

Prenatal cocaine exposure alters default mode brain activity: functional and resting state MRI evidence

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Introduction Prenatal cocaine exposure (PCE) is associated with attention/arousal dysregulation and possible inefficiencies in certain cognitive functions [1]. As an important indicator of mental processing resource allocation [2, 3], the “default mode” brain activity (high baseline metabolic activity at rest) may also be affected by the PCE. By examining the default mode responses with functional and resting state MRI, the present neuroimaging study revealed that PCE may affect behavior and functioning by increasing baseline arousal and altering brain mechanisms involved in cognitive resource allocation.

Method Eleven control (age 13±1, 5M6F) and eleven PCE (age 13±0.9, 8M3F) subjects were scanned with a 3T Siemens scanner. In the functional MRI (2 EPI-BOLD fMRI scans with 120 volume measurements in each, matrix=64×64, 30 axial slices, thickness/gap=3mm/0mm, TR/TE/FA/FOV=3000ms/30ms/90°/192cm), participants were asked to perform a working memory task by pressing a button either when “RR” was displayed (0-back condition) or when the displaying letter pair matched with the previous one (1-back condition). There were also distracting pictures placed between the memory stimuli list to assess the emotion responses (results shown elsewhere). In the resting state MRI (1 EPI-BOLD scan with 210 volume measurements, matrix=64×64, 20 axial slices, thickness/gap=4mm/0mm, TR/TE/FA/FOV=2000ms/30ms/90°/192cm), subjects were instructed to simply gaze at a fixation cross on the screen.

AFNI (<http://afni.nimh.nih.gov>) was used for imaging data analysis. **Functional MRI:** After the data preprocessing steps (slice timing correction, scan concatenation, spatial registration, signal normalization to change%, and 5mm FWHM Gaussian smoothing), regression coefficients (β -weights), which represent the BOLD signal level for the 0- and 1-back conditions were derived for each subject with a multiple regression analysis. For the group comparison of default mode activity, voxels with a negative memory effect (higher BOLD signal level in the 0-back as compared to the 1-back condition) were submitted into a group t-test. **Resting state MRI:** The preprocessing includes slice timing correction, spatial registration, 0.08-0.01Hz band pass filtering and 5mm FWHM Gaussian smoothing. The time course from an anterior cingulate seeding voxel (Talairach coordinates x/y/z=0/-40/4) was used for subsequent whole brain cross-correlation analysis. The correlation coefficients, after being converted to Z-scores, were compared between the control and PCE subjects by group t-test.

Result The behavioral data (not shown here) showed no significant group difference in memory performance. For the default mode activity (signal decrease with higher memory load), control subjects showed a larger decrease in the BOLD signal in the medial prefrontal and posterior cingulate areas than the PCEs. In the resting state MRI, PCE subjects had a stronger default mode network correlation as compared to the controls. The group t-test comparison maps are shown in the Fig.1. Although the activation and resting state connectivity group differences do not exactly overlap, these differences were all in the default mode network.

Discussion The default mode activity represents intrinsic neural responses associated to environment monitoring and/or stimulus independent thoughts [3]. As shown by fMRI, control subjects reduced default mode activity more when cognitive demand increased, possibly reflecting a higher ability to shift mental processing resources to the cognitive task when necessary. Furthermore, resting state results showed stronger default mode connectivity in the PCE subjects. This observation provides more evidence supporting the view that PCE subjects exhibit an increased level of baseline arousal which may account for an increased risk for cognitive deficit as well as antisocial personality [4].

References [1] Mayes, L. 2002. *Neurotoxicol Teratol.* 24:385. [2] McKiernan et. al., 2003. *J Cogn Neurosci.* 15:394. [3] Gusnard & Raichle. 2001. *Nat Rev Neurosci.* 2:685. [4] Coles & Bard. 1999. *Neurotoxicol Teratol.* 21:527.

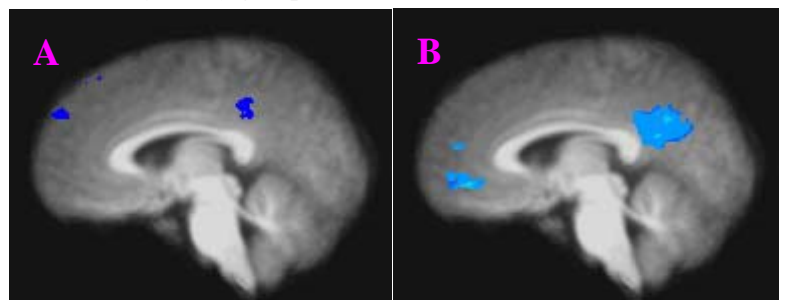


Fig.1. Group t-test map of the functional (A) and resting state (B) MRI data. Both maps had a threshold of $p < 0.05/\text{voxel}$ plus 200 μL cluster. (A). In the high memory load condition, control subjects exhibit more BOLD signal decrease in the medial prefrontal and posterior cingulate areas. (B). PCE subjects show stronger default mode connectivity in the anterior and posterior cingulate areas.

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