Corticostriatal Connectivity in Violent Offenders with Schizophrenia

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Target Audience: Those who are interested in applying functional magnetic resonance imaging (fMRI) to the neuroscience, psychiatry and forensic fields.

Purpose: The association between schizophrenia and violent behavior has significant clinical and social implications [1]. Although previous studies had proved that alterations in the basal ganglia, predominantly the striatum, constitute important characteristics of neural pathology in schizophrenia [2], the relationship between its functional connectivity (FC) and severely violent behaviors remains unknown. The aim of the current study is to explore the characteristic functional connectivity in a subgroup of schizophrenia patients with severe violent behavior and its relationship with clinical measurements.

Methods: The study was approved by the local ethical committee and written informed consent was obtained from guardians of all subjects. 18 male violent offenders appraised as schizophrenia (VS) according to DSM-IV were recruited from the forensic psychiatry department (mean age = 38.17±10.42 years) and 24 age and handedness matched male healthy controls (HC) (mean age=35.83±14.25 years) were also recruited through advertisement. Modified Overt Aggression Scale (MOAS), Wisconsin Card Sorting Test (WCST) and Positive and Negative Syndrome Scale (PANSS) for schizophrenia were used for clinical evaluation in the VS group. The MRI examinations were performed via a 3-Telsa GE MRI system with an 8 channel phase array head coil. The resting-state fMRI (rsfMRI) sensitized to changes in BOLD signal levels were obtained via a GE-EPI sequence (TR/TE=2000/30msec, flip angle=90°, slice thickness=5mm with no gap, 30 axial slices, 200 volumes in each run). Subjects were instructed to relax with their eyes closed without falling asleep during MR examination. FC of subregions of the striatum within bilateral caudate nucleus, bilateral pallidum and bilateral putamen was examined via fMRI using a seed-based approach. A reference time series for each seed was extracted by averaging the rfMRI time series of voxels within each seed. Correlation analysis was carried out between each seed and the filtered time series in the rest of the brain. The correlation coefficients in each voxel were transformed to z values, and then spatial smoothing (8-mm full width half-maximum). Voxel-based analyses of FC between two groups were performed using two-sample t-test in SPM8 and P value of less than 0.05 after Alphasim correction was deemed to be significant. Pearson correlation analyses between altered FC and clinical ratings of VS group were performed using SPSS 16.0.

Results: At the threshold we set, various regions were found to have significant differences in FC between two groups for most seeds regions except for right caudate nucleus ($P < 0.05$, corrected for Alphasim). Comparing to HC, VS showed decreased FC between (1) dorsal anterior cingulate cortex (dACC) and left pallidum as well as left putamen; and (2) right hippocampus and left putamen. Increased FC in VS was revealed between (1) left middle frontal gyrus (MFG) and left putamen; (2) right MFG and left caudate nucleus as well as right pallidum and (3) bilateral MFG and right putamen (Figure 1. Left). For correlation analysis, increased FC between right MFG and right putamen correlated positively with MOAS ($r = 0.502$, $p = 0.034$) (Figure 1. Right).

Discussion & Conclusion:

To the best of our knowledge, this is the first study investigating the alterations of striatal FC in VS and evaluating its relationship to severely violent behaviors. In line with the currently accepted model of schizophrenia pathophysiology, the present findings supported the key role of cortico-striatal functional dysconnectivity in schizophrenia [3] and showed its complexity. Furthermore, the positive correlation between FC of right putamen and right MFG and MOAS scores suggests the specific role of these regions in violence behavior in schizophrenia. Decreased FC in limbic system gave more support for the therapeutic effect of antipsychotic drugs. Meanwhile, our findings of FC changes in cerebellum with various striatal structures compliment the current hypothesis about cerebellum in pathology model of schizophrenia.

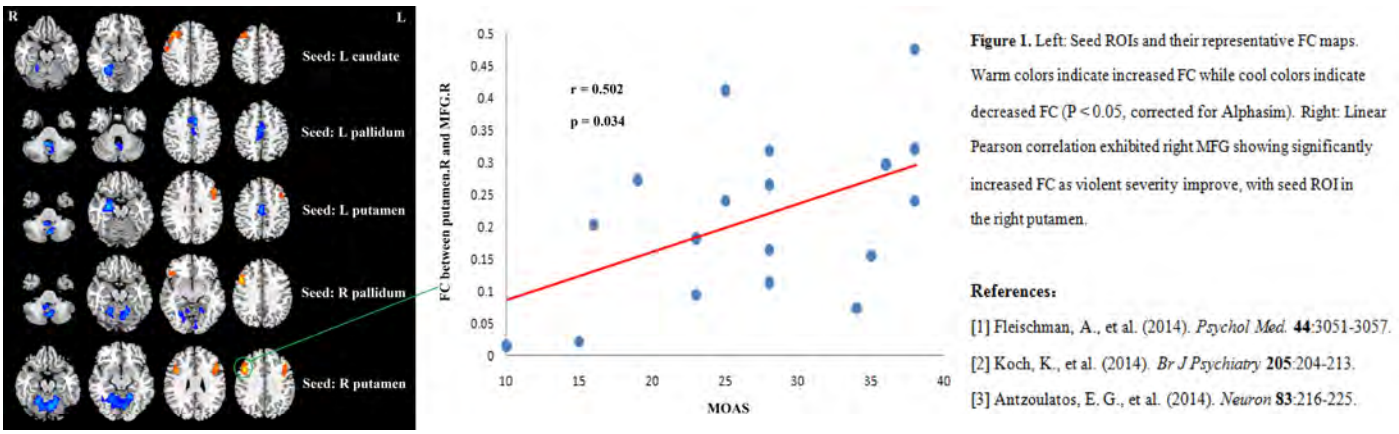

Figure 1. Left: Seed ROIs and their representative FC maps. Warm colors indicate increased FC while cool colors indicate decreased FC ($P < 0.05$, corrected for Alphasim). Right: Linear Pearson correlation exhibited right MFG showing significantly increased FC as violent severity improve, with seed ROI in the right putamen.

References:

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[3] Antzoulatos, E. G., et al. (2014). *Neuron* **83**:216-225.