Neurite Orientation Dispersion and Density Imaging (NODDI) of the Prefrontal Cortex in Psychosis

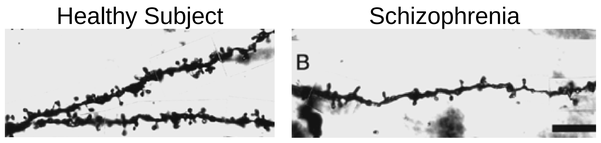
Neil D. Woodward[1], Prasanna Parvathaneni[2], Baxter P. Rogers[3], Stephen M. Damon[2], Bennett A. Landman[2,3]

[1]Deparment of Psychiatry and Behavioral Sciences, Vanderbilt University Medical Center
[2]School of Engineering, Vanderbilt University
[3]Vanderbilt University Institute of Imaging Sciences

Introduction

There is considerable evidence from post mortem investigations that prefrontal cortex (PFC) micro-circuitry is altered in psychosis. Key findings include reduced lower spine density and shorter total dendritic length (see below). In vivo evidence of altered PFC micro-circuitry is lacking. We used neurite orientation dispersion and density imaging (NODDI) to investigate cortical micro-circuitry in vivo in individuals with psychosis.

Figure: Dendritic spine density in schizophrenia.



* Figure adapted from Glantz & Lewis, 2000

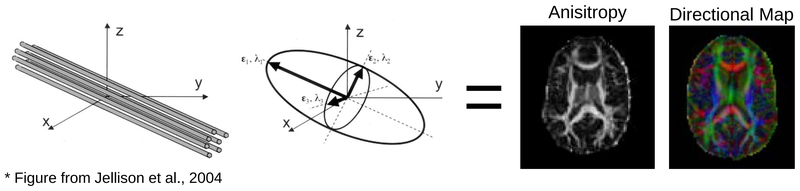
Methods

Procedures

Multi-shell diffusion-weighted imaging (DWI) and high resolution anatomical T1-weighted imaging acquired on 67 individuals with a psychotic disorder (schizophrenia, psychotic bipolar disorder) and 47 healthy individuals. Using the NODDI model, neurite orientation dispersion index (ODI), a putative marker of dendritic structure and complexity, was calculated on a voxel-wise basis throughout the brain and compared between healthy subjects and psychosis patients.

NODDI Compared to Diffusion Tensor Imaging (DTI)

DTI: Diffusion modeled as an ellipsoid. A diffusion tensor is fit to the data to calculate fractional anisitropy (FA) and infer directionality of underlying white matter tracts.

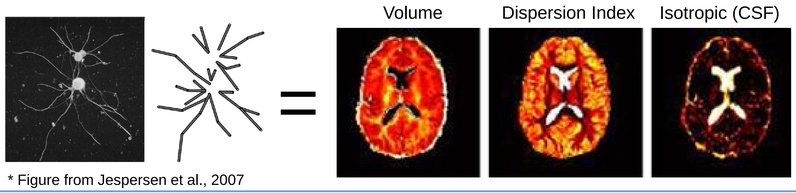


* Figure from Jellison et al., 2004

NODDI: Uses a 3-compartment tissue model to characterize diffusion in both white matter and grey matter.

1) Intracellular: neurites modelled as a set of sticks- diffusion is restricted by the membranes.
2) Extracellular: space outside the neurites- water is hindered by membranes.
3) CSF: space occupied by CSF- modelled as isotropic diffusion.

ODI is derived from intracellular and extracellular compartments. ODI reflects the orientation distribution of 'sticks' and models the spectrum of neurite orientation from highly coherent (low ODI) observed in white matter to complex dendritic processes (high ODI) observed in grey matter.



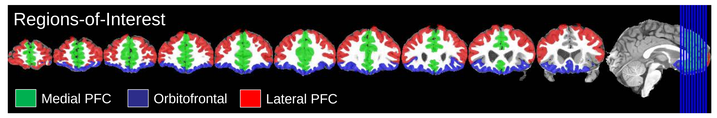
* Figure from Jespersen et al., 2007

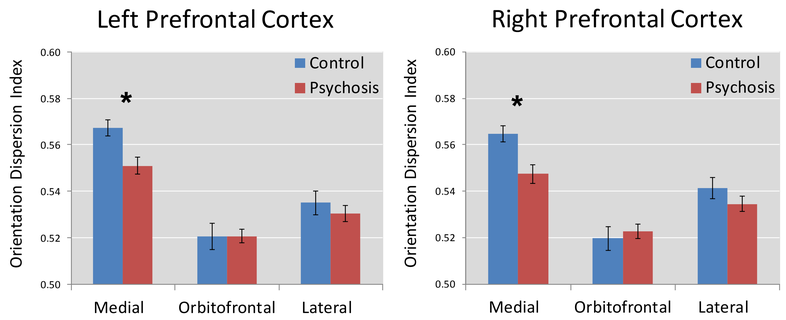
Results

Table 1. Sample Demographics

	Healthy Subjects N=47		Psychosis N=67		Statistics F/t/x^2	df	p
Sex (m:f)	29:18		40:27		0.05	1	.830
Ethnicity (White:AA:O)	33:10:4		49:15:3		0.78	1	.677
Antipsychotic (Yes/No)	--		60:7		--	--	--
	Mean	**SD**	**Mean**	**SD**			
Age	30	9.9	27.8	8.8	1.25	112	.214
Premorbid IQ	113.1	10.0	103.5	14.1	9.56	111	<.001
Education	16.2	1.9	13.8	1.9	6.51	112	<.001
Maternal Education	14.7	2.3	14.6	2.7	0.39	110	.694
Paternal Education	15.2	2.7	14.8	3.8	0.60	109	.552
Age of Illness Onset	--	--	22.0	6.2	--	--	--
Duration of Illness (yrs)	--	--	5.8	5.9	--	--	--
PANSS Positive	--	--	12.7	6.3	--	--	--
PANSS Negative	--	--	13.2	5.4	--	--	--
PANSS General	--	--	26.5	6.9	--	--	--

Region-of-Interest (ROI) Analysis

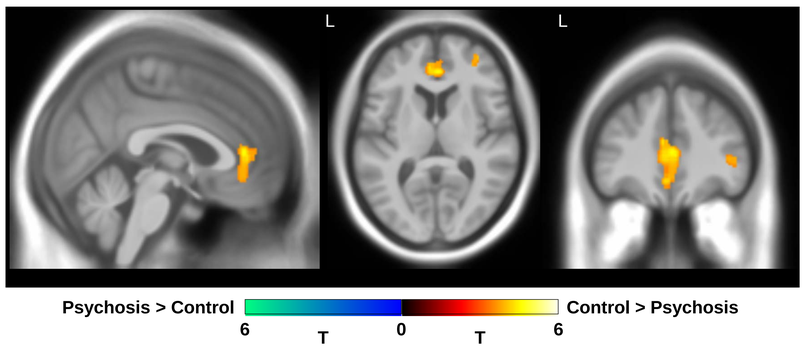




PFC region x group interaction: F(1,111)=5.29, p=.006
* Independent group t-test p<.05

Methods: Each subjects' ODI image coregistered to their anatomical T1. Anatomical-T1 image segmented using Multi Atlas. ODI extracted from 50 cortical ROIs spanning the entire cortical mantle. Mean ODI calculated for three PFC sub-regions: lateral PFC, medial PFC, and orbitofrontal PFC. Data entered into multivariate repeated measures ANOVA to asses for group, region, and hemisphere effects, and interactions.

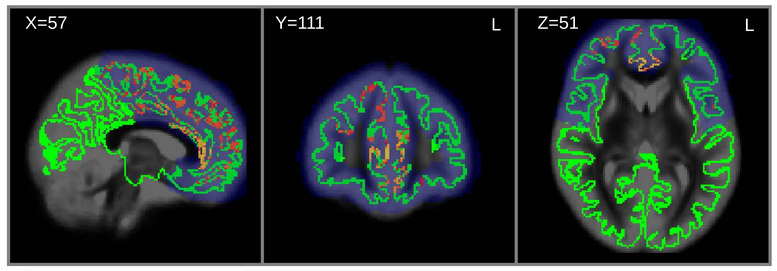
Voxel-wise Analysis



- ODI reduced in two clusters located in midline anterior cingulate (522 voxels) and right middle frontal gyrus (259 voxels).

Methods: Voxel-wise Analysis- Biological Parametric Mapping (BPM): Each subjects ODI and coregistered grey matter density image normalized to MNI space and entered into second-level voxel-wise analysis comparing ODI between healthy subjects and psychosis. Grey matter volume included as a covariate to control for grey matter volume at the voxel-wise level. Results thresholded at p=.05 (Family-wise error corrected) for voxel-wise p=.001 (uncorrected).

Grey Matter Surface-Based Spatial Statistics (GS-BSS)



- ODI reduced in medial PFC, primarily anterior cingulate, and, to a lesser extent, lateral PFC.

Methods- Grey Matter Surface Based Spatial Statistics (GS-BSS): Following normalization to standard space, grey matter segmented images and ODI images projected onto cortical surface (green voxels) using diffeomorphic spectral matching on cortical surfaces. ODI surface projected maps compared between healthy subjects and psychosis patients. Results thresholded at p=.05 (corrected) using Threshold Free Cluster Enhancement (TFCE) masked to include only voxels in the frontal lobe (blue shading in above image).

Conclusions

- Orientation dispersion index (ODI) is a putative in vivo MR diffusion measure of dendritic density
- ODI is reduced in the PFC, especially medial PFC, in individuals with a psychotic illness
- Results are consistent with post-mortem findings of reduced dendritic spine density and total dendritic length in PFC of schizophrenia patients
- Further work is needed to determine the clinical and cognitive correlates, and diagnostic specificity of reduced ODI
- Additional work is also needed to clarify the effects of antipsychotic treatment and illness stage (i.e. early stage vs. chronic) on ODI in psychosis

References

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