# Baseline Functional Corticostriatal Circuitry Predicts Response to Antipsychotic Drug Treatment

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Background: Clinical response to antipsychotic drug treatment is highly variable, yet prognostic biomarkers are lacking. Recently, we demonstrated that successful antipsychotic drug treatment alters resting state functional connectivity of the striatum. The goal of the present study was to test whether intrinsic striatal connectivity patterns provide prognostic information, and can be used as a biomarker that predicts treatment response to antipsychotic drugs.

Methods: We first identified a biomarker in a discovery dataset of 41 first-episode schizophrenia patients. Resting state functional MRI scans were collected at the initiation of randomized, controlled treatment with a second-generation antipsychotic medication. Whole brain functional connectivity maps were generated for each subject from striatal seed regions. A stringent measure of clinical response was calculated that required sustained improvement over two consecutive study visits. Clinical response was entered into a survival analysis that was applied to our functional connectivity data. A striatal connectivity index was created, comprised of functional connections of the striatum that predicted treatment response. This striatal connectivity index was then tested on an independent cohort of 40 patients with psychotic disorders who were hospitalized for acute psychosis.

Results: A total of 91 regions functionally connected with the striatum provided significant prognostic information. The pretreatment striatal connectivity index predicted response to antipsychotic treatment in both the discovery (P <0.001) and generalizability cohorts (P<0.05) with high sensitivity (80%) and specificity (75%).

Conclusions: These results provide evidence that individual differences in striatal functional connectivity predict response to antipsychotic drug treatment in acutely psychotic patients. This has potential for use as a prognostic biomarker with clinical utility and to reduce the overall burden associated with psychotic illnesses.