

# Analysis of White Matter Tracts of Resting State Cognitive Networks in Multiple Sclerosis

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## BACKGROUND

Cognitive impairment affects 40-70% of patients with multiple sclerosis (MS)<sup>1.</sup> These impairments are seen in multiple domains of cognition including attention, memory, and speed of information processing<sup>2</sup>. In a previous study using resting-state fMRI, we found abnormal connectivity links for most patients with MS in the default mode network as well as other cognitive networks including attention, memory, language, and visual-spatial memory.

### **OBJECTIVES**

To analyze the white matter damage and topological organization of white matter tracts in specific brain regions responsible for cognition in MS patients compared with healthy controls.

### METHODS

MRI measurements of DTI, T1, T2, and T2 FLAIR were acquired by GE clinical 3T system of 32 healthy subjects and 20 MS patients. DTI images were preprocessed in MATLAB to calculate the fractional anisotropy (FA) maps<sup>3,4,5,6</sup>.



#### We investigated five circuits in the brain responsible for cognitive functions:

• <u>Default Mode Network (DMN)</u>: (1) Medial Prefrontal Cortex (MPFC), (2) Rostral Anterior Cingulate Cortex (RACC), (3) Posterior Cingulate Cortex (PCC), (4) Precuneus (PC), and (5) Lateral Parietal Cortex (LPC)

•Attention: (1) Thalamus (Superior Colliculus and Pulvinar) (THAL), (2) Superior Parietal Lobule (SPL), (3) Middle Frontal Gyrus (MFG), (4) Superior Frontal Gyrus (SFG), (5) Angular Gyrus (AG), and (6) Supramarginal Gyrus (SMG)

•<u>Verbal memory:</u> (1) Inferior Temporal Gyrus (ITG), (2) Medial Occipitotemporal Gyrus (MOG), (3) Middle Temporal Gyrus (MTG), (4) Temporal Pole (TP), (5) Angular Gyrus (AG), and (6) Inferior Frontal Gyrus (IFG)

•<u>Memory:</u> (1) Angular Gyrus (AG), (2) Fusiform Gyrus (FG), (3) Superior Parietal Lobule (SPL), (4) Supramarginal Gyrus (SMG), (5) Hippocampal Formation (HF), and (6) Superior Frontal Gyrus (SFG)

•<u>Visual-Spatial Working Memory:</u> (1) Cingulate Region (CR), (2) Superior Frontal Gyrus (SFG), (3) Fornix, (4) Superior Parietal Lobule (SPL), and (5) Supramarginal Gyrus (SMG)

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#### RESULTS

Sociodemographic and clinical characteristics of subjects

	RRMS	CONTROLS
Gender		
Female	15	16
Male	5	22
Race		
White	14	
Black	6	
Others	0	
Age (median/range)	39.6 (26-54)	34.92 (17-64)
Median disease duration (range)	7 (5-20)	
EDSS (mean/range)	3 (1-8)	
Cognitive complains	6	

The percentile of the MS patients (N=20) having significant FA reduction (p < 0.05) of  $\geq 50\%$ 

Side	Anterior Limb of Internal Capsule	Frontal Lobe WM	Globus Palladus	Hippocam pal Formation	Lateral Occipito- temporal Gyrus	Occipital Lobe WM	Parietal Lobe WM	Tempor al Lobe WM	Uncus	Corpus Callosum
Right	60%	60%	55%	65%	50%	50%	65%	60%	85%	70%
Left	60%	60%	60%	55%	0	30%	60%	60%	55%	

The percentile of the MS patients (N=8) having increase in FA reduction at 1 year follow up

Side	Anterior Limb of Internal Capsule e		Fro Lobe	ntal WM	Glo Palla	bus adus	Hippo Forn	campal nation	Lat Occ tempor	teral ipito- al Gyrus	Occ Lobe	ipital e WM	Parie Lobe	etal WM	Tempora WN	al Lobe M	Un	cus	Cor Callo	pus osum
Time point	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd
Right	62.5	62.5	62.5	75	37.5	62.5	62.5	75	50	62.5	50	62.5	75	75	87.5	75	62.5	75		
Left	75	75	75	75	75	62.5	62.5	62.5	0	0	37.5	37.5	62.5	75	62.5	62.5	75	75	75	75

#### Sociodemographic, clinical, and radiological characteristics of subjects used for DTI and fMRI connectivity analysis

VARIABLE	MS subjects N=7	Healthy Controls N=18	p-value
Mean age at scan years (range)	35.7 (28-54)	36.4 (17-62)	
Mean (range) disease duration, years	4.8 (2-10)		
Median (range) EDSS score	2.25 (1-7.5)		
Use of disease-modifying therapies (Y/N)	7/0		
Complains of cognitive deficit	4		
	Mean (SD)	structural MRI metrics	
Brain Volume (cm <sup>3</sup> )	1051.00 (154.17	1196.84 (99.84	0.005
Thalamic Volume (cm <sup>3</sup> )	13.52 (1.01)	16.32 (1.59)	0.0006
White matter Volume (cm <sup>3</sup> )	427.90 (94.26)	500.76 (40.92)	0.008
Grey matter Volume	623.10 (67.96)	696.09 (66.21)	0.01

#### **DEFAULT MODE NETWORK**

Bilateral decreased DTI connectivity in MS subjects compared to controls. Asymmetric decreased fMRI connectivity involving left cingulate and parietal cortex. Higher functional connectivity was observed in bilateral posterior cingulate cortex and left precuneus.

	L MPFC	L RACC	L PCC	L PC	L LPC	R MPFC	R RACC	R PCC	R PC	R LPC	<b>P-Value</b>	fr vi
L MPFC		0.2202	0.1123	0.1424	0.2202	I		0.1155	I	_	0.3	
L RACC	- 0.1832		0.2202	0.1800	0.2202			0.2202		_	0.2	
L PCC	- 0.0001	0.0000		0.2202				0.3000		_	Increased Connectivit in MS	y
L PC	- 0.0001	0.0000	0.0003		0.2202			0.2202		-	0.1	
L LPC	- 0.0006	0.0782	0.1208	0.0022						-		
R MPFC	- 0.0000	0.0002	0.2852	0.0411	0.0638					-	0	
R RACC	- 0.0007	0.3000	0.2382	0.3000	0.1655	0.0992				-	0.1	
R PCC	- 0.0019	0.0013	0.0197	0.0027	0.1123	0.0003	0.0034			_	Decreased Connectivity in MS	y
R PC	- 0.0281	0.0037	0.0385	0.0024	0.0027	0.0001	0.0001	0.0050		-	0.2	
R LPC	- 0.1479	0.3000	0.3000	0.0020	0.0145	0.0001	0.3000	0.3000	0.0022			

DTI





