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Title

Disordered fronto-limbic interactions during emotion processing in the vulnerable brain: fMRI and Dynamic Causal Modeling applied to the study of adolescents

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Abstract

Background: Disordered organization of cortico-limbic circuits in the brain may underlie documented social impairments in schizophrenic offspring (SCZ-Off; Philips and Seidman, 2008). Advanced techniques such as Dynamic Causal Modeling (DCM; Stephan et al., 2007) are ideally suited to understand network interactions in the brain, yet have never been applied to this important developmental question. Here we use a combination of DCM and fMRI to investigate cortico-limbic network interactions during affective appraisal in a group of adolescent (10 ≤ age ≤ 20 yrs) SCZ-Off (n=19) and controls (n=24).

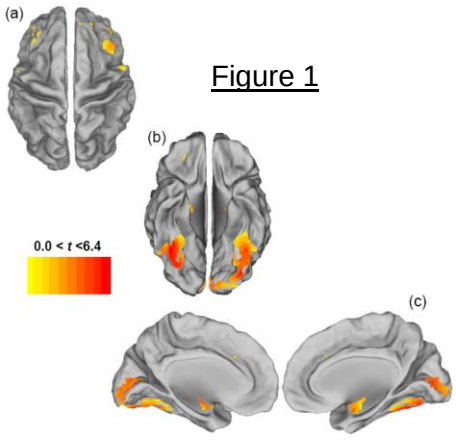
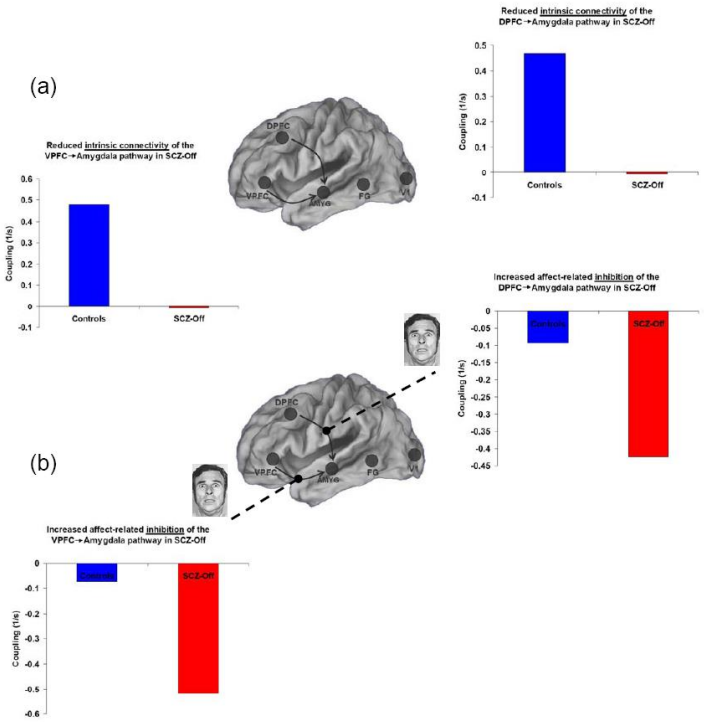


Figure 1

Methods: All subjects provided consent or assent before performing an event-related affective appraisal task (continuously presented faces; Ekman & Oster, 1979). DCM was conducted (SPM8) on fMRI data (4.0T) using time series (p<.05, effects of interest) from five cortico-limbic regions (V1, FG, Amyg, DPFC, VPFC). To comprehensively address model fit, we employed 100 models per subject to explore a combination of intrinsic and modulatory interactions between regions. Finally, Bayesian model selection (Stephan et al., 2009) identified the appropriate models within and across groups.

Figure 2



Results: Results of a conjunction analysis (activation to faces) in Controls and SCZ-Off are depicted in Figure 1 and show activation in both groups in our network of interest. Significant clusters (p<.05) are depicted on dorsal (a; bilateral DPFC), ventral (b; visual, fusiform, amygdala, and VPFC) and medial (c; amygdala, fusiform, and visual) views of the brain. Figure 2 shows, (a) Reduced intrinsic DPFC → Amygdala and VPFC → Amygdala connectivity/coupling (in 1/s) in SCZ-Off, relative to HC and (b) in SCZ-Off, markedly increased modulatory *inhibition* of activity in these pathways by the valence of the face.

Conclusions: Aberrant cortico-limbic responses appear to characterize the impaired affective response in adolescent SCZ-Off and may reflect a substantive disordering of this important pathway.

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Disclosure

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Keywords

Emotion processing; Fronto-limbic connectivity; Dynamic Causal Modeling; fMRI; Adolescents