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DISRUPTED EFFECTIVE CONNECTIVITY OF EMOTIONAL CIRCUITRY IN SCHIZOPHRENIA: A DYNAMIC CAUSAL MODELING STUDY

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BACKGROUND:

Impaired emotional processing is a core feature of schizophrenia (SKZ). Structural and functional brain imaging studies defined the neural circuitries engaged in emotion processing, which involve amygdala (Amy) and several cortical areas, such as dorsolateral prefrontal cortex (DLPFC) and anterior cingulate cortex (ACC). Consistent findings suggested that abnormal emotional processing in SKZ could be paralleled by a disrupted functional and structural integrity of these structures. Moreover several studies using connectivity techniques, such as Psycho-physiological Interaction, confirmed alterations in fronto-limbic network in SKZ [1,2]. Nevertheless these techniques didn't allow to explore the causal relationships and directionality among the involved regions.

For this reason, using Dynamic Causal Modeling (DCM), we explored differences in effective connectivity between Amy, DLPFC and ACC in SKZ patients and HC, during an emotional processing task.

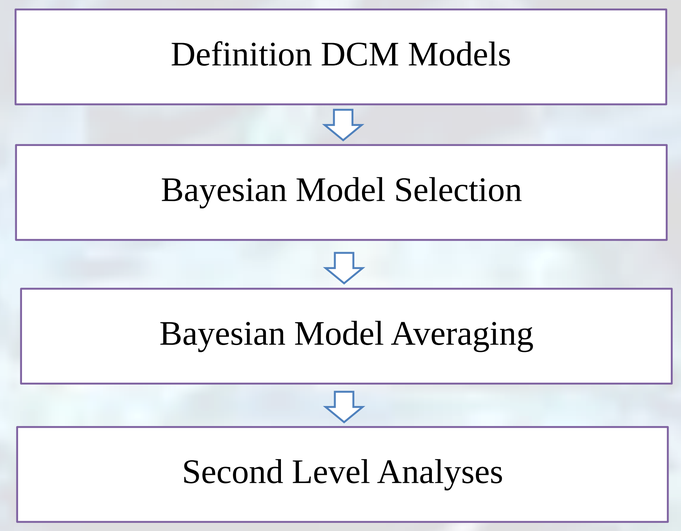

Fig. 1. Summerized DCM analyses.

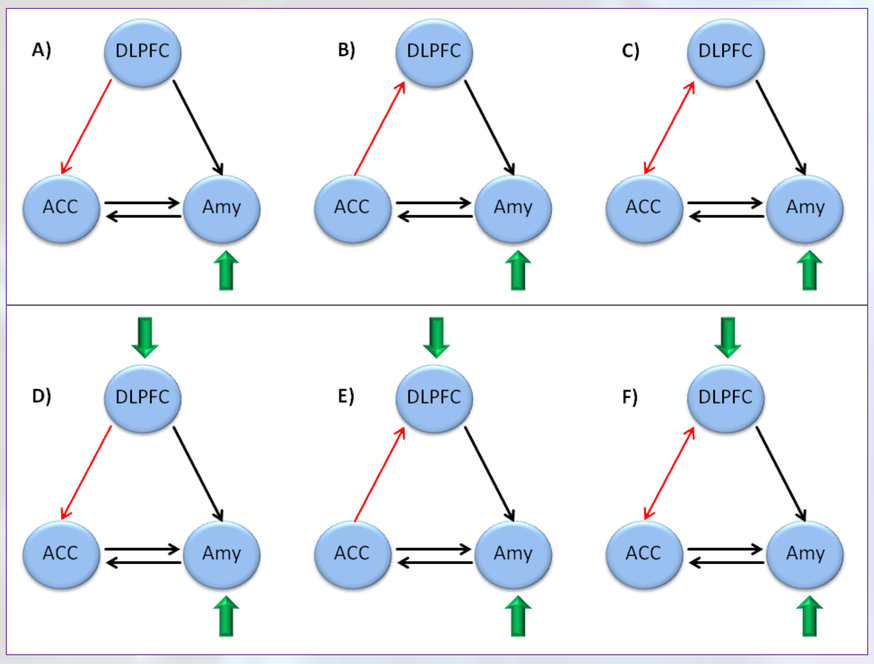

Fig.2. Six competive DCMs

METHOD:

A 3.0 Tesla fMRI acquisition was used to study 24 SKZ patients and 38 healthy controls (HC). The activation paradigm was the emotional faces task developed by Hariri et al [3]. The seed regions were identified using a task-related contrast. Afterwards six competitive DCM models were constructed: in all models the ACC-Amy connection was bidirectional and unidirectional from DLPFC to Amy. We also tested all the possible combinations in ACC/DLPFC connectivity. Moreover the input might enter the network from both Amy and DLPFC or from Amy only (fig.2).

Bayesian model selection was used to determine the best model from a structural perspective, whereas Bayesian Model Averaging was performed to extract DCM parameters. Afterwards the endogenous parameters were included in a second level analyses to assess:

(1) differences between groups (ANOVA)

(2) correlations (Person correlation) with Positive and Negative Symptoms Scale (PANSS).

RESULTS

In both groups, SKZ and HC, the best model showed a forward connection from DLPFC to Amy and from DLPFC to ACC, and a bidirectional connection between ACC and Amy (fig. 3). The connection from DLPFC to Amy was significantly reduced in SKZ compared to HC (fig. 4).

Finally, the strength of the ACC-Amy connection correlated significantly with PANSS positive symptomatology (r=0.64, p=0.13).

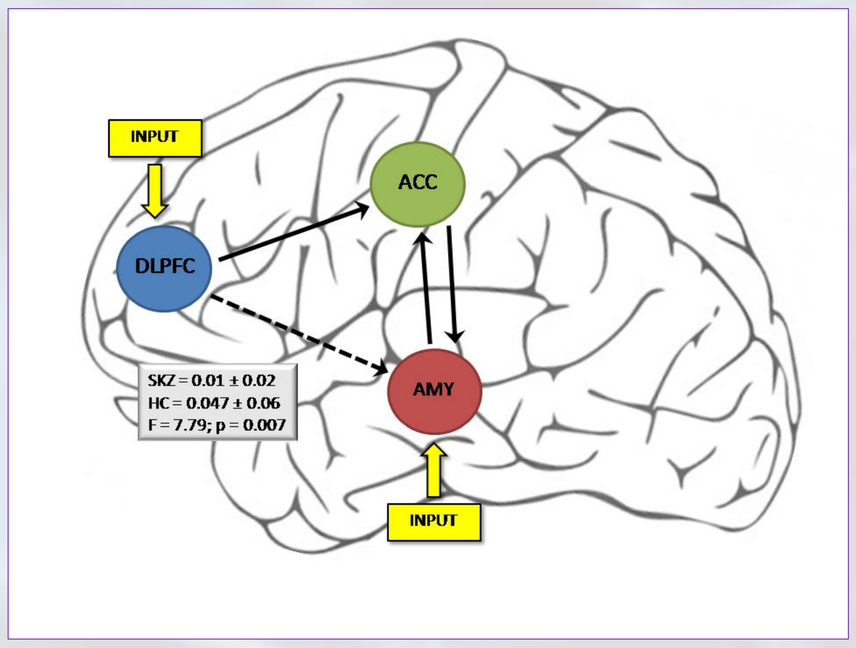

Fig. 3. DCM results

	SKZ n=24	Controls n=38	F(1,57)	p	R^2
DLPFC to Amy	0.01 ± 0.02	0.047 ± 0.06	7.79	0.007*	0.114
ACC to Amy	0.038 ± 0.07	0.022 ± 0.06	0.21	0.64	0.003
DLPFC to ACC	0.044 ± 0.06	0.048 ± 0.06	0.05	0.81	0.000
Amy to ACC	0.038 ± 0.08	0.022 ± 0.04	0.94	0.33	0.008

Fig. 4. Results ANOVAs between groups

CONCLUSIONS:

Patients showed a reduced top-down DLPFC-Amy connectivity that can reflect a deficit in amygdala modulation. Specifically an altered inhibitory function may provide a neural basis for the enhanced sensitivity to negative stimuli common in schizophrenia psychopathology. Another interesting finding is the correlation between ACC-Amy parameters and positive symptomatology in SKZ patients. These findings can suggest a crucial role of this disrupted network in schizophrenic psychopathology.

To our knowledge this is the first study which explore the causal relationships of the neural system involved in emotional regulation in schizophrenic patients. Our results suggest a functional disconnection in the social brain network of these patients. The disrupted connectivity of this circuitry may contribute to the behavioral and symptomatic outcome of the disorder and might be proposed as one of the possible neural biomarkers of treatment efficacy studies.

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