Effective connectivity of resting state networks in patients prenatally exposed to cocaine shows higher emotional arousal

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Introduction

Behavioral [1] and imaging research [2] has led to the hypothesis that prenatal cocaine exposure (PCE) alters emotional regulation. Preliminary functional connectivity evidence suggests that resting state BOLD fluctuations in the emotional network are more synchronized in PCE patients than in healthy controls [3]. In this study, we evaluate Granger-based resting state effective connectivity in the emotional network in PCE subjects to examine the above hypothesis. We found interhemispheric connections between homologous areas in both PCE subjects and controls, but additional bidirectional connectivity between amygdala and parahippocampal gyrus in only PCE subjects.

Methods

Twenty two control and 32 PCE participants (13-18 years of age) were recruited from longitudinal samples first identified in the postpartum unit. Mothers of children in the PCE group reported cocaine use during pregnancy or had EMIT (enzyme-multiplied immunoassay technique) screens indicating cocaine use. EPI data were obtained using a 3T Siemens scanner while they were instructed to simply gaze at a fixation cross. Scanning parameters were: in-plane resolution of 64×64, 20 slices (4 mm wide each), 220×200 mm in-plane FOV, TR=2 s, 210 images, TE=30 ms, FA=90°. Bilateral amygdala were chosen as seeds due to their importance in the emotional network [4] and correlated with the other voxel time series within the brain. Twelve ROIs showing significant resting state functional connectivity ($p \leq 0.01$) with the amygdala seed in either of the groups – bilateral anterior cingulate (ACC), posterior cingulate (PCC), mid cingulate (CG), middle frontal gyrus (MFG), parahippocampal gyrus (PHG) and amygdala (Amyg) – were identified from a t-test. The mean functional BOLD time series from each of the ROIs were extracted and fed into the multivariate Granger connectivity model [5] to obtain effective connectivity networks for the PCE and control groups, respectively.

Results

The resting state Granger-based effective connectivity networks for the control and PCE groups are shown in Fig.1. We predominantly observed strong interhemispheric connectivity between the homologous regions. However, in the PCE subjects, there was additional bidirectional connectivity between right amygdala and right PHG, which was absent in the control group. Also, effective connectivity between bilateral PHG was significantly higher in PCE as compared to control subjects ($p < 0.05$).

Discussion

The predominant interhemispheric connectivity is expected due to the absence of a driving input in resting state. PHG, identified as a part of the resting state functional connectivity networks, has been hypothesized to have a role in episodic memory retrieval [6,7] when subjects are asked to do nothing but gaze at a fixation cross. The significantly higher connection between bilateral PHG in the PCE group may suggest stronger episodic memory retrieval in them. Amygdala-PHG interaction has been previously observed in the processing of emotional memory [8]. Therefore, the additional bidirectional connection between PHG and amygdala in PCE subjects suggests higher baseline emotion-memory interaction in them compared to controls. While dysregulation of the emotional network in PCE subjects has been shown previously during a working memory task [2], the present results demonstrate the same in terms of resting state effective connectivity. This supports the hypothesis of emotional dysregulation in PCE subjects, wherein disinhibition of emotional arousal affects other cognitive functions leading to behavioral impairments.

Conclusions

We obtained effective connectivity differences between healthy and PCE subjects and found that the latter had higher bilateral PHG connectivity and additional connectivity between PHG and amygdala as compared to the former. Our results support the hypothesis of disinhibition of emotional arousal in PCE subjects.

References

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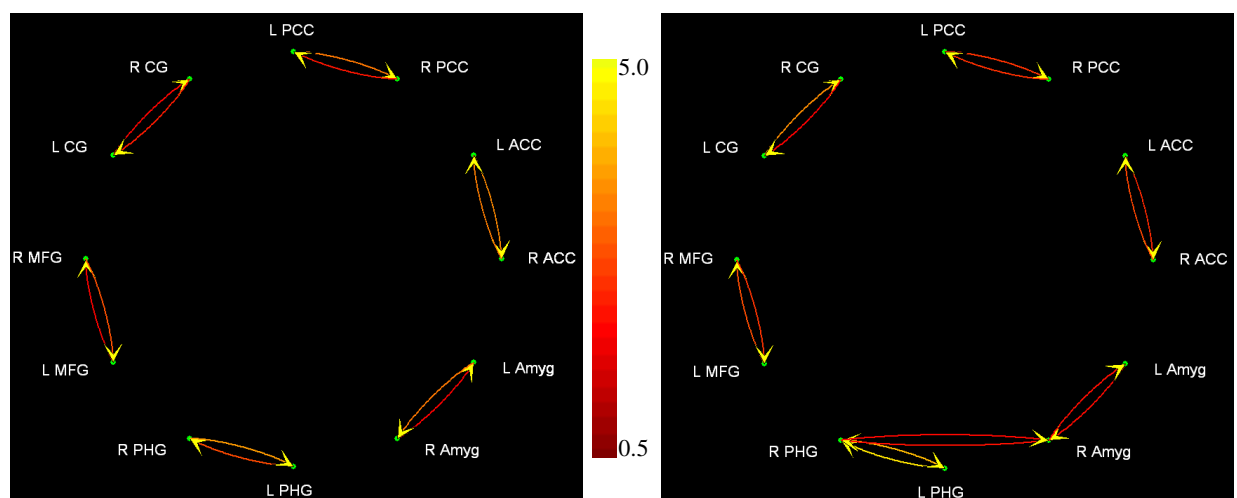
Fig.1 Granger based effective connectivity networks for the control group (left) and PCE group (right)