

## Prenatal cocaine exposure alters ventromedial prefrontal activity associated with emotion regulation

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**Introduction** Prenatal cocaine exposure (PCE) is associated with arousal dysregulation and possible inefficiencies in some cognitive functions [1]. Previous data showed that PCE subjects could not effectively suppress the amygdala response to emotional distracters, which in turn affects their working memory function [2]. As the ventromedial prefrontal cortex (VMPFC) is structurally connected to bilateral amygdalae [3], and functionally suppresses their emotional responses [4], the present study examines the hypothesis that PCE alters the VMPFC activity associated with emotion regulation. Our fMRI data showed that PCE subjects, unlike the controls, did not exhibit an increased VMPFC activation when working memory load was increased, indicating the absence of increased suppression of emotional distraction.

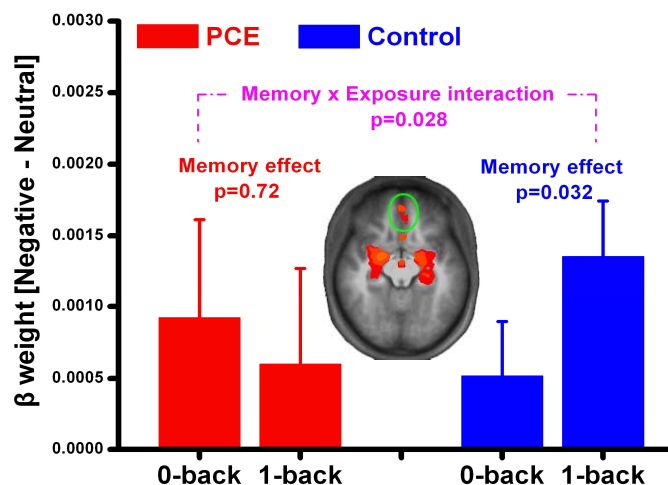
**Method** Twenty-two control and twenty-three PCE teenagers (12-18 yrs. old) were scanned with a 3T Siemens scanner. In the task state fMRI (30 axial slices, thickness/gap=3mm/0mm, TR/TE/FA/FOV=3000ms/30ms/90°/192cm, matrix=64×64, 2 EPI-BOLD scans, 120 volume measurements each), participants were asked to perform a block design “n-back” working memory task with two memory load levels (0- and 1-back). Emotionally neutral or negative pictures were also imbedded in the memory stimuli, thus producing 4 different task blocks (neutral 0-back, neutral 1-back, negative 0-back, and negative 1-back). We also collected resting state fMRI data (same acquisition parameters as the task fMRI except 20 slices in 4mm thickness, TR=2000ms) while subjects looked at a fixation cross on the screen.

Using the task fMRI data, bilateral amygdalae were functionally localized by the negative vs. neutral contrast. The VMPFC was then defined by resting state fMRI as the ventral medial prefrontal voxels that have a strong low frequency (0.01-0.08Hz) correlation with bilateral amygdalae. Because the subjects needed to focus on the memory task, the VMPFC fMRI signal difference between the negative and neutral conditions (Negative-Neutral) is expected to represent the brain activity related to the effort to suppress the emotional distraction. This effort needs to be increased if the memory load goes high. We compared this emotional regulation associated VMPFC signal between groups and conditions with a 2 (PCE vs. control) x 2 (0- vs. 1-back) ANOVA (confounding factors: gender, alcohol and marijuana exposure were statistically controlled as covariates).

**Result** With resting fMRI, we successfully located the VMPFC region that is functionally connected to bilateral amygdalae. A higher VMPFC signal in the negative condition than neutral indicates more emotional suppression exerted when the memory task was challenged by emotional arousal. In the control subjects, this suppression associated VMPFC activation increased significantly when memory load changed from 0- to 1-back. However, this VMPFC activation of the PCEs was not significantly changed by memory load. The group and condition comparison are depicted in Fig.1.

**Conclusion and Discussion** The present study reveals more imaging evidence supporting the view that PCE has a long-term effect on arousal regulation. It was previously reported that control subjects could decrease their amygdalae emotional response when cognitive demand increases while PCE subjects could not [2]. The present data complement this previous finding and provide more in-depth understanding about the neurobiological basis associated to PCE.

**References** [1] Mayes, 2002. Neurotoxicol Teratol. 24:385. [2] Li et al., 2007. Proc.ISMRM. 15:100. [3] Cohen et al., 2008. NeuroImage. 39:1396. [4] Urry et al., 2006. J.Neurosci. 26:4415.



*Fig.1 Emotional regulation associated VMPFC signal in different experimental conditions and subject groups. The central brain map shows the brain regions that are functionally connected to bilateral amygdalae. The resting correlation defined VMPFC is depicted by the green circle. Error bars here represent standard error.*

**Supported by:** GA Research Alliance, NIH grant RO1 DA17795