Title

75. Disrupted Network Cross Talk, Hippocampal Dysfunction, and Hallucinations in Schizophrenia

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74. THE NEUROCHEMICAL BASIS OF ANTIPSYCHOTIC RESPONSE IN PSYCHOSIS: A PROSPECTIVE MULTIMODAL 18 F-DOPA AND 1-H MRS STUDY IN FIRST-EPISODE PSYCHOSIS.

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Background: Antipsychotic medication remains the primary treatment for symptoms of psychosis. The dopamine system, in particular, the presynaptic system, has been linked to treatment response, leading to the suggestion that dopaminergic and nondopaminergic forms of schizophrenia exist. This has been examined in vivo, using PET to index presynaptic dopamine (linking elevated dopamine to good treatment response), and Magnetic Resonance Spectroscopy (MRS) to measure glutamatergic function, linking elevated anterior cingulate glutamate to poor antipsychotic response. To date, no study has utilised these measures to examine antipsychotic response prospectively, in first episode patients. We sought to examine both neuroimaging methods in antipsychotic-naïve, first-episode psychosis patients, before and after treatment.
Methods: 18F-DOPA PET and 1-H MRS study, in people witfirst episode psychosis, naive of antipsychotic medication, those minimally treated with antipsychotic medication (for less than 2 weeks) and those not taking antipsychotic medication.
Baseline and follow-up whole striatum Kicer, anterior cingulate glutamate and baseline and follow-up PANSS after antipsychotic treatment
Results: There was a significant positive correlation between baseline Kicer and subsequent improvement in PANSS positive (rho =0.64, $P < .01$), negative (rho=0.48, $P = .03$), total symptoms (rho=0.56, $P = .01$) and GAF score (rho=0.54,. There was no relationship between glutamate levels and any clinical measure. There was a significant effect of group on Kicer ($F(2,25)=5.73$, $P < .01$). Kicer was significantly higher in responders than both non-responders ($P = .03$) and healthy volunteers ($P < .01$). Cohen's d effect size for the elevation in the responders relative to nonresponders was 1.28. No difference in dopamine synthesis capacity was found after treatment for at least 4 weeks of antipsychotic medication, $t(20) = 0.73$, $P = 0.49$. A positive correlation was found between change in dopamine synthesis capacity and change in PANSS positive symptoms (Pearson's $r = .47$, $P = .04$), though not PANSS negative ($r = .4$, $P = .1$) or total symptoms ($r = .42$, $P = .08$).
Conclusion: Dopamine, and not glutamate function, predicts the response to antipsychotic treatment. Change in dopamine synthesis capacity is related to positive symptom change. Variability exists in the effects of antipsychotic medication on presynaptic dopamine function.

75. DISRUPTED NETWORK CROSS TALK, HIPPOCAMPAL DYSFUNCTION, AND HALLUCINATIONS IN SCHIZOPHRENIA

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Background: Individuals with schizophrenia (Sz) show abnormal functional connectivity between resting state networks (RSNs), yet the relation between disrupted connectivity and symptoms remains unclear. Using a combination of resting-state fMRI analyses – independent component analysis (ICA) and analysis of the mean amplitudes of low-frequency fluctuations (ALFF)—we probed the relation between cross-network communication, low frequency fluctuations and reported experience(s) of auditory hallucinations (AH) and visual hallucinations (VH) in Sz.
Methods: Resting-state fMRI data were analyzed (143 Sz, 155 controls) from the Function Biomedical Informatics Research Network (FBIRN) dataset. Sz were divided into subgroups: patients reporting AH, patients reporting VH and patients reporting neither AH nor VH (NH). Most patients reporting VH also reported AH. Group spatial ICA and ALFF analyses were performed on preprocessed images using GIFT and REST software respectively. Eight RSNs were selected (two insular components, two precuneus components, along with anterior cingulate cortex (ACC), superior temporal gyrus (STG), hippocampus and putamen components). ALFF was calculated across two frequency ranges ([0.01–0.027 Hz]; [0.027–0.08 Hz]). General linear models examined the impact of group on functional network connectivity (FNC) ($P < .05$ FDR-corrected) and ALFF ($P < .05$, corrected for multiple comparisons at cluster level).
Results: AH and VH were not different in FNC, but VH had significantly elevated left hippocampal ALFF. The 2 hallucination subgroups (VH, AH) were combined to form a larger (HALL) subgroup. Both NH and HALL showed elevated FNC between STG and hippocampus relative to healthy controls (HC). In comparison to HC, HALL in particular, showed significantly increased FNC between two precuneus RSNs, precuneus-ACC, STG-ACC, and STG-putamen. They also showed decreased FNC between insula-precuneus and the two insular RSNs. In post-hoc analyses, we examined the relationship between left hippocampal ALFF variation, FNC values, and symptom severity. AH ($b = -.28$, $t = -2.857$, $P < .001$) and VH ($b = 0.40$, $t = 4.054$, $P < .001$) severity, but not overall positive symptoms, were significantly linked to hippocampal ALFF. Hippocampal ALFF was negatively correlated with FNC between insular RSNs, but positively correlated with FNC between two precuneus RSNs, precuneus-ACC, STG-putamen, and STG-hippocampus.
Conclusion: Our results suggest that hippocampal low-frequency fluctuations are linked to cross-network functional communication. More severe VH are associated with elevated hippocampal low-frequency fluctuations, while more severe AH is associated with decreased hippocampal low-frequency fluctuations. We propose a novel hypothesis of hallucinations in Sz in which altered hippocampal oscillation dynamics disrupt functional communication between dispersed networks.

76. FMRI RESPONSE DURING ERROR PROCESSING IN CLINICAL HIGH RISK AND EARLY ILLNESS SCHIZOPHRENIA

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Background: Error detection is a critical part of the self-monitoring functions that guide efficient, goal-directed behaviors. Error-monitoring deficits are well described in schizophrenia, but the extent to which error processing deficits and their associated functional neuroanatomy are evident in