

From the Knight to the Right: an event-related fMRI study of schizophrenic thinking

Gina R Kuperberg^{1,3,4}, Daya P Gulabani⁴, Donald Goff¹, Karin Blais⁴, David Caplan², Phillip Holcomb³

¹*Dept. Psychiatry, Mass. General Hospital*

²*Dept. Neurology, Mass. General Hospital*

³*Dept. Psychology, Tufts University*

⁴*Athinoula A. Martinos Center for Biomedical Imaging*

Objective: From its earliest inception, loosening of associations with tangential or ‘knight’s-move’ thinking – the generation of inappropriate links between unrelated sentences and concepts – has been considered a fundamental feature of schizophrenia (1). Cognitive neuroimaging studies of language in schizophrenia have reported abnormal modulation of a bilateral temporal-prefrontal network, sometimes with increased engagement of the right hemisphere, in patients relative to controls (2). Such studies, however, have generally focused on the processing of single words and sentences. Lesion studies suggest that the right hemisphere, particularly the right prefrontal cortex, plays a specific role in generating inferences that link sentences together into a coherent whole (3). We hypothesized that the inappropriate tendency of schizophrenia patients to generate links between unrelated concepts would be reflected by the inappropriate engagement of the right prefrontal activity to unrelated (relative to related) sentences.

Methods: Over eight functional runs on a 3T Siemens scanner (T2*-weighted EP images; 33 slices, 3 mm skip 1 mm; TR 2s; TE 25 ms), fifteen patients with schizophrenia and fifteen demographically-matched right-handed healthy volunteers read 240 three-sentence scenarios in which final sentences were: (a) causally linked to their preceding contexts, (b) related to their preceding contexts only if participants generated bridging inferences, and (c) unrelated to their preceding contexts. Subjects judged how related the final sentence was to the preceding two sentences. Scenario trials were randomly interspersed with fixation trials of variable durations. High-resolution structural images provided detailed anatomic information for the reconstruction of each participant’s cortical surface. Following selective averaging without assumptions about the shape of the underlying hemodynamic response (4), each subject’s functional data was resampled into a common spherical space (derived from each individual’s cortical surface) and then averaged using a random effects model within and between subject group (5,6).

Results: Both patient and control groups rated the inference-requiring sentences as more related than the unrelated sentences and less related than the causally-linked sentences.

Both patient and control groups exhibited more activity to inference-requiring than causally-linked sentences within a bilateral lateral and inferior temporal-prefrontal network. Patients showed significantly more right prefrontal cortical activity than controls to the inference-requiring sentences. In comparing unrelated and causally-linked sentences, patients, unlike controls, inappropriately engaged a subset of this network: bilateral inferior temporal-prefrontal cortices and, once again, the right prefrontal cortex. All these hemodynamic differences were maximal at the point of presentation of the final sentence that differentiated between the three experimental conditions.

Conclusions: The inappropriate increase in right prefrontal activity to both inference-requiring and unrelated discourse (relative to causally-linked sentences) might contribute to the bizarre, knights-move thinking that characterizes the schizophrenia syndrome.

References & Acknowledgements:

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