

Functional neuroanatomy of abnormal real-world comprehension in schizophrenia

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Introduction: Deficits in building up an overall meaning representation of perceived information have been proposed as a fundamental cognitive dysfunction underlying schizophrenia¹. Previous studies of this dysfunction have focused primarily on language¹. Clinically, however, schizophrenia is characterized by abnormalities in both verbal and non-verbal domains. To examine the time-course and neuroanatomy of semantic processing during the comprehension of visual real-world events in schizophrenia, we conducted two experiments using event-related potentials (ERPs) and event-related fMRI.

Methods: 20 patients with schizophrenia and 20 matched healthy participants viewed 80 silent, 8-sec-long movies of common real-world activities. The final movie scenes were either congruous or anomalous (e.g., in a congruous movie, a man in a bathroom smeared shaving cream on his face, and then shaved; in an anomalous movie, instead of shaving, he stroked a rolling pin across his face). ERPs at 63 scalp locations were time-locked to final scenes and selectively averaged across trials from each condition. Mean ERPs were analyzed between 300-500 msec and 500-1000 msec post-stimulus onset – the time-windows corresponding to the N400 and LPC components, respectively. fMRI data was recorded using a 3T Siemens MR scanner (T2*-weighted echoplanar images covering the whole brain, 33 slices, 3 mm thickness, 1 mm skip, TR = 2 sec, TE = 25 msec). After motion correction and normalization, each subject's hemodynamic response was selectively averaged across trials from each condition and resampled into spherical² and Talairach space for inter-subject averaging.

Results: In the ERP experiment, an N400 effect to anomalous relative to congruous movie endings was larger in patients with schizophrenia than in healthy participants. In contrast, an LPC effect to anomalous relative to congruous scenes was found only in the healthy participants but not in the patients.

In the fMRI experiment, an increase in fMRI BOLD signal to anomalous relative to congruous scenes was comparable between the participant groups in the left inferior-prefrontal and temporal cortices (fronto-temporal system). However, in the left dorsolateral prefrontal cortex and the basal ganglia (fronto-striatal system), a congruency effect was seen only in the healthy controls but not in the patients.

Discussion: The N400 and the fronto-temporal hemodynamic effects have been consistently reported in semantic congruency paradigms, and are thought to reflect an analysis based on semantic knowledge of common real-world associations². Although their relationship is poorly understood, both LPC and fronto-striatal effects have recently been reported when readers attempted to interpret the meaning of unusual³ or impossible⁴ real-world actions. These effects might reflect a slower, more exhaustive analysis of incoming information that serves as a double check on initial expectations and is crucial for flexible and adaptive comprehension. The dysfunction of the fronto-striatal mechanism in schizophrenia might lead to an over-reliance on analysis of the semantic associations between stimuli by the fronto-temporal system. This could lead to a tendency to “jump to conclusions”, and in turn, to delusions and the non-goal-directed, disorganized thought that characterize the schizophrenic syndrome.

References:

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