Supplement

A Broken Filter: Prefrontal Functional Connectivity Abnormalities in Schizophrenia During Working Memory Interference

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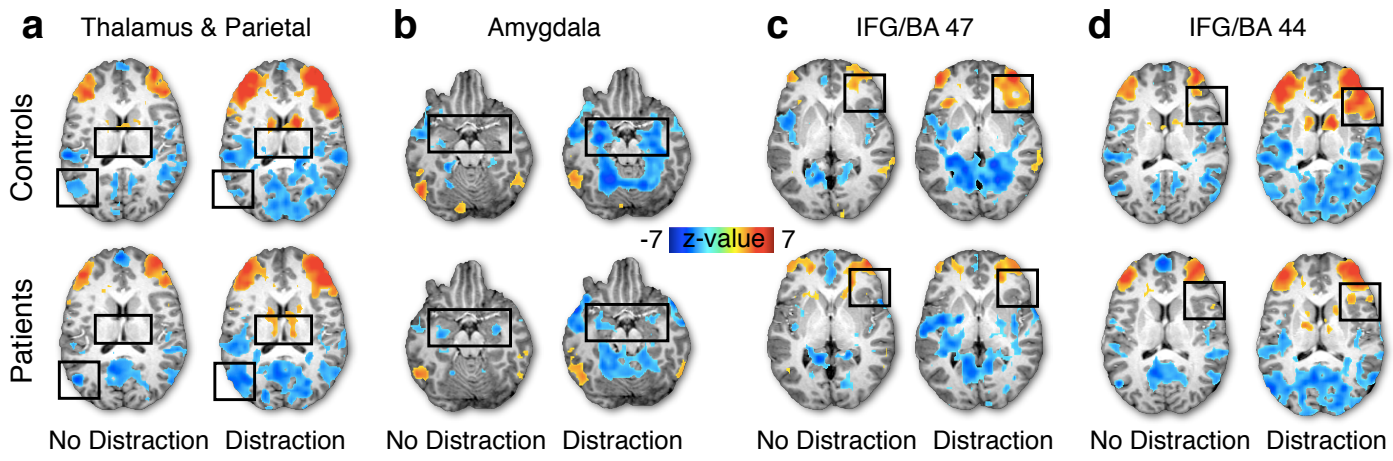
Supplemental Information [SI]

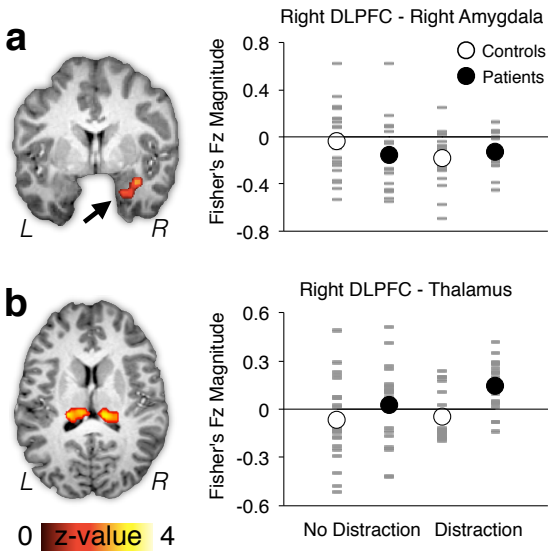
SI 1: Additional Task Details and Considerations. As illustrated in the main text (**Figure 1**) we used a slow event-related design such that a block of trials with no distraction was presented first, followed by trials containing distracters presented during the delay phase of working memory (WM). This design was chosen because our pilot work, and previous studies conducted in healthy adults using the same design (Anticevic et al., 2010a; Anticevic et al., 2010b), showed that mixing the no distraction trials along with distraction trials generates an 'expectation' for there to be a distraction the majority of the time (as no distractor trials constitute ¼ of all trials). Therefore, somewhat unexpectedly, the no distracter trials became surprising in this context and resulted in worse performance. That is, a subject expects a distracter and perhaps engages preparatory strategies most of the time in anticipation of a distracter; however, when a distracter does not appear in a minority of the trials this violates the general expectation of a distracter occurring. Hence, in our subsequent studies we opted for a blocked design with no distracter trials presented initially to avoid this context effect. This modification improved performance and was adopted in the present design. This choice of design may create a 'power' issue between the two conditions such that there exists an uneven number of trials across distraction vs. no distraction trials. However, this difference in trial numbers was present for both groups (as the design was identical for both patients and controls). In that sense, the between group effects cannot be confounded by this issue. Nevertheless, we acknowledge this as a limitation of the present design.

SI 2: Behavioral Results. As noted in the main text, groups differed in response to distraction vs. no distraction on WM task whereby patients were distracted irrespective of distracter category, whereas controls were more specifically distracted by emotional distracters. As reported in our prior work (Anticevic et al., 2011), this was confirmed using repeated-measures ANOVA, with *Diagnosis* (2 levels, SCZ versus CON) and *Distraction Type* (4 levels - no distraction, neutral, negative, task-relevant) as factors. Results revealed a trend-level main effect of *Diagnosis* [$F(1,50)=3.85$, $p<0.055$], with overall lower accuracy for SCZ versus CON; significant main effect of *Distraction Type* [$F(3,150)=9.43$, $p<0.0001$] and a significant *Diagnosis* X *Distraction Type* interaction [$F(3,150)=2.93$, $p<0.04$], indicating different across-group *Distraction Type* effects. Patients and controls did not differ significantly in the no distraction condition [$t(50)=1.2$, $p=0.23$, two-tailed, NS]. As described in detail previously (Anticevic et al., 2011), there was no main effect of *Distracter Type* [$F(1,50)=0.88$, $p=0.45$, NS] nor *Distracter Type* X *Diagnosis* interaction [$F(1,50)=0.83$, $p=0.47$, NS] when using reaction time (RT) as the dependent variable, although numerically, patients performed more slowly across all distracter conditions [$F(1,50)=1.93$, $p=0.17$, NS].

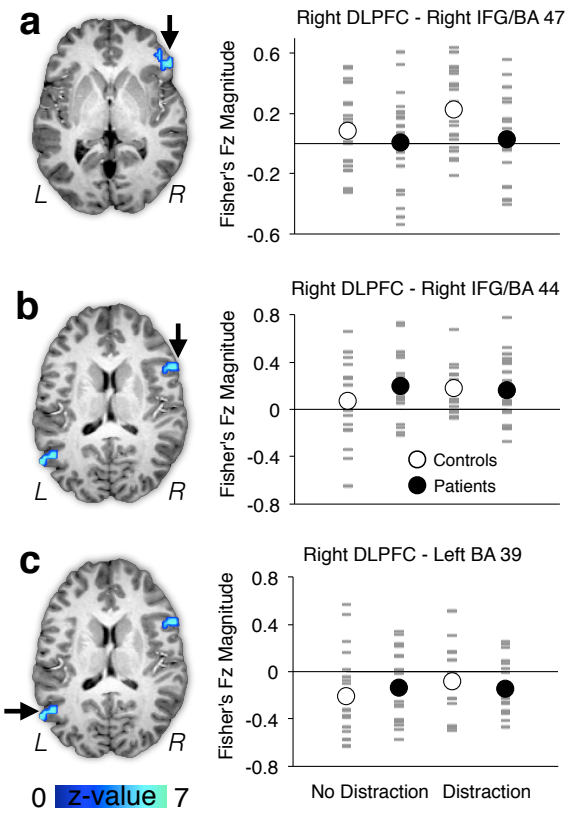
SI 3: Covariate & Symptom Analyses. We conducted additional co-variate analyses to further rule out that third variables may be in part driving observed effects. First, we computed an analysis with distracter-related performance for each subject as a covariate to rule out possible performance-related confounds driven by task response difference between groups. Reported results remained unchanged. Next, we explored whether positive or negative symptoms as measured using the Scale for Assessment of Positive and Negative Symptoms (SAPS/SANS) correlated with observed tb-fcMRI group differences. We found no significant effects (all p values > .14 across 10 correlations). We also tested whether performance differences in the two conditions of interest (no distraction minus distraction) correlated with differences in connectivity between the two conditions, in patients and controls. This analysis tests whether connectivity modulation between nodes of interest is linearly correlated with performance differences between these conditions. To this end, we computed a difference score for each subject where we deviated the performance following distraction vs. performance with no distraction. We did the same for the connectivity modulation across conditions. This yielded 5 indexes for each of the identified foci: thalamus, extended amygdala, inferior frontal gyrus, middle frontal gyrus and parietal cortex. We computed a linear correlation between these indexes and the performance difference score. Results revealed no significant relationships (all p values > .23). Lastly, we found that when co-varying for IQ reported tb-fcMRI results were not altered. In summary, these additional individual-difference covariate analyses did not reveal further significant findings. We acknowledge that identifying individual difference effects would have aided our interpretation of effects in the main text. However, we find that the lack of such effects may be more consistent with the 'trait' interpretation presented in the Discussion section.



SI Figure 1. Patterns of task-based functional connectivity (tb-fcMRI) across groups and conditions. (**a-d**) We show patterns of tb-fcMRI across the five foci identified in the main text. All maps are visualized at a somewhat lower threshold (Z>2.5) to facilitate qualitative inspection of patterns. Each general region of interest is highlighted with a black box outline.



SI Figure 2. Subcortical regions showing significant tb-fcMRI group differences with right DLPFC following WM interference. Vertical scatterplots are shown for **(a)** the extended amygdala and **(b)** bilateral dorsal thalamic region to facilitate inspection of outliers. The color scheme is preserved as in the main text: control subject mean data is shown using white circles, whereas patient mean data is shown using black circles. Each gray line marks an individual subject for a given group. As illustrated by the scatter around the means, outlier subjects did not impact the results.



SI Figure 3. Cortical regions showing significant tb-fcMRI group differences with right DLPFC following WM interference. Vertical scatterplots are shown for **(a)** the right IFG region, **(b)** a more inferior portion of the right IFG, and **(c)** left parietal cortex to facilitate inspection of outliers. The color scheme is preserved as in the main text: control subject mean data is shown using white circles, whereas patient mean data is shown using black circles. Each gray line marks an individual subject for a given group. As illustrated by the scatter around the means, outlier subjects did not impact the results.

Supplemental References

Anticevic, A., Repovs, G., Barch, D.M., 2010a. Resisting Emotional Interference: Brain Regions Facilitating Working Memory Performance During Negative Distraction. Cogn. Affect. Behav. Neurosci. 10(2), 159-173.
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