Supplementary Online Content


eAppendix. Supplemental Methods.

eTable. Summary of Significant Between Scan Differences in Functional Connectivity in FEP.

This supplementary material has been provided by the authors to give readers additional information about their work.
eAppendix. Supplemental Methods

Participants

All received a physical exam and laboratory screening to rule out medical causes for their initial psychotic episode. Exclusion criteria for the HC group included present use of any psychotropic medications, and the presence of any lifetime history of a major mood or psychotic disorder as determined by clinical interview using the SCID, Non-Patient edition. Exclusion criteria for all study participants included magnetic resonance imaging contraindications, neurologic conditions (Gilles de la Tourette's, Huntington's Disease, Parkinson's Disease, encephalitis, strokes, aneurysms, tumors, central nervous system infections or degenerative brain diseases), and any serious medical disorder that could affect brain functioning or the participant’s capacity to provide informed consent.

Patients were treated with diphenhydramine or benztropine as needed for extrapyramidal symptoms, and lorazepam for akathisia, agitation, and anxiety. Nineteen patients received at least one dose of lorazepam during the study (ranges 0.5 - 8mg). Five patients were being treated with benztropine at follow-up (dose 0.5 mg -2 mg). Concurrent treatment with mood stabilizers or antidepressants was not allowed. Medications were administered orally, once per day by research psychiatrists (DR, JG). Compliance was assessed by pill count and medication logs. Clinical ratings were performed by raters trained according to our standardized NIMH protocol (P50MH080173), and conducted ratings blind to medication status.

Resting State fMRI Image Acquisition

For image registration we acquired anatomical scans in the coronal plane using an inversion-recovery prepared 3D fast spoiled gradient (IR-FSPGR) sequence (TR = 7.5 ms, TE = 3 ms, TI = 650 ms matrix = 256x256, FOV = 240 mm) producing 216 contiguous images (slice thickness = 1mm) through the whole brain. Five minutes of resting-state functional scans were acquired, comprising a total of 150 echo-planner imaging (EPI) volumes with the following parameters: TR = 2000 ms, TE = 30 ms, matrix = 64*64, FOV = 240 mm, slice thickness = 3 mm, 40 continuous axial oblique slices (one voxel = 3.75x3.75x3 mm).

Image Analysis and Preprocessing
Standard preprocessing included removal of the first four scans. This was followed by standard registration and normalization to MNI152 space with the resulting transformation then applied to each individual's functional dataset (12 parameter affine transformation). Motion correction was performed with FLIRT, images were spatial smoothed (6-mm FWHM Gaussian kernel), and skull stripping was performed with BET. The resulting time series was then high- and low-pass filtered (cutoff frequencies were 0.05 Hz and 0.1 Hz, respectively). Each individual's 4D time series data was regressed with eight predictors in a general linear model: white matter (WM), cerebrospinal fluid (CSF), and six motion parameters. We did not regress out global signal because it would have shifted the correlation distribution to the middle and interfered with the connectivity strength calculation described below.

**Functional Connectivity Masks**

Our masks on average consisted of 53420 (standard deviation 10640) voxels, and accounted for a mean of 16% (standard deviation 3.2%) of whole brain volume.

**Power analysis for medication effects**

In our patient group 11 participants were treated with aripiprazole and 13 with risperidone. To assess for power within our study to differentiate effects of medication we randomly choose a subset of 11 patients and re-analyzed our symptom-dependent correlations with this group of patients. Our results were no longer significant in our symptoms dependent or between scan analyses. Thus, we concluded that the sample sizes in our medication groups were not powered to tease apart drug-specific effects.
### eTable. Summary of Significant Between Scan Differences in Functional Connectivity in FEP

<table>
<thead>
<tr>
<th>Seed region</th>
<th>Contrast</th>
<th>Region</th>
<th>Montreal Neurological Institute Coordinates</th>
<th>T-score</th>
<th>Z-score</th>
<th>FDR corrected p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right VSS</td>
<td>Follow-up &gt; baseline</td>
<td>Left Thalamus</td>
<td>-16, -10, 16</td>
<td>5.12</td>
<td>4.15</td>
<td>0.041</td>
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<tr>
<td></td>
<td>Follow-up &gt; baseline</td>
<td>Right Nucleus Accumbens</td>
<td>8, 14, -8</td>
<td>5.99</td>
<td>4.60</td>
<td>0.039</td>
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</tbody>
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