Longitudinal changes of functional connectivity with amygdala and prefrontal cortex in adolescents prenatally exposed to cocaine

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TARGET AUDIENCE Researchers interested in resting-state functional connectivity and/or prenatal substance exposure.

PURPOSE Prenatal cocaine exposure (PCE) is associated with long-term effect of arousal dysregulation [1] with specific functional alterations reported in both amygdala and prefrontal cortex [2]. However, all neuroimaging studies of this population to date are cross-sectional and interactions of the exposure and neural development over adolescence has not been directly explored. In this study, we measured resting-state functional connectivity in the same groups of PCE and control adolescents while they were scanned at two different times averagely 26.7 months apart. With correlation seeds placed in amygdala and left dorsal lateral prefrontal cortex (LDLPFC), control participants were expected to exhibit network architecture associated with improved stress coping and executive control [3,4], but this improvement was hypothesized to be compromised in adolescents with PCE.

METHOD Sixteen control (7M9F, Age_{1st}=14.2±2.3, Age_{2nd}=16.4±2.3) and twenty-five PCE (14M11F, Age_{1st}=14.4±1.8, Age_{2nd}=16.7±2.1) adolescents were scanned during rest (no specific task other than eye fixation) with exactly the same imaging parameters at both visits (3T Siemens, EPI-BOLD, TR/TE/FA/FOV=2000ms/30ms/90°/192cm, volume=210, 20 axial slices, thickness/gap=4mm/0mm, matrix=64×64). AFNI (http://afni.nimh.nih.gov) was used for connectivity analysis with regular approach of seeding-correlation (despiking, slice timing correction, volume registration, noise reduction [5], band pass filtering with 0.08Hz<f<0.009Hz, spatial smoothing with FWHM=5mm, spatial normalization, and Pearson correlation). The seeding regions were bilateral amygdala ($coordinates_{left}$=23.4,5.4,-12.8, $volume_{left}$=1809mm^3; $coordinates_{right}$=-22.6,5.1,-12.2, $volume_{left}$=1539mm^3) and LDLPFC (coordinates=43.4,-29.8,35.6, volume=1323mm^3) defined by emotion and memory activation data acquired in the same imaging session [2]. Once the connectivity maps were obtained, they were compared between GROUP (PCE vs. control) and TIME (1st vs. 2nd visit) through a voxel-wise ANOVA. In addition, potential group confounding factors of other substance (tobacco, alcohol, and marijuana) exposures were controlled through covariates in the statistical model.

RESULTS The two groups exhibited significant (p<0.05/voxel plus 1620mm^3 cluster, p<0.05 corrected) developmental differences in connectivity maps of both amygdala and LDLPFC. For the amygdala, its functional connection with lateral occipital cortex (LOC) and inferior temporal cortex (ITC) are generally reduced with increasing age for the controls; but this developmental effect was not observed in the PCE group (Fig.1 top row). For the LDLPFC, its functional connection with dorsal anterior cingulate cortex (dACC) was reduced with increasing age for the controls; but this effect was much weaker in the PCE group (Fig.1.bottom row).

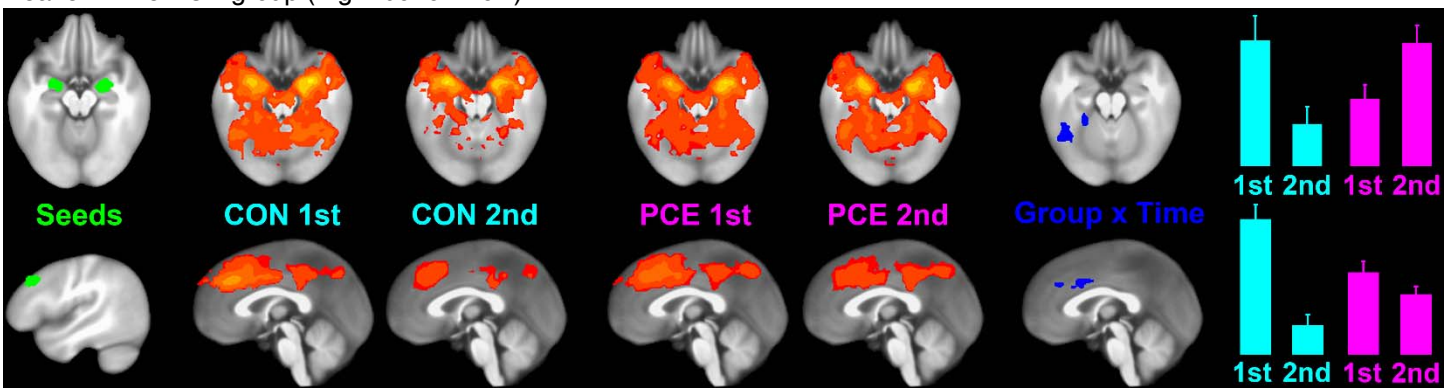

Figure 1. Development effect of functional connectivity with amygdala (top) and LDLPFC (bottom). Significant mapping results are shown in cyan for control group, in pink for PCE group, and in blue for Group x Time interaction. The bar plots compare connectivity z-scores in the blue regions.

DISCUSSION AND CONCLUSION The maturation of functional connectivity in the control group has reflected an improved capacity for stress coping [3] and network segregation in typical development [4]. The absence or weaker pattern of this maturation in the PCE group is consistent with their impaired capacity in processing conflicting information on task-relevant cognitive stimuli and task-irrelevant emotional stimuli [2]. The present results provide further and direct evidence supporting the view of PCE associated long-term effect on arousal regulation.

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