SU72. Abnormal Frontal Synaptic Gain Mediating the P300 in Patients With Psychosis and Their Unaffected Relatives

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Background: The 'dysconnection hypothesis' of psychosis suggests that a disruption of functional integration underlies cognitive deficits and clinical symptoms. Impairments in the P300 potential are well documented in psychosis. We investigated intrinsic (self-)connectivity in a cortical hierarchy during a P300 experiment. We used Dynamic Causal Modelling to estimate how evoked activity results from the dynamics of coupled neural populations and how neural coupling changes with the experimental factors.

Methods: Twenty-four patients with psychosis, twenty-four unaffected relatives and twenty-five controls underwent EEG recordings during an auditory oddball paradigm. We analyzed sixteen frontoparietal models (primary auditory, superior parietal, and superior frontal sources) and identified an optimal model of neural coupling, explaining diagnosis and genetic risk effects, as well as their interactions with task condition.

Results: The winning model included changes in connectivity at all three hierarchical levels. Patients showed decreased self-inhibition (i.e., increased cortical excitability) in left superior frontal gyrus across task conditions, compared to unaffected participants. Relatives had similar increases in excitability in left superior frontal and right superior parietal sources, and a reversal of the normal synaptic gain changes in response to targets, relative to standard tones.

Conclusion: We confirmed that both subjects with psychosis and their relatives show a context-independent loss of synaptic gain control at the highest levels of the hierarchy. The relatives also showed abnormal gain modulation responses to task-relevant stimuli. These may be caused by NMDA-receptor and/or GABAergic pathologies that change the excitability of superficial pyramidal cells and may be a potential biological marker for psychosis.