



City Research Online

City St George's, University of London

Citation: Diez, A., Ranlund, S., Pinotsis, D. A., Calafato, S., Shaikh, M., Hall, M-H., Walshe, M., Nevado, Á., Friston, K. J., Adams, R. & et al (2017). SU72. Abnormal Frontal Synaptic Gain Mediating the P300 in Patients With Psychosis and Their Unaffected Relatives. Schizophrenia Bulletin, 43(suppl_1), S187-S187. doi: 10.1093/schbul/sbx024.070

This is the accepted version of the paper.

This version of the publication may differ from the final published version. To cite this item please consult the publisher's version.

Permanent repository link: <https://city-ref-test.eprints-hosting.org/id/eprint/19649/>

Link to published version: <https://doi.org/10.1093/schbul/sbx024.070>

Copyright and Reuse: Copyright and Moral Rights remain with the author(s) and/or copyright holders. Copies of full items can be used for personal research or study, educational, or not-for-profit purposes without prior permission or charge, unless otherwise indicated, provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way. For full details of reuse please refer to [City Research Online policy](#).

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

Alvaro Diez*¹, Siri Ranlund², Dimitris Pinotsis³, Stella Calafato⁴, Madiha Shaikh⁵, Mei-Hua Hall⁶, Muriel Walshe⁴, Ángel Nevado¹, Karl Friston⁴, Rick Adams⁴, Elvira Bramon⁴

¹*Universidad Complutense de Madrid*, ²*King's College London*, ³*Massachusetts Institute of Technology*, ⁴*University College London*, ⁵*North East London NHS Foundation Trust*, ⁶*Harvard Medical School*

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.