Title
Impaired associative learning in schizophrenia assessed with fMRI: Inefficiently increased activation, but decreased fronto-hippocampal connectivity

Authors
Wadehra, S
Pruitt, P
Murphy, E
Diwadkar, VA

Affiliation
1Dept of Psychiatry & Behavioral Neurosciences, Wayne State University SOM
2Dept of Psychology, Georgetown University

Abstract
Background: fMRI studies in schizophrenia (SCZ) have suggested inefficiently increased activation during demanding tasks (Manoach, 2003). However, few studies have assessed activation and connectivity differences in the same study. With increased focus on using fMRI to study the functional integration of information (Stephan, 2004), comparing patterns of disordered activation and connectivity in SCZ assumes significance. Here, we compared differences in activation and connectivity between SCZ and controls (HC) during paired-associate learning (Diwadkar et al., 2008), a domain particularly dependent on fronto-hippocampal connectivity (Friston, 2003).

Methods: Subjects (18 ≤ age ≤ 35 yrs; SCZ, n=12; HC; n=10) participated in an object-location associative learning paradigm (Buchel et al., 1999). Activation differences were assessed using standard approaches. Connectivity differences using a hippocampal seed were compared using Psychophysiological Interaction (PPI)(Friston et al., 1997). Seeds were identified (effects of interest: $p_{FWE}<.05$) and convolved with contrasts of interest (learning epochs > rest epochs). First-level activation and PPI maps were submitted to second-level random effects analyses to assess differences between groups, using group (HC vs. SCZ) as a factor and learning performance as a covariate.

Results: Figure 1.

Conclusions: SCZ were characterized by increased learning related activation but reduced learning-related connectivity. fMRI analyses in clinical syndromes such as schizophrenia must assess potentially complementary patterns of activation and connectivity differences to provide a clearer picture of their neural bases.
Figure 1: Using group as a factor and performance as a covariate interacting with group, results of A) inter-group two-sample t-test comparing activation between HC and SCZ during encoding and B) PPI analysis investigating positive HIP modulatory effects between HC and SCZ during encoding, are depicted. Significant clusters of increased activity (pFWE < 0.05, corrected at cluster level) are shown on lateral views for (a) HC and (b) SCZ. Note that activation across the network is significantly increased in SCZ (relative to controls), whilst connectivity is significantly decreased.