

# CORTICO-STRIATAL DYSFUNCTION DURING 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 schizophrenia. Previous studies of this dysfunction have focused on language<sup>1</sup>. Clinically, however, schizophrenia is characterized by both verbal and non-verbal abnormalities.

The present study examined the functional neuroanatomy of comprehending real-world events in schizophrenia. We recorded functional magnetic resonance imaging (fMRI) data while patients with schizophrenia and matched healthy participants viewed silent video clips of common real-world activities. The final scene in these movies was either congruous or anomalous (Figure 1).

In our previous study with young healthy adults, anomalous movie endings evoked increased fMRI BOLD response in the left temporal and inferior-prefrontal cortices (fronto-temporal system), relative to congruous movie endings. This activity has been suggested to reflect comprehension processes based on semantic knowledge of real-world associations<sup>2</sup>. In addition, the BOLD activity in the left dorsolateral prefrontal cortex and basal ganglia (fronto-striatal system) was increased to anomalous relative to congruous final scenes. Similar effects have been previously reported during comprehension of verbally described unusual goal-directed events<sup>3</sup>, and when participants evaluated relationships between goal-relevant elements in complex events<sup>4</sup>. Therefore, we hypothesize that this fronto-striatal response might reflect more exhaustive analysis of incoming information reevaluating initial expectations that is crucial for flexible comprehension in unfamiliar situations.

**QUESTIONS: Are there neurocognitive abnormalities during real-world comprehension in schizophrenia? Is there a general abnormality or a specific deficit in a particular comprehension mechanism?**

## Experimental Design

**Subjects:** 20 patients with schizophrenia (mean age 42) and 20 matched healthy controls (mean age 41)

**Materials:** 80 silent video-clips (40 congruent and 40 anomalous) – Figure 1; average clip length 8 sec.

**Task:** Anomaly detection

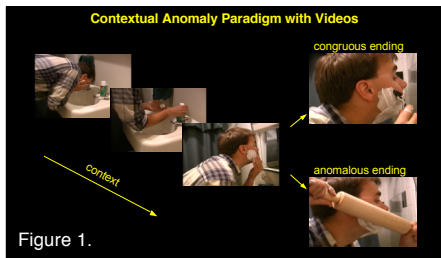


Figure 1.

## fMRI Recording

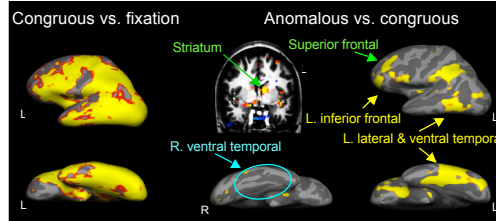
- Pseudorandom stimulus presentation including fixation trials
- Counterbalanced design
- 3T Siemens MR scanner
- Event-related fMRI:

TR 2 s, TE 25 ms, 33 slices, 3 mm skip 1 mm  
Talairach and spherical space

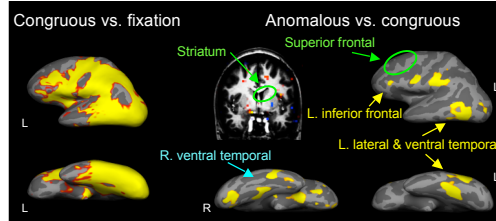
## Results

Healthy participants showed increased BOLD response to anomalous relative to congruous movie endings in both fronto-temporal and fronto-striatal systems that was comparable to our earlier study with young adults – Figure 2A. In patients with schizophrenia, anomalous scenes evoked relatively intact fronto-temporal response but strongly attenuated fronto-striatal response – Figure 2B. Direct comparisons between the groups (Figure 2C); (1) in the congruous condition patients showed less activity in the bilateral temporal and prefrontal cortices; (2) the enhanced response to anomalous relative to congruous scenes was increased in the patient relative to control group in the right ventral temporal cortex but was reduced in the fronto-striatal system.

### A. Brain regions with fMRI BOLD response differences in healthy participants



### B. Brain regions with fMRI BOLD response differences in patients with schizophrenia



### C. Between-group differences:

Yellow - increased activity in healthy controls relative to patients with schizophrenia  
Blue - increased activity in patients with schizophrenia relative to healthy controls

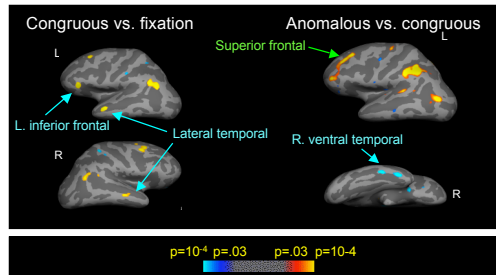


Figure 2.

## Discussion

**Fronto-temporal system:** Processing of anomalous movie endings in patients with schizophrenia appeared not only to recruit the same inferior-frontal and temporal regions in the left hemisphere as in healthy controls, but also the right ventral temporal cortex. Furthermore, bilateral regions in the inferior frontal and temporal cortices appeared to be engaged less by the patients than healthy controls during processing of congruous movie endings, suggesting increased contextual priming in schizophrenia. Taken together, these findings suggest that patients with schizophrenia might excessively depend on the fronto-temporal associative semantic system during real-world comprehension.

**Fronto-striatal system:** Some evidence suggests that the fMRI BOLD response in the fronto-striatal system might reflect a comprehension process serving as a double check on our initial expectations formed on the basis of associative semantic knowledge<sup>3,4</sup>. Our world is repetitive but is never the same. This comprehension mechanism would account for our remarkable ability to make sense of unfamiliar and unusual situations quickly and intuitively. The reduced fronto-striatal effect in schizophrenia suggests abnormalities in this more flexible comprehension processing.

The fronto-striatal dysfunction 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.

## Conclusion

Our results suggest that in schizophrenia comprehension of the world is compromised by a disruption of the fine balance between taking advantage of the repetitiveness in our world, while still being able to comprehend novel information. This finding is consistent with previous results in the language domain<sup>1,5</sup> and illustrates a potential pathogenic pathway to symptoms of this disorder.

## References

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## Acknowledgements

This research was supported by the grants from the Massachusetts General Hospital Fund for Medical Discovery to T.S., from NIMH to G.K. & C.W. (K23 MH02034, MH071635-01, MH065356-03), from NARSAD and the Sidney Baer Trust to T. S. and G.K., and from NICHD to P.H. (HD25889), and by the Institute for Mental Illness and Neuroscience Discovery (MIND).