Longitudinal comparison of the "default mode" deactivations in adolescents prenatally exposed to cocaine

Zhihao Li[1], Priya Santhanam[1], Claire Coles[2], Mary Ellen Lynch[2], Stephan Hamann[3], and Xiaoping Hu[1]

[1]*Biomedical Engineering, Emory University & Georgia Institute of Technology, Atlanta, Georgia, United States,* [2]*Psychiatry and Behavioral Science, Emory University, Atlanta, Georgia, United States,* [3]*Psychology, Emory University, Atlanta, Georgia, United States*

TARGET AUDIENCE Researchers interested in fMRI of the default mode network and/or prenatal drug exposure.

PURPOSE Prenatal cocaine exposure (PCE) is associated with arousal dysregulation [1] with an unbalanced allocation of mental resource between different streams of information processing [2-4]. Specifically in the "default mode" network (DMN), the brain regions known for balancing internal and external attention, previous data has shown PCE related alterations on both functional activation and connectivity [3]. However, neuroimaging studies of this population to date has been cross-sectional, and the interaction of this particular effect with neural development over adolescence has not been directly explored. In this study, we measured DMN deactivations with fMRI in the same groups of PCE and control adolescents while they performed the same cognitive task at two different time points (~26 months apart). Due to maturity and/or familiarity with the stimuli and task, control participants were expected to exhibit improved behavioral performance and attenuated DMN deactivation at the second time while this developmental effect was hypothesized to be compromised in adolescents with PCE.

METHOD Twelve control (6M6F, Age_{1st}=14.4±2.2, Age_{2nd}=16.8±2.3) and twenty-one PCE (13M8F, Age_{1st}=14.3±1.8, Age_{2nd}=16.7±2.1) adolescents were scanned (3T Siemens, EPI-BOLD, TR/TE/FA/FOV=3000ms/30ms/90o/192cm, 30 axial slices, thickness/gap=3mm/0mm, matrix=64×64) while performing an n-back working memory task with emotional distracting pictures [2]. The task instruction, stimuli, and imaging settings were identical for the two study sessions. AFNI (http://afni.nimh.nih.gov) was used for fMRI data analysis via general linear modeling. Specifically, the DMN was identified by the BOLD signal contrast between the conditions of high and low memory loads. The DMN typically shows a functional deactivation with an increased memory load, and this deactivation was compared between the groups and imaging sessions through a Group (PCE vs. control) x Time (1^{st} vs. 2^{nd} visit) ANOVA. In addition, potential group confounding factors of gender, family income, birth weight, and other substance (tobacco, alcohol, and marijuana) exposures were controlled through covariates in the statistical model.

RESULTS Both groups improved their memory performance at the 2^{nd} visit (table 1) but no significant main effect was noted on Group, on Time, or on Group x Time interaction (table 1). However, the two groups exhibited significant ($p<0.05$/voxel plus 37 voxels cluster, $p<0.05$ corrected) developmental differences on DMN deactivation in the anterior and posterior cingulate areas. For the controls, this deactivation was much reduced at the 2^{nd} visit but it was increased in the adolescents with PCE. This Group x Time interaction in DMN also remained its significance when potential group confounding factors were statistically controlled.

Table 1. Summary of behavioral performances.

	Control		*PCE*		*Effect significance (p values)*		
	1st	*2nd*	*1st*	*2nd*	*group*	*time*	*group x time*
Reaction Time (ms)	*420*	*416*	*439*	*424*	*0.55*	*0.49*	*0.69*
Accuracy (%)	*92*	*95*	*90*	*91*	*0.17*	*0.17*	*0.74*

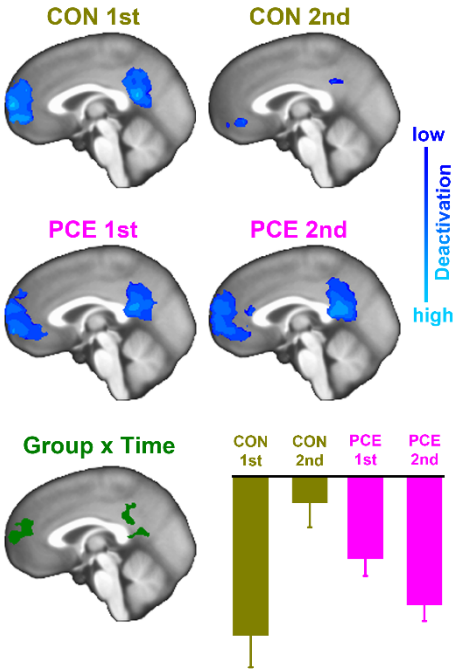

Figure 1. Group comparison of the DMN deactivations.

DISCUSSION AND CONCLUSION Due to maturation and familiarity with the task/distractors, both groups improved their behavioral performances at the 2^{nd} visit. However, while this improvement is achieved with a lower cost of attentional resource in typically developing adolescents, those with PCE have to pay a higher cost for a comparable achievement. The present results provide direct evidence supporting the view of PCE associated long-term effect on arousal regulation [1]. With a weaker distractor suppression [2-3], the altered DMN functionality may compromise performances of exposed individuals with increased cognitive demand or interference.

REFERENCES [1] Mayes, L. 2002. Neurotoxicol Teratol. 24:385. [2] Li et al., 2009. Neurotoxicol Teratol. 31:342. [3] Li et al., 2011. Hum. Brain Mapp. 32:759. [4] Li et al., 2013. Psychiat Res Neuroim. 213:47.

This work was supported by: GA Research Alliance, NIH grant RO1 DA033393