Disruption of posterior parietal cortex and striatum during spatial working memory in schizophrenia and bipolar disorder

Anna S. Huang[1], Baxter P. Rogers[2], Alan Anticevic[3], Jennifer U. Blackford[1], Stephan Heckers[1], Neil D. Woodward[1]

[1] Department of Psychiatry and Behavioral Sciences, Vanderbilt University Medical Center
[2] Vanderbilt University Institute of Imaging Sciences
[3]Department of Psychiatry, Yale University School of Medicine

Background

Working memory (WM) is impaired in psychosis and associated with functional outcome[1].

Neurobiological models emphasize prefrontal cortex (PFC) dysfunction in WM impairment[2].

Neural bases of WM sub-processes (encoding, maintenance, retrieval) are poorly understood in schizophrenia and bipolar disorder[3,4].

The current study seeks to:

1. **Characterize neural responses of WM sub-processes in schizophrenia and bipolar disorder**
2. **Determine whether schizophrenia and bipolar disorder exhibit similar abnormalities**
3. **Elucidate associations between WM-related brain function, task performance and neuro-psychological functioning.**

Methods

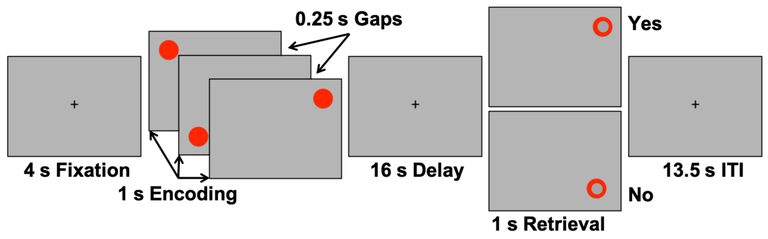
Table 1. Demographics of study participants

	Healthy Subjects (N=58)		Schizophrenia Spectrum Disorders (N=72)		Psychotic Bipolar Disorder (N=41)				
Variable	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**df**	**X^2/t/F**	**p**
Gender (M:F)	37:21		48:24		24:17			.75	.688
Age	29.2	9.5	27.9	9.4	31.3	12.0	2,168	1.48	.232
Accuracy (d')	2.27	.71	2.08	.76	2.02	.76	2,167	1.60	.204
Reaction Time (WM)	999	322	1159	490	1235	409	2,167	4.27	.016
SCIP Z score	.30	.60	-.74	.77	-.53	.94	2,167	30.98	<.001

Abbreviations: F=Female; M=Male; SCIP=Screen for Cognitive Impairment in Psychiatry;

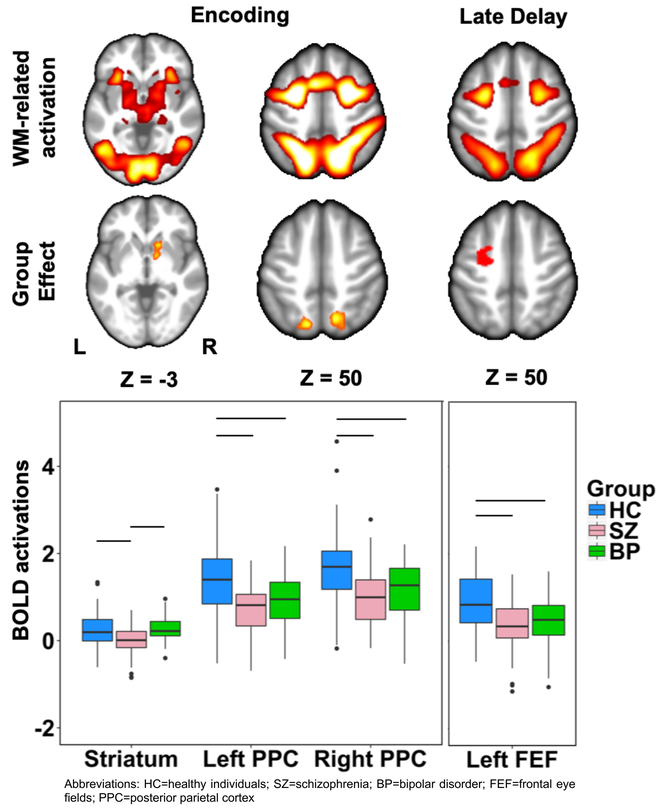
Analyses:

- Spatial delayed-match-to-sample task used in a prior study of WM[4]
- WM stages were fit to a GLM and used in complementary region-of-interest (ROI)[4,5,6] and whole-brain voxel-wise analyses.



Results

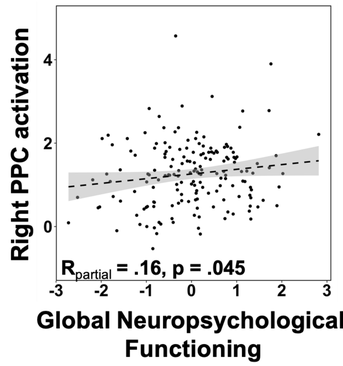
Whole Brain Encoding- and Maintenance-related Group Effect



Abbreviations: HC=healthy individuals; SZ=schizophrenia; BP=bipolar disorder; FEF=frontal eye fields; PPC=posterior parietal cortex

FEF and PPC deficits found in both schizophrenia and bipolar disorder.
Ventral striatum activation differentiated the schizophrenia group.

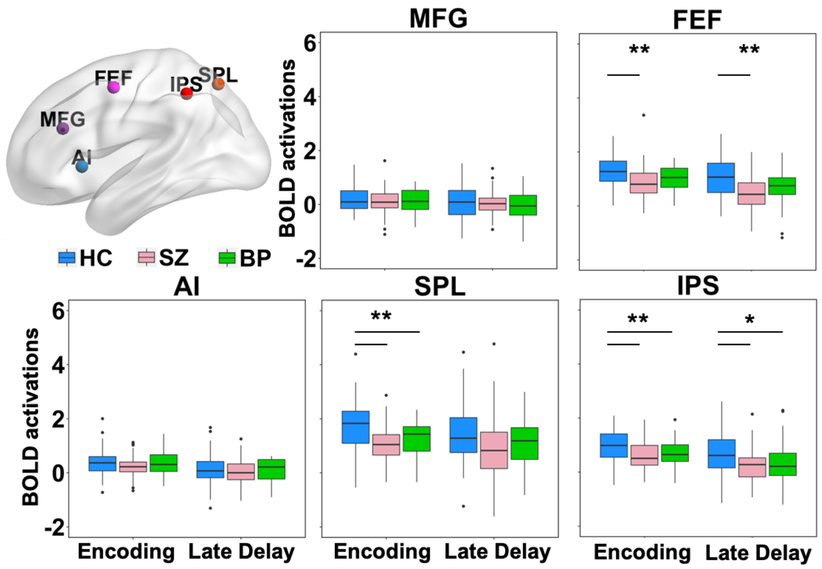
Association with Task Performance and Neuropsychological functioning



PPC activation was associated with neuropsychological functioning independent of group.

Encoding- and maintenance-related activation in FEF and PPC regions were associated with task performance independent of group ($R_{partial}$'s>.2, p's<.01).

Group Differences in WM Network Regions-of-Interest



Abbreviations: HC=healthy individuals; SZ=schizophrenia; BP=bipolar disorder; AI=anterior insula; FEF=frontal eye fields; MFG=middle frontal gyrus; IPS=intraparietal sulcus; SPL=superior parietal lobule; (*p<.01,**p<.001)

Schizophrenia and bipolar disorder show similar encoding- and maintenance-related deficits in FEF and PPC regions (SPL and IPS).

Conclusions

- **Our results are consistent with emerging evidence implicating PPC dysfunction in WM impairment[7] and show that these deficits occur during encoding and maintenance.**
- **Interventions targeting PPC activation and behavioral training targeting encoding processes may improve WM and general cognitive functioning in psychosis.**
- **Future investigation may better elucidate differential ventral striatal activation during cognition in psychosis.**

References

1. Gold, J. M., et al. (2018). *Schizophrenia Bulletin.*
2. Glahn, D. C., et al., (2005). *Human Brain Mapping*, 25(1), 60–69.
3. Anticevic, A., et al., (2011). *Schizophrenia Bulletin*, 39(1), 168–178.
4. Driesen, N. R., et al., (2008). *Biological Psychiatry,* 64(12), 1026–1034.
5. Leung, H.-C., et al. (2002). *Journal of Cognitive Neuroscience*, 14(4), 659–671.
6. Rottschy, C., et al. (2012). *NeuroImage*, 60(1), 830–846.
7. Hahn, B., et al., (2018). *The Journal of Neuroscience*, 38(39), 8378–8387.

This work was supported by NIMH grants RO1 MH102266 (awarded to NDW) the Charlotte and Donald Test Fund

Correspondence to: anna.s.huang@vumc.org
PDF available at www.woodwardlab.com