra Scanner: whole-brain axial T1-weighted images
- Cortical reconstruction and volumetric segmentation completed in Freesurfer

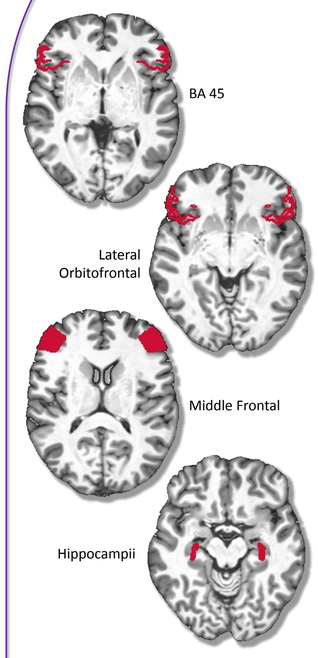
Analysis Models

Five statistical models (total cortical gray matter covaried for all volumetric analyses):

1. No behavioral covariates
2. Age at scan, gender covariates
3. Age, gender, IQ covariates
4. Age, gender, IQ, prenatal alcohol/cigarette exposure covariates
5. Age, gender, IQ, prenatal alcohol/cigarette exposure, caregiver depression and changes by age 7

Results

Volumetric Segmentation

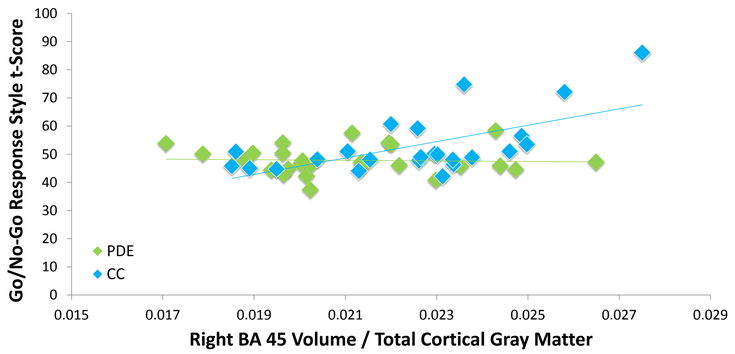


	PDE (n=28)	CC (n=24)	Statistical Models				
	Mean [SD]	Mean [SD]	Model 1	Model 2	Model 3	Model 4	Model 5*
Whole Brain			*F(1,50)>0.1*	*F(1,48)>0.01*	*F(1,47)>0.00*	*F(1,45)>0.00*	*F(1,37)>0.00*
Total cortical gray	460774.83 [38234.44]	460453.19 [41042.05]	p=0.98	p=0.93	p=0.95	p=0.92	p=0.95
Total white matter	417663.25 [42461.69]	412024.65 [41766.86]	p=0.63	p=1.00	p=0.97	p=0.99	p=0.63
Subcortical gray	185454.21 [20699.10]	181948.25 [20414.85]	p=0.54	p=0.41	p=0.33	p=0.33	p=0.81
Intracranial volume	$1.27x10^6$ [$2.12x10^5$]	$1.29x10^6$ [$1.75x10^5$]	p=0.75	p=0.22	p=0.22	p=0.59	p=0.94
BA 45			*F(1,49)>3.00*	*F(1,47)>3.60*	*F(1,46)>4.80*	*F(1,44)>1.00*	*F(1,36)>0.10*
Left BA 45	6960.96 [943.33]	7328.83 [1048.78]	p=0.09	p=0.06	**p=0.03**	p=0.32	p=0.66
Right BA 45	9648.21 [1059.93]	10372.50 [1396.17]	**p=0.01**	**p=0.01**	**p=0.01**	**p=0.00**	**p=0.01**
Lateral Orbitofrontal			*F(1,49)>1.90*	*F(1,47)>1.60*	*F(1,46)>1.80*	*F(1,44)>3.70*	*F(1,36)>1.30*
Left LOF	7752.79 [1047.64]	8257.00 [1194.05]	**p=0.02**	**p=0.02**	**p=0.03**	**p=0.03**	p=0.08
Right LOF	7829.04 [979.27]	8083.92 [1020.25]	p=0.17	p=0.21	p=0.19	p=0.06	p=0.26
Rostral Middle Frontal			*F(1,49)>1.70*	*F(1,47)>2.60*	*F(1,46)>2.09*	*F(1,44)>9.50*	*F(1,36)>6.20*
Left RMF	16508.68 [1901.16]	17583.42 [2530.45]	**p=0.01**	**p=0.01**	**p=0.00**	**p=0.00**	**p=0.02**
Right RMF	17824.14 [2630.62]	18552.38 [3113.89]	p=0.19	p=0.11	p=0.16	**p=0.00**	**p=0.00**
Hippocampii			*F(1,49)>5.50*	*F(1,47)>6.30*	*F(1,46)>6.30*	*F(1,44)>6.80*	*F(1,36)>1.40*
Left hippocampus	4046.71 [409.68]	3810.88 [327.61]	**p=0.00**	**p=0.00**	**p=0.00**	**p=0.00**	**p=0.00**
Right hippocampus	4081.25 [381.31]	3877.42 [346.46]	**p=0.02**	**p=0.02**	**p=0.02**	**p=0.01**	p=0.24

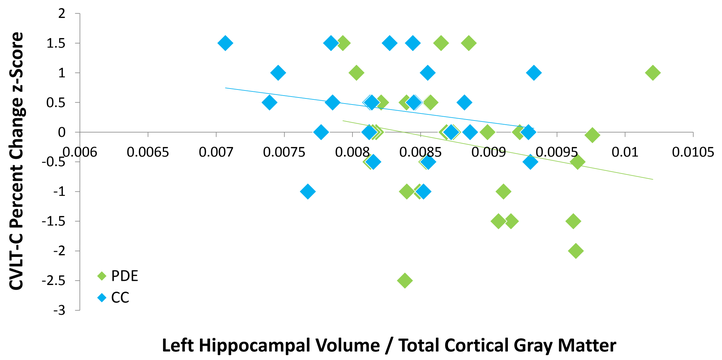
* Model 5 includes only n=46 (18 CC, 28 PDE) as 6 CC participants did not have caregiver depression scores; all other models contain n=52 (24 CC, 28 PDE)

Correlation to Behavior

Go/No-Go Response Style and Right BA 45



CVLT-C Percent Change and Left Hippocampal Volume



	Go/No-Go Response Style t-Score				CVLT-C Percent Change z-Score			
Model	PDE(27) vs CC(24)	Correlation to BA 45: PDE, CC, Both			PDE(28) vs CC(24)	Correlation to Hippocampus: PDE, CC, Both		
1	**p=0.026**	p=0.818	**p=0.001**	**p=0.002**	**p=0.036**	p=0.212	p=261	**p=0.020**
2	**p=0.031**	p=0.752	**p=0.003**	**p=0.002**	**p=0.049**	p=0.225	p=0.363	**p=0.020**
3	**p=0.027**	p=0.853	**p=0.005**	**p=0.002**	p=0.062	p=0.166	p=0.413	**p=0.020**
4	p=0.175	p=0.971	**p=0.004**	**p=0.002**	p=0.123	p=0.135	p=0.453	**p=0.029**
5*	p=0.249	p=0.988	---	**p=0.009**	p=0.441	p=0.152	---	p=0.066

Discussion

Whole Brain Volumes

There were no significant differences on whole brain volumes between the PDE and CC groups. This is inconsistent with some previous studies which have found lower mean cortical gray matter[5] but notably, significant head circumference differences are often present at birth between cohorts which were not present in this sample.

Frontal and Subcortical Volumes

PDE adolescents had significantly smaller volumes than CC adolescents in the right BA 45, left lateral orbitofrontal, and left rostral middle frontal. This direction of difference is consistent with previous literature on cortical and subcortical structures [5,6]. CC adolescents had significantly smaller volumes in the bilateral hippocampii. This was expected given that better care giving quality has been associated with smaller hippocampal volume during adolescence [7].

Correlations

Larger right BA 45 volumes were correlated with higher/"safer" response style t-scores (more errors of omission than errors of commission). This neural correlate is in line with previous research showing the PDE have more behavioral and attention problems. Smaller left hippocampal volumes were correlated with better memory performance on the CVLT-C (less proactive interference). This is in line with previous research indicating smaller hippocampal volume is related to better memory performance in typically developing groups [8].

Future Directions

We plan to investigate cortical thickness differences between groups, re-test volumetric differences at late adolescence (16-20 years old) and analyze volume differences across time.

References

1. Lester BM, Tronick EZ. The effects of 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,, SAMHSA, CBHSQ. Available at: http://oas.samhsa.gov/NSDUH/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. Rivkin MJ, Davis PE, Lemaster JL, et al. Volumetric MRI study of brain in children with intrauterine exposure to cocaine, alcohol, and marijuana. *Pediatrics*. 2008;121(4):741-750.
6. Avants BB, Hurt H, Giannetta JM, et al. Effects of heavy in utero cocaine exposure on adolescent caudate morphology. *Pediatric Neurology*. 2007;37(4):275-279.
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://respository.upenn.edu/neuroethics_pubs/68
8. Sowell ET, Delis D, Stiles J, Jerigan, TL, et al. Improved memory functioning and frontal lobe maturation between childhood and adolescence: a structural MRI study. *Journal of the International Neuropsychological Society*. 2001;7(3):312-322.

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