

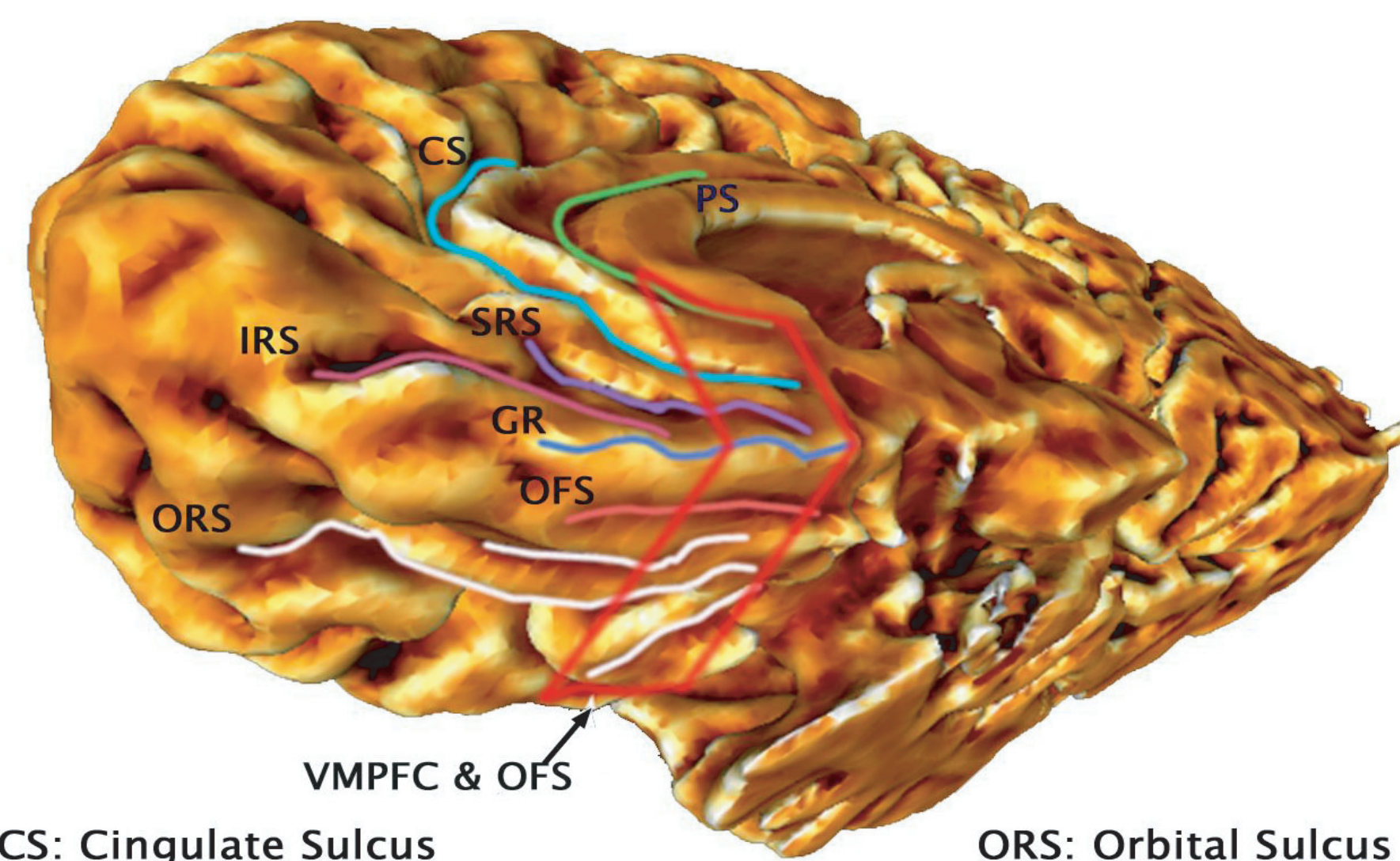
Ventral Medial Prefrontal Cortex Metrics in Early Onset Depression: A Twin MRI Study

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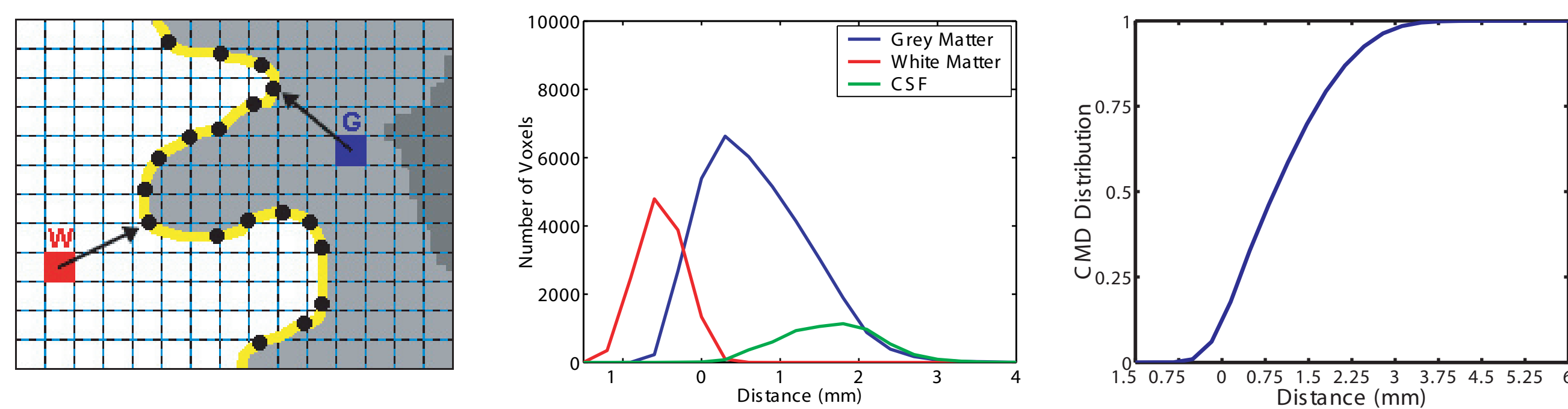
Introduction

Structural and functional imaging studies have shown the medial prefrontal cortex is implicated in major depressive disorder (MDD) [1,2]. Using automated methods of cortical analysis [3,4], we demonstrate the application of statistical tests on Labeled Cortical Mantle Distance Maps in the Ventral Medial Prefrontal Cortex (VMPFC) - shown on the right - to quantify cortical changes.

A population of 34 right-handed female twin pairs between 13-23 years was studied, of which 14 pairs were control and 20 pairs were affected with Major Depressive Disorder (MDD). Both monozygotic and dizygotic twins were included. The inclusion criteria for the affected twin pairs were onset prior to age 16 and the DSM IV criteria for Major Depression being greater than a duration of 4 weeks. Control twin pairs had no personal or first degree family history of Major Depression.



CS: Cingulate Sulcus
GR: Gyrus Rectus
IRS: Inferior Rostral Sulcus
OFS: Olfactory Sulcus
ORS: Orbital Sulcus
PS: Pericallosal Sulcus
SRS: Superior Rostral Sulcus
VMPFC: Ventral Medial Prefrontal Cortex



Labeled Cortical Distance Maps (LCDM)

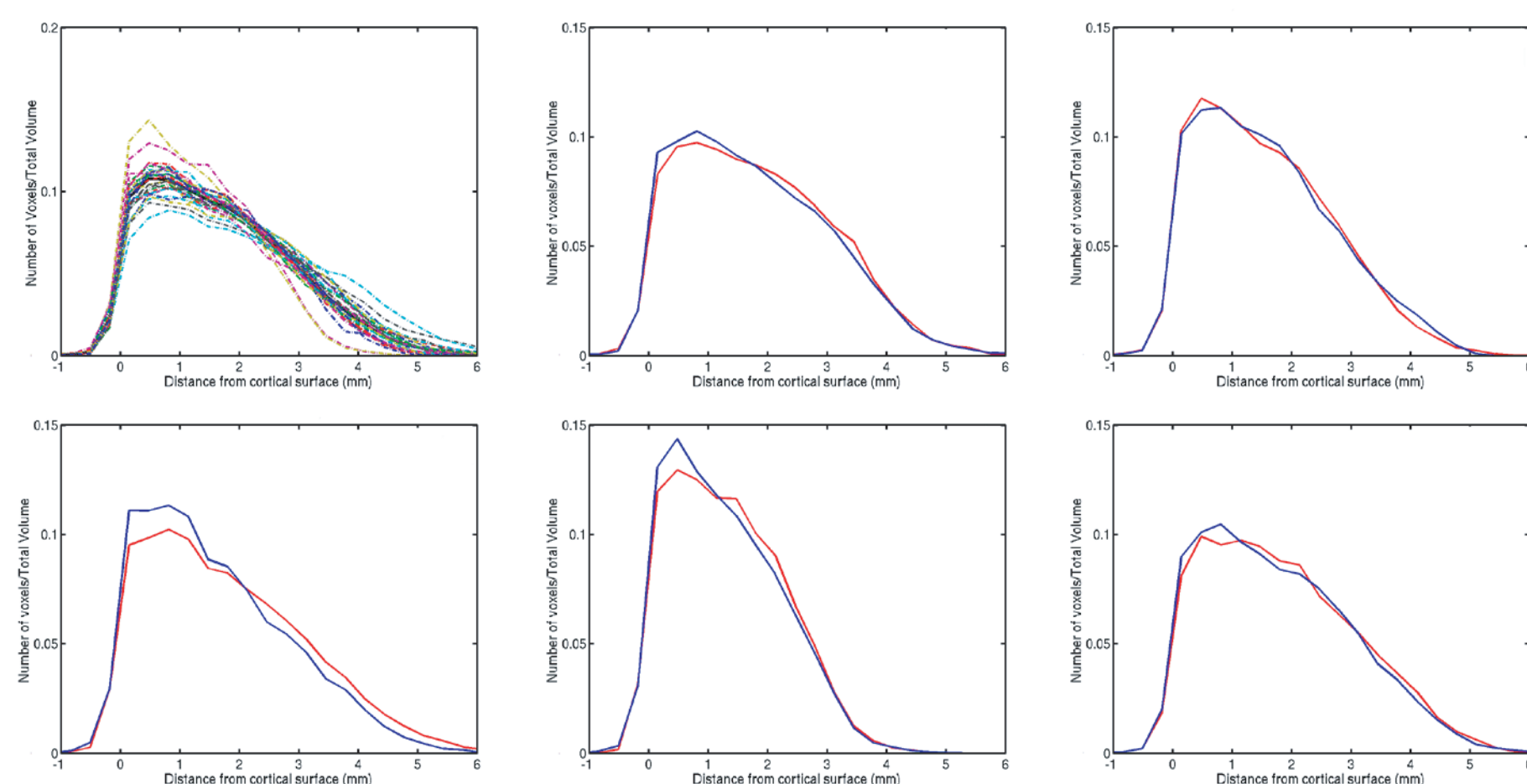
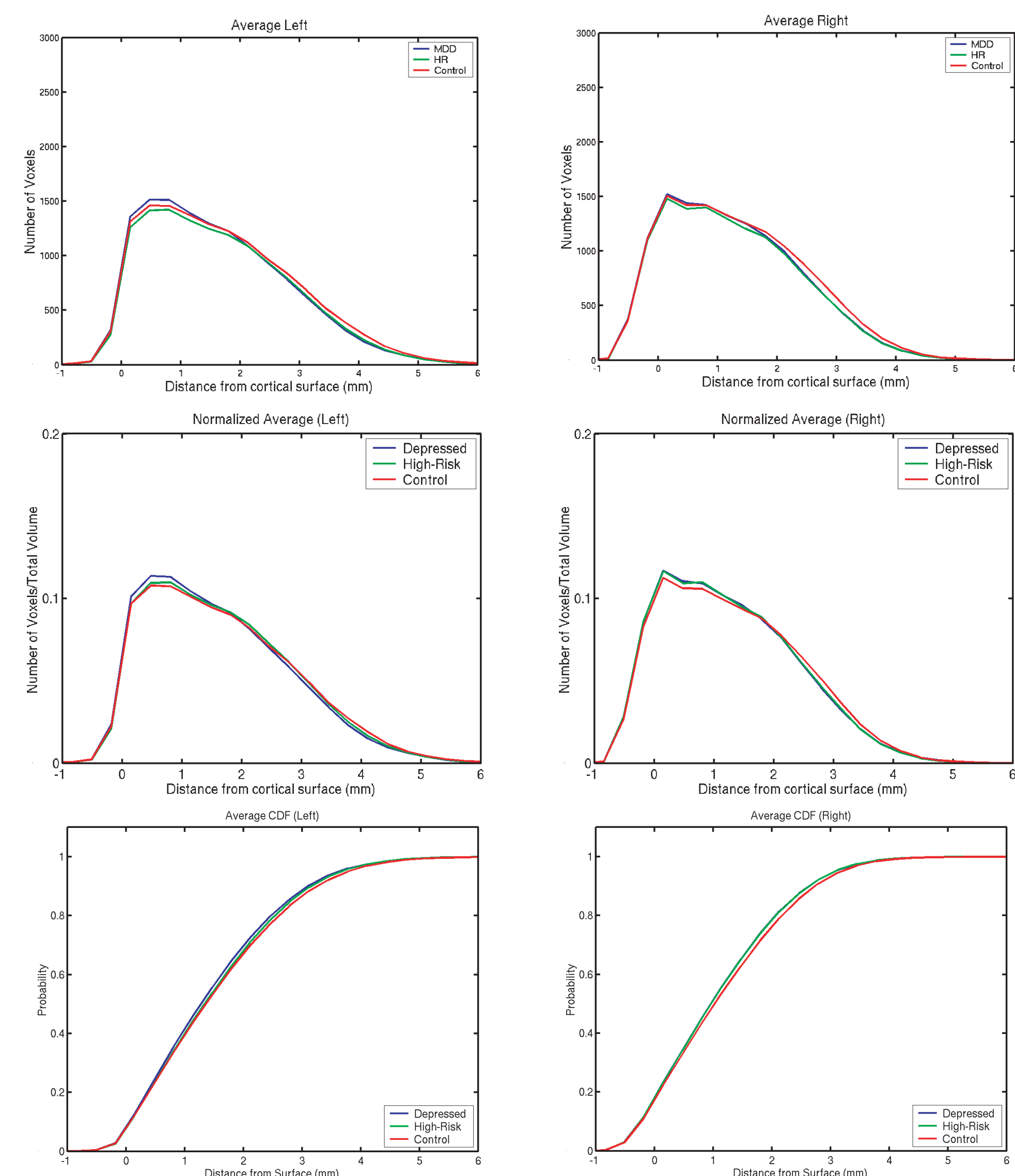
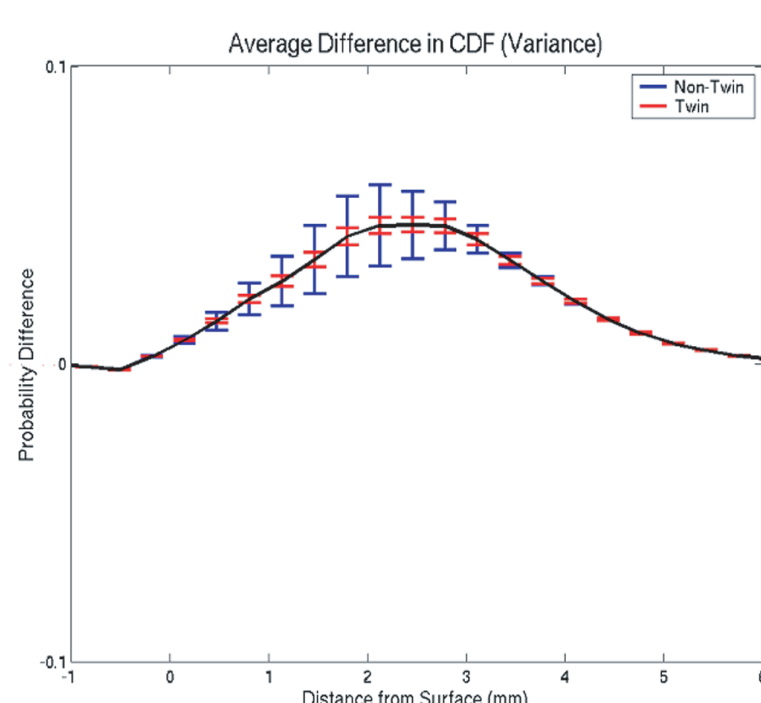
The flow chart on the left describes the sequence of methods used to quantify cortical changes in the VMPFC. Following Ratnanather et al. [4], Bayesian segmentation was used to classify tissues in MRI ROI subvolumes of the VMPFC as Gray Matter (GM), White Matter (WM) and cerebrospinal fluid (CSF). Using the threshold intensity between the GM and WM, isosurfaces representing GM/WM interface were generated. Following Miller et al. [3], we generated LCDMs which are histograms of labeled tissue compartments of GM, WM and CSF computed as a function of distance from the GM/WM isosurface as illustrated on the left (panel 1 and 2). Normalizing the histograms by the corresponding total volume yielded Cortical Mantle Distance (CMD) profiles of GM distribution as a function of distance independent of total GM volume (panel 3).

Results

On the right, we show graphs of average LCDM grey matter profiles (row 1), average normalized LCDM grey matter profiles (row 2) and CMD profiles (row 3) for the left and right VMPFC. Wilcoxon Rank-Sum Tests for cortical thinning [3] were performed to test for stochastic ordering between populations with average p-values and standard deviations summarized in the table below. For the left VMPFC, the High Risk (HR) population is stochastically larger than the MDD (depressed) population and the control population is stochastically larger than the MDD population. For the right VMPFC, the control population is stochastically larger than both HR and MDD populations.

The figure next to the table shows the average difference in variance for the MZ control twin pairs vs. randomly paired controls. The six figures at the bottom show the left VMPFC profiles from control pairs with combined profiles in the top left and 5 randomly selected twin pairs profiles separately. Notice how close the LCDM profiles are for the MZ control twin pairs.

Population	LEFT		RIGHT	
	p-value	S.D.	p-value	S.D.
Depressed vs High Risk	0.0188*	0.0516	0.4298	0.2854
Depressed vs Control	0.0009*	0.0064*	0.0041*	0.0180*
High Risk vs Control	0.1416	0.1807	0.0071*	0.0288*



Summary

These results demonstrate cortical thinning in the left VMPFC for the MDD population when compared to the HR and control populations, and cortical thinning in the right VMPFC for the MDD and HR populations when compared to the control population. These orderings may be confirmed by the graphs of the normalized LCDM and CMD profiles shown above (rows 2-3). These distance maps coupled with statistical testing provide another way to examine neuromorphometric differences associated with MDD. Finally, comparison of LCDM profiles and demonstration of reduced variance in MZ healthy control twins shown on the left strongly support significant genetic influence on healthy VMPFC cortical structure.

References:

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