

## Background

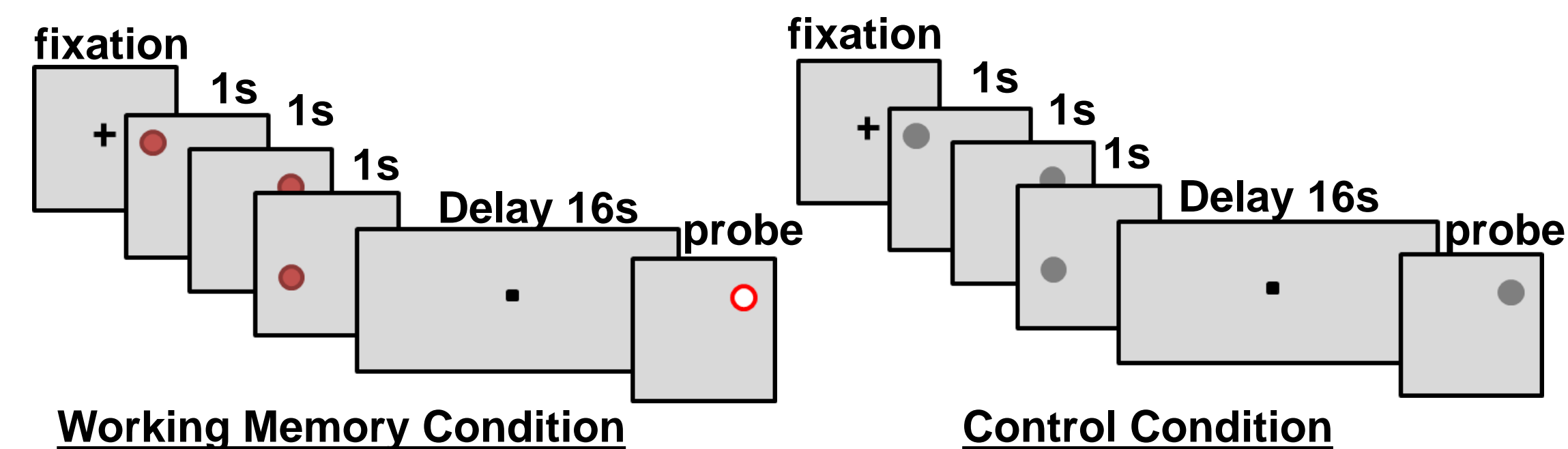
- Psychosis is associated with impaired cognition, altered brain activation, and abnormal cortical micro-circuitry<sup>1-3</sup>
- We used neurite orientation dispersion and density imaging (NODDI)<sup>4</sup>, a method for quantifying grey matter integrity, and working memory (WM) fMRI to test the following hypotheses:
  - Brain activation during WM maintenance is reduced in psychosis;
  - Grey matter integrity is reduced in regions showing altered WM brain activity; and
  - Grey matter integrity is associated with WM activation and cognition

## Methods

### Procedures

Multi-shell diffusion-weighted imaging (DWI) and event-related spatial WM fMRI collected on 53 healthy subjects and 103 individuals with a psychotic disorder during a single scanning session on a 3T MR scanner.

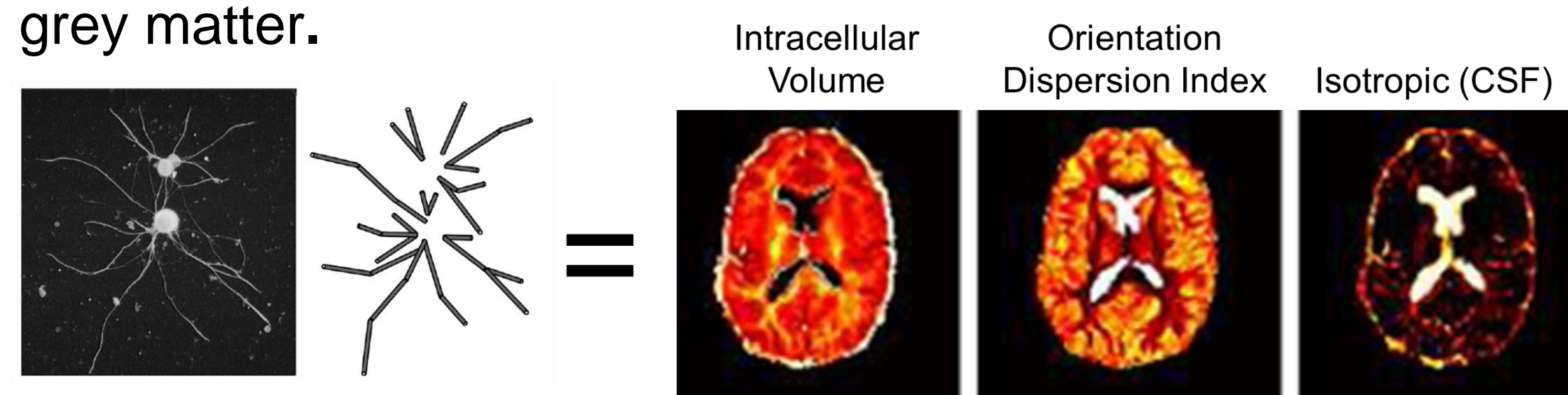
### Spatial Working Memory (WM) Task



### Neurite Orientation Dispersion and Density Imaging

NODDI applies a 3 compartment tissue model (intracellular, extracellular, CSF)<sup>5</sup> to multi-shell DWI data to characterize:
 

- Intracellular Volume Fraction (V<sub>ic</sub>):** Fraction of tissue volume restricted within neurites, a measure of neurite density.
- Orientation Dispersion Index (ODI):** Spectrum of neurite orientation from highly coherent (low ODI) observed in white matter to complex dendritic processes (high ODI) observed in grey matter.



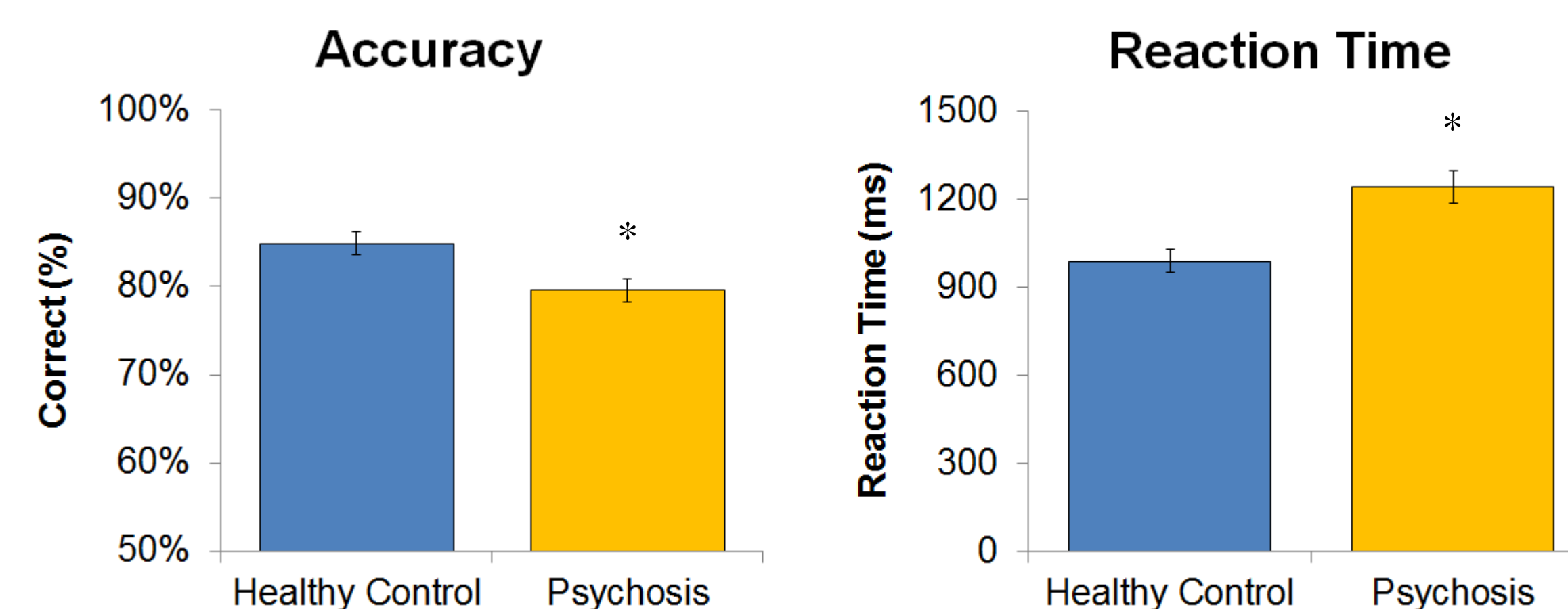
\* Figure from Jespersen et al., 2007

### Imaging Analysis

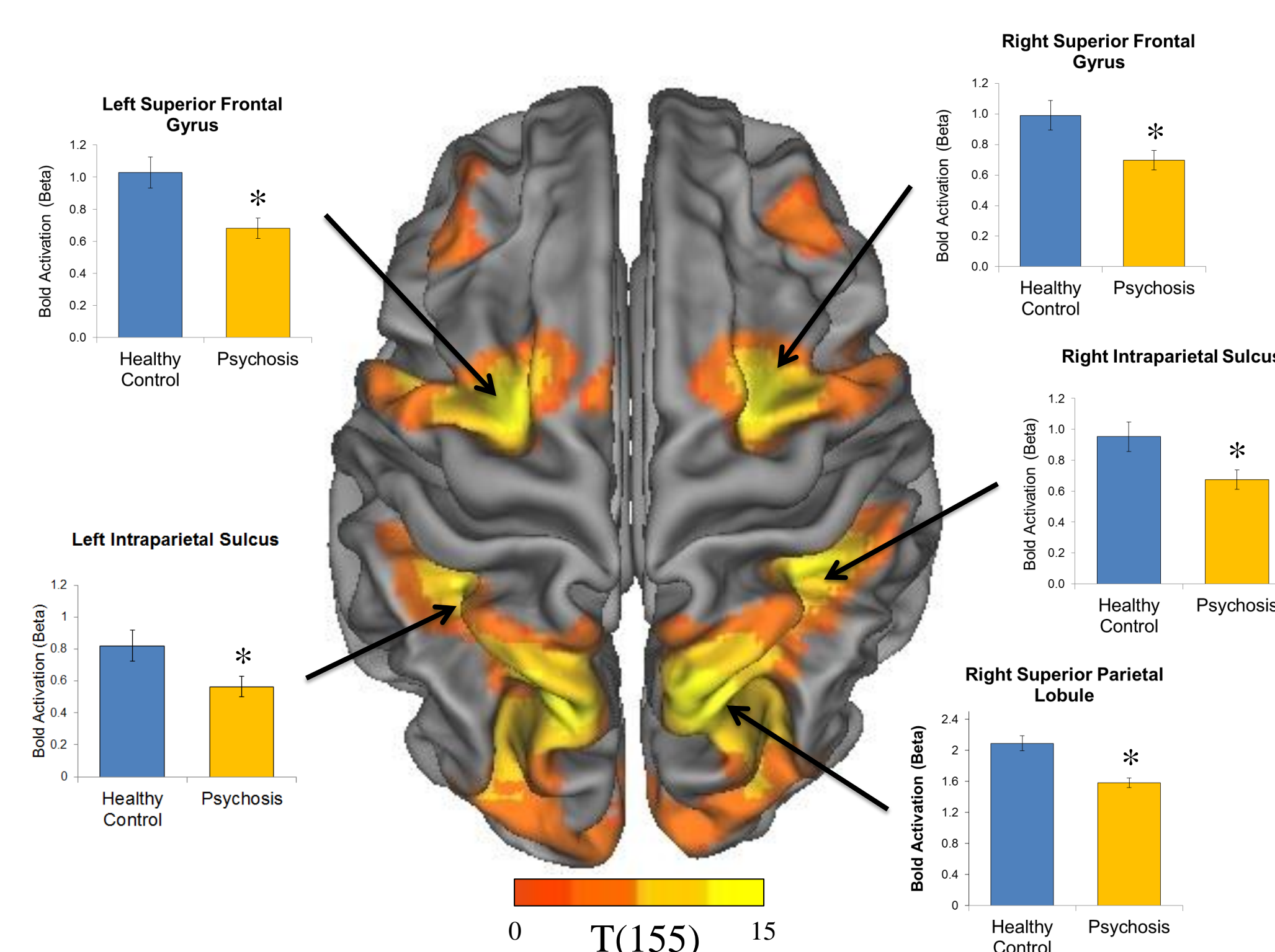
Brain regions involved in WM maintenance were identified by contrasting WM delay vs. control trial delay period (all subjects (n=156), correct trials only). Mean activation, V<sub>ic</sub>, and ODI extracted from each region for group comparisons.

## Results

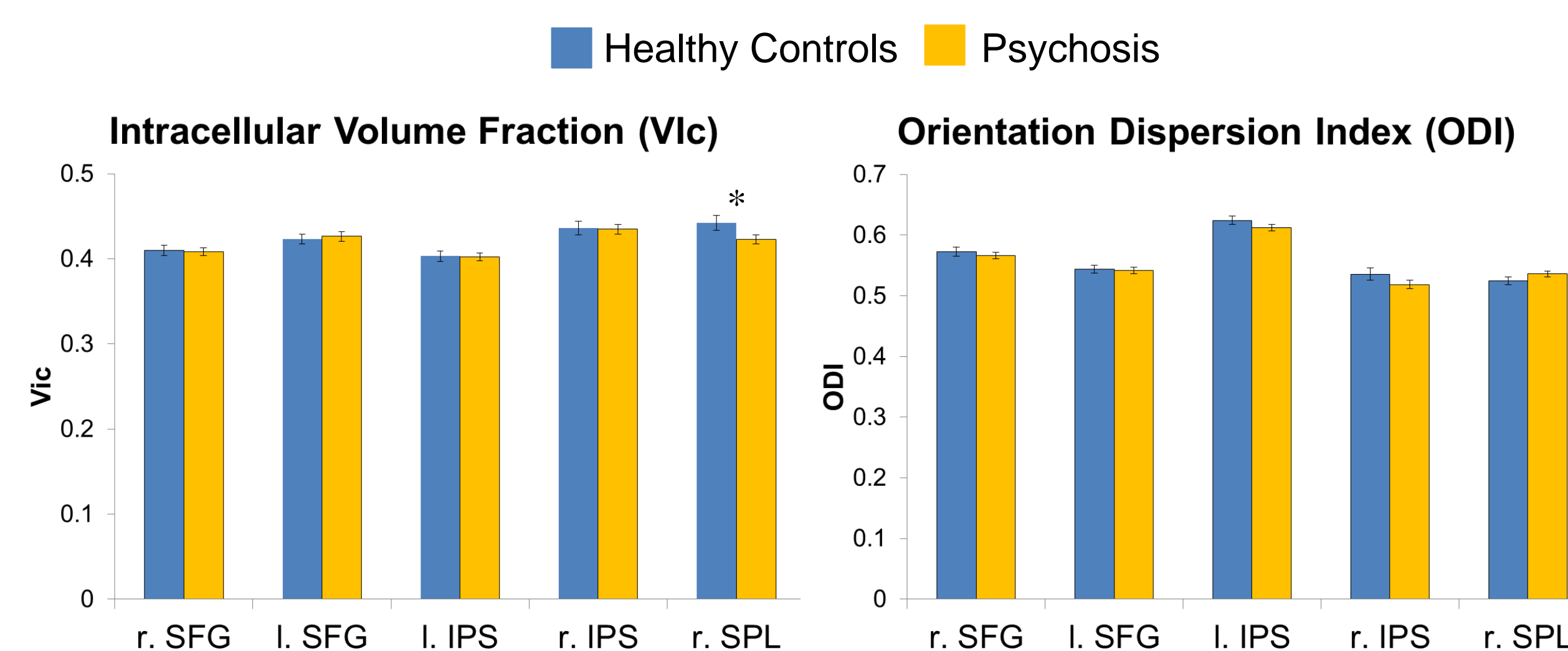
### Spatial Working Memory (WM) Task Performance



### Brain Activation: WM Delay > Control Delay



### Neurite Orientation Dispersion and Density Imaging



r. = right; l. = left; SFG = superior frontal gyrus; IPS = intraparietal sulcus; SPL = superior parietal lobule; \* = p<.05

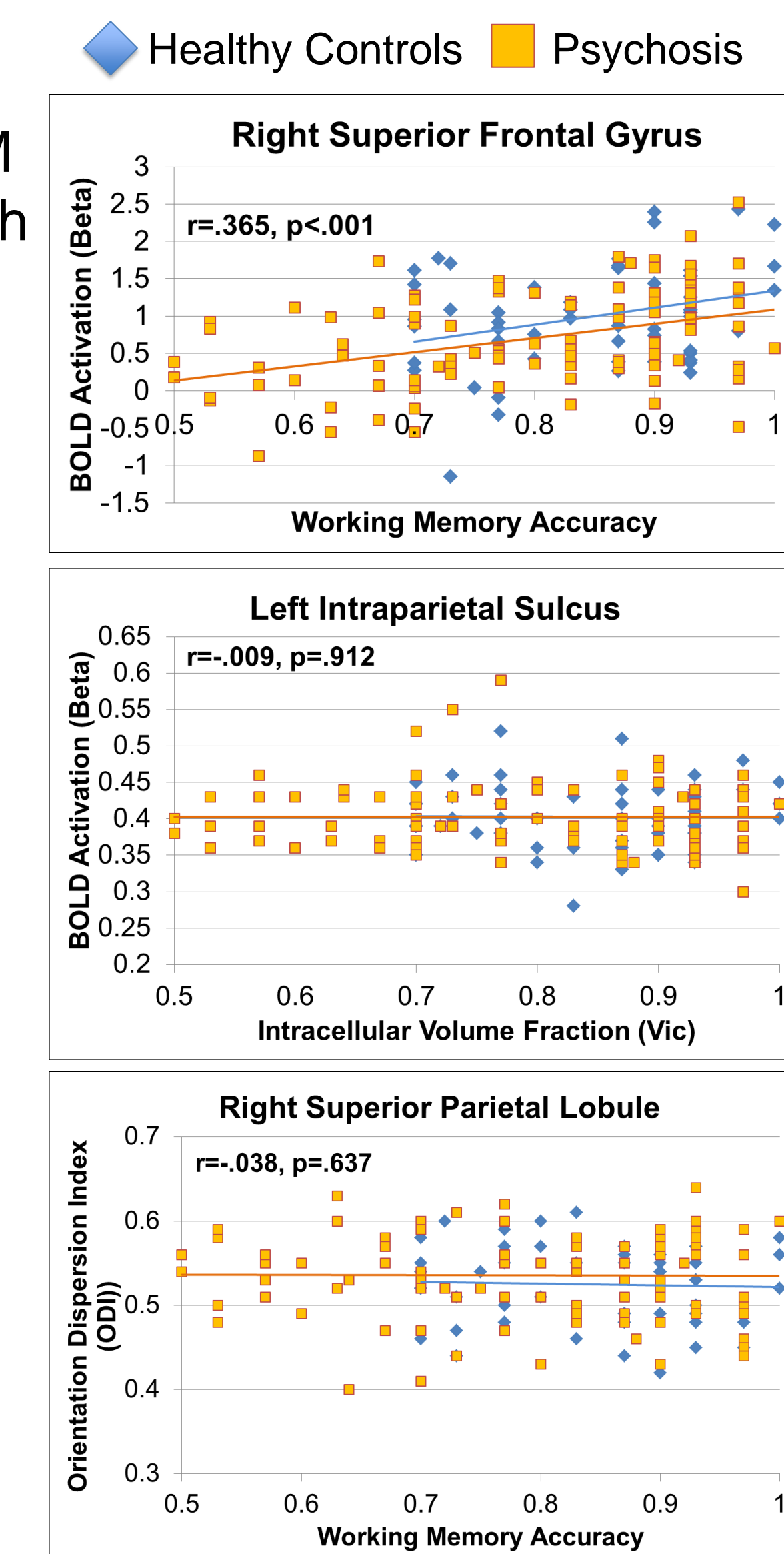
### Sample Demographics

	Healthy Controls N=53	Psychosis N=103	Statistic
Age (SD)	29.53 (9.81)	28.41 (9.99)	t(154)=.67, p=.51
Gender (F/M)	19/34	39/64	χ <sup>2</sup> =.81, p=.86
Race (B/W/O)	10/37/6	22/78/3	χ <sup>2</sup> =5.90, p=.21
Personal Education	16.00 (1.95)	13.84 (1.95)	t(154)=6.54, p<.001
Maternal Education	14.87 (2.34)	14.63 (2.55)	t(152)=.56, p=.23
Paternal Education	15.33 (2.82)	15.01 (3.37)	t(150)=.58, p=.56

## Results

### Associations Between Working Memory (WM) Brain Activation, Cognition, and Grey Matter Integrity

- BOLD response during WM maintenance correlated with task performance in both healthy controls and psychosis patients (e.g. right SFG)
- Grey matter integrity unrelated to activity during WM maintenance (e.g. left IPS)
- Grey matter integrity unrelated to WM task performance and cognition (e.g. right SPL)



## Conclusions

- Activation in fronto-parietal regions is reduced in psychotic disorders during WM maintenance.
- Grey matter microstructure is largely intact in brain regions demonstrating reduced BOLD response.
- Grey matter integrity is unrelated to BOLD response during WM maintenance and task performance.
- Next steps include investigation of diagnostic (i.e. SSD, BPD) and illness stage effects (i.e. chronic, early stage)

### References

- Glantz LA, Lewis DA. (2000) Decreased dendritic spine density on prefrontal cortical pyramidal neurons in schizophrenia. *Archives of General Psychiatry*, 57(1):63-73.
- Simonsen C, Sundet K, Vaskinn A et al. (2011) Neurocognitive dysfunction in bipolar and schizophrenia spectrum disorders depends on history of psychosis rather than diagnostic group. *Schizophrenia Bulletin*, 37:73-83.
- Minzenberg MJ, Laird AR, Thelen S, Carter CS, Glahn DC. (2009) Meta-analysis of 41 functional neuroimaging studies of executive function in schizophrenia. *Am J Psychiatry*, 166(8):811-22.
- Zhang, H., Schneider, T., Wheeler-Kingshott, C. A., & Alexander, D. C. (2012) NODDI: practical in vivo neurite orientation dispersion and density imaging of the human brain. *Neuroimage*, 61(4), 1000-1016.
- Jespersen SN, Kroenke CD, Ostergaard L, Ackerman JJ, Yablonskiy DA. (2007) Modeling dendrite density from magnetic resonance diffusion measurements. *Neuroimage*, 34(4):1473-86.