

Altered Prefrontal-Amygdala Structural Connectivity in Adolescents Prenatally Exposed to Cocaine

P. Santhanam¹, Z. Li¹, L. Li¹, C. Coles², M. Lynch², and X. Hu¹

¹Department of Biomedical Engineering, Georgia Institute of Technology/Emory University, Atlanta, GA, United States, ²Department of Psychiatry and Behavioral Sciences, Emory University

INTRODUCTION

Prenatal cocaine exposure (PCE) is known to affect emotional regulation [1]. Reciprocal modulation between the ventral medial prefrontal cortex (VMPFC) and amygdala is associated with emotional control in healthy populations [2], and disconnection between is associated with behavioral dysregulation [3,4]. Previously our PCE cohort was shown to lack emotional suppression during cognitive demand; as compared to controls, the PCE group could not raise VMPFC activity during a higher cognitive load condition that contained negatively emotive distracters [5]. As these results imply a functional disconnect between the VMPFC and amygdala in the PCE group, and since VMPFC and amygdala are known to be structurally connected [6], the present study examined possible PCE-induced alterations to underlying structural connectivity.

METHODS

Participants were adolescents recruited from a longitudinal cohort and were divided into two groups: those with PCE (n=25) and socio-economic status matched controls (n=12). DTI data was acquired with a diffusion-weighted, single-shot, spin-echo EPI sequence. Diffusion gradients were applied in 12 directions with a b-value of 1000 sec/mm². Contiguous axial slices (34 with 2.5mm thickness) were acquired, with TR/TE/FOV of 6500ms/90ms/22cm, and total scan time of 8:34 minutes. Probabilistic tractography in FSL (<http://www.fmrib.ox.ac.uk/fsl/>) was used to identify white matter tracts connecting the VMPFC and bilateral amygdala. To derive seed and target regions, masks from the previous study [5] were transformed to native space for all subjects individually. To ensure that the VMPFC mask was equally distributed in both hemispheres, the final VMPFC mask used was the product of the union of the original functional mask and its mirror image along the R-L axis. The left and right amygdala, respectively, were used as seeding regions, and the VMPFC region was used as target. The output of the probabilistic tractography was a group of fibers representing the connectivity distribution between regions of interest (ROIs), along with the total number of fibers between them (i.e., waytotal). Structural integrity between ROIs was quantified by total tract volume and FA along the thresholded tracts derived from tractography. To ensure that the tracts were present and continuous at a range of thresholds (p<0.1 to p<0.01), the thresholded tract data was examined visually. Differences in total tract volume and FA were determined between groups by t-test.

RESULTS

Figure 1 shows continuous tracts identified by probabilistic tractography, in one representative participant from each group, between the VMPFC and left and right amygdala, respectively. Tract volume between the VMPFC and left amygdala (red) appears to be larger in the control group than the PCE group. Total tract volume and mean FA for thresholded tracts (p<0.1) connecting the ROIs are shown in Table 1. VMPFC-left amygdala tracts in the PCE group have lower total tract volume and FA along the tracts as compared to the healthy control group.

Figure 1. Probabilistic tractography results for one representative participant from each group. Continuous tracts are identified connecting the ROIs in serial axial slices (control: z=7-10, PCE: z=9-12).

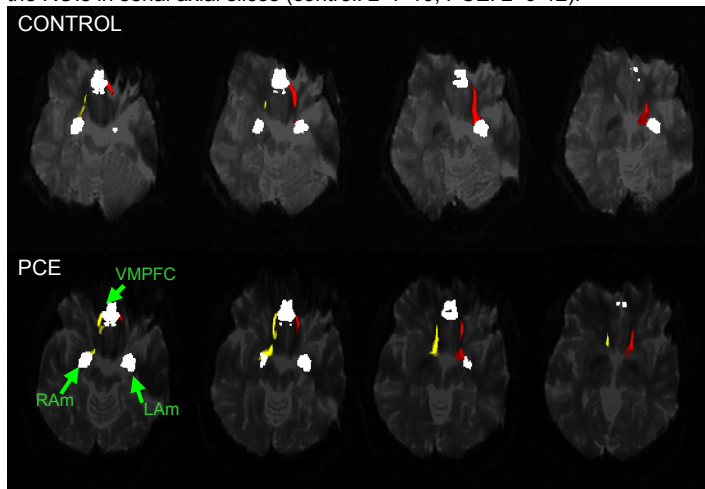


Table 1. Tractography measures between the VMPFC and bilateral amygdala. *= significantly different from control group (p<0.05). SEM = standard error of mean.

| ROI network | Tractography Measures (SEM) | | |
|----------------------------|-----------------------------|---------------------------------|----------------|
| | | Tract volume in mm ³ | FA |
| Left amygdala-VMPFC (SEM) | Control | 105.2 (12.7) | 0.421 (0.016) |
| | PCE | 50.8* (6.48) | 0.361* (0.028) |
| Right amygdala-VMPFC (SEM) | Control | 100.2 (9.35) | 0.364 (0.014) |
| | PCE | 67.7 (12.4) | 0.368 (0.029) |

DISCUSSION

In addition to a functional disconnect between the VMPFC and amygdala regions [5], individuals with PCE had reduced structural connectivity between these regions, indicated by reduced tract volume and FA over the tracts connecting the left amygdala to the VMPFC. Normal hemispheric differences in white matter density and FA may explain the different structural connectivity result for

the left and right amygdala. The findings imply that the structural damage seen in the PCE group may be responsible for reduced functional connectivity, leading to emotionally dysregulated behavioral outcomes in adolescents with PCE. This adds to the growing body of knowledge about the neurobiological basis for PCE-related teratogenic effects.

ACKNOWLEDGEMENTS: This work is supported in part by the NIH (R01 DA17795).

REFERENCES: [1] Bendersky M, and Lewis M 1998 Dev Psychol 34(3):555-64. [2] Beaugreard M, et al. 2001 J Neurosci 21(18):RC165. [3] Gilboa A, et al. 2004 Biol Psychiatry 55(3):263-72. Hoptman MJ, et al. April 16 2009 Schizophr Bull. [5] Li, Z. Proc. of ISMRM, Abstract #430, April 2009. [6] Cohen MX, et al. 2008. Neuroimage 39(3):1396-407.