46. Role of Medial Prefrontal Cortex in Intention Deficit in Schizophrenia

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Background: In schizophrenia, an intention disorder is revealed in many patients in the form of reduced spontaneous language and reduced task initiation. Likewise, the finding of reduced output during verbal fluency tasks is one of the most consistently reported neurocognitive deficits in schizophrenia. The intention deficit that underlies poor language and task initiation interferes with successful social and occupational functioning, as well as optimal utilization of healthcare services. The purpose of this study was to determine if this intention deficit is associated with disordered medial prefrontal function in the pre-supplementary motor area (pre-SMA), a region known to be consistently active during healthy word production performance, and during other cognitive tasks that place a heavy demand on internally mediated initiation.
Methods: An event-related overt word fluency paradigm and functional magnetic resonance imaging (fMRI) were used to investigate medial prefrontal function. Data was collected on 5 patients and 4 controls. Single word generation to semantic categories alternated with single word repetition and rest. Motion correction was applied after which time series analysis was performed using a deconvolution algorithm available through AFNI software. To generate a region of interest in medial prefrontal cortex, a one-sample t-test was used to identify brain regions in which the area under the curve (AUC) of the hemodynamic response (HDR) to generation trials was significantly different than zero across the groups. A functional region of interest was present in the pre-SMA. Averaged hemodynamic responses within this functional ROI were compared between groups.
Results: Relative to word repetition and rest, the semantic word generation task led to robust medial prefrontal activity in the pre-supplementary motor area for healthy comparison patients. In contrast, patients demonstrated significantly reduced or absent activity in this region despite behavioral performance equivalent to the healthy comparison group. Thus, a significant difference was observed between the averaged hemodynamic response in the pre-SMA between patients and controls.
Discussion: Preliminary findings are consistent to suggest that the pre-SMA region functions abnormally in chronic schizophrenia patients during a word production task. This likely relates to a more general deficit in intentional aspects of cognition. The intentional deficit has been linked to social skills deficits in this population. In conclusion, the pre-SMA region appears to be an excellent candidate as an outcome measure in pharmacological and psychosocial treatments that target the debilitating intentional disorder observed in many chronic schizophrenia patients.

47. Amygdala Hyperactivity to Angry Faces in Patients with Intermittent Explosive Disorder

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Background: Patients with intermittent explosive disorder (IED), characterized by impulsive aggression, exhibit affective dysregulation, lack of anger control, and impaired recognition of negative emotions in facial expressions. This social-emotional phenotype resembles the affective and behavioral patterns observed in humans with amygdala and orbitofrontal (OFC) lesions. However, little is known about the functional neuroanatomy these deficits in patients with IED, or about the neural mechanisms of human aggression.
Methods: The present study employed BOLD-sensitive whole-brain functional magnetic resonance imaging at 3Tesla (reverse spiral: TR=2s; TE=25ms) to examine the neural correlates of social-emotional processing. Ten patients with IED (5 females; age 34.3 ±7.3 years) were studied along with 10 healthy controls (HC) matched on gender, age, and socio-economic status. Subjects performed a gender identification task while viewing alternating 20-sec blocks of Ekman Faces expressing discrete emotions (anger, fear, disgust, happy, sad, surprise, neutral), interleaved with 20-sec blocks of blank screens. Imaging data were analyzed with a standard, random effects model ($p<0.05$, SVC) using statistical parametric mapping software (SPM2). Estimates of activation (e.g., BOLD response) were extracted from a priori atlas-based regions of interest (e.g., amygdala, OFC).
Results: Patients with IED had exaggerated activation of the left amygdala ([-14, -8, -18], Z=2.78) and OFC ([-12, 64, -6]; Z=2.60) in response to faces expressing harsh emotions (anger, fear, and disgust), relative to healthy controls. Follow-up voxel-wise analyses revealed that the amygdala hyperactivity was driven predominantly by faces of anger ([-22, 0, -26], Z=3.06), which was confirmed by extraction of BOLD parameter estimates of activation extracted from a 10mm atlas-derived amygdala ROI centered at [-20, -4, -20] showing a significant group-difference to anger (IED: 0.32 ± 0.19 vs. HC: 0.05 ± 0.22; t=2.93, df=18, $p < 0.01$, 2-tailed), but not to other emotional expressions.
Discussion: The results suggest that amygdala dysfunction in patients with IED is specifically linked to faces of anger. More generally, these preliminary findings suggest that altered responses in the amygdala and OFC, regions important for social cognition, threat perception, and emotion/anger regulation, may contribute to the deficits in social-emotional processing observed in impulsive aggression.

48. Prefrontal Neurochemical Abnormalities in Adolescent Bipolar Disorder

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Background: Recent findings suggest that adolescents with bipolar disorder exhibit abnormalities in ventral prefrontal cortical development. Indeed, the results of magnetic resonance spectroscopy studies suggest that compared with healthy controls, bipolar youth have increased anterior cingulate myo-inositol (mI) levels and elevated ventral prefrontal glx (glutamate/glutamine), indicating abnormalities in putative biomarkers of second messenger and cell membrane metabolism and neuronal excitation, respectively. However, most of the patients in these studies were treated with a variety of medications and were in variable mood states making it difficult to interpret whether the neurochemical alterations were due to medication effects or an acute mood episode, or were core features of the underlying illness. The aim of our study was to examine neurochemical differences in glx and mI in prefrontal cortical regions among unmedicated bipolar adolescents with a mixed episode, unmedicated bipolar adolescents with a depressive episode, and healthy adolescents.
Methods: Unmedicated adolescents (ages 12-18 years) hospitalized for a mixed (N=18) or depressive (N=31) episode of bipolar I disorder were recruited. Demographically matched control adolescents without a psychiatric disorder (n=10) were also recruited. Three single voxels (8cc) were positioned from the sagittal T1 weighted series each based upon anatomical landmarks for the left and right ventral prefrontal cortex (VPFC) and anterior cingulate (ACC). Spectra were acquired using the point resolved spectroscopy (PRESS) sequence with the following parameters: TE=35 msec and TR=5 sec with 64 averages. Each of the spectral areas associated with mI and glx were quantified using the LC Model program. Gray and white matter and cerebral spinal fluid contribution to voxel volumes were determined and concentrations of metabolites were adjusted accordingly.
Results: There were no statistically significant group differences in gender, race, or socioeconomic status among the three groups, and