

# **Cognitive impairment and magnetic resonance diffusion tensor imaging (MRDTI) of the brain in multiple sclerosis**

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## **List of abbreviations**

<b>ACHE-I:</b>	Acetyl Choline Esterase- Inhibitor
<b>AD:</b>	Alzheimer Disease
<b>AD:</b>	Axial diffusivity
<b>ADC:</b>	Apparent diffusion coefficient
<b>AMPA:</b>	$\alpha$ -Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
<b>APCs:</b>	Antigen Presenting Cells
<b>APOE :</b>	Apolipoprotein E
<b>ATP:</b>	Adenosine Tri Phosphate
<b>AWM:</b>	Abnormal White Matter
<b>BAMA:</b>	Brief Assessment of Memory & Attention
<b>BBB:</b>	Blood Brain Barrier
<b>BDI:</b>	Beck Depression Inventory
<b>BICAMS:</b>	Brief International Cognitive Assessment for Multiple sclerosis
<b>BPF:</b>	Brain Parenchymal Fraction
<b>BVMT-R:</b>	Brief Visuospatial Memory Test- Revised
<b>BVRT:</b>	Benton Visual Retention Test
<b>CC:</b>	Corpus Callosum
<b>CCI:</b>	Corpus Callosum Index
<b>CIS:</b>	Clinically Isolated Syndrome

<b>CNS:</b>	Central Nervous System
<b>COWAT:</b>	Controlled Oral Word Association Test
<b>CSF:</b>	Cerebro Spinal Fluid
<b>CST:</b>	California Sorting Test
<b>CTL:</b>	Cytotoxic T- Lymphocyte
<b>CVLT:</b>	California Verbal Learning Test
<b>DC:</b>	Dendritic Cells
<b>DIR:</b>	Diffusion Inversion Recovery
<b>DTI:</b>	Diffusion Tensor Imaging
<b>DWI:</b>	Diffusion Weighted Imaging
<b>EAA:</b>	Excitatory Amino Acids
<b>EAE:</b>	Experimental Autoimmune Encephalitis
<b>EBV:</b>	Epstein- Barr virus
<b>EDSS:</b>	Extended Disability Survey Scale
<b>FA:</b>	Fractional Anisotropy
<b>fMRI:</b>	functional Magnetic Resonance Imaging
<b>FOXP3:</b>	Fork head box P3f
<b>FSS:</b>	Fatigue severity scale
<b>GAP-43:</b>	Growth Associated Protein-43
<b>GCA:</b>	Global Cortical Atrophy

<b>GM-CSF:</b>	Granulocyte- Macrophage Colony Stimulating Factor
<b>gWM:</b>	global White Matter
<b>HDRS:</b>	Hamilton Depression Rating Scale
<b>HLA:</b>	Human Leukocyte Antigen
<b>ICAM:</b>	Intercellular Adhesion Molecule
<b>ICR:</b>	Inter Caudate Ratio
<b>ICV:</b>	Intracranial Volume
<b>Ig:</b>	Immunoglobulin
<b>iNO:</b>	inducible Nitrous Oxide synthase
<b>INF:</b>	Interferon
<b>IL:</b>	Interleukin
<b>JLO:</b>	Judgment of Line Orientation test
<b>Kir:</b>	inwardly rectifying potassium channel
<b>MACFIMS:</b>	Minimal Assessment of Cognitive Function In Multiple Sclerosis
<b>MAG:</b>	Myelin Associated Glycoprotein
<b>MBP:</b>	Myelin Basic Protein
<b>MCI:</b>	Mild Cognitive Impairment
<b>MD:</b>	Mean Diffusivity
<b>MHC:</b>	Major Histocompatiblity Complex
<b>MLBV:</b>	Maximal Lifetime Brain Volume

<b>MMP:</b>	Matrix Metalloproteinase
<b>MMSE:</b>	Mini Mental State Examination
<b>MMMS:</b>	Modified Mini Mental State Examination
<b>MRI:</b>	Magnetic Resonance Imaging
<b>MOG:</b>	Myelin Oligodendrocyte Glycoprotein
<b>MS:</b>	Multiple Sclerosis
<b>MSNQ:</b>	Multiple Sclerosis Neuropsychological Questionnaire
<b>MTR:</b>	Magnetization Transfer Ratio
<b>NAA:</b>	N-Acetyl Aspartate
<b>NAWM:</b>	Normally Appearing White Matter
<b>NK:</b>	Natural Killer
<b>NMO:</b>	Neuromyelitis Optica
<b>NO:</b>	Nitrous Oxide
<b>NOs:</b>	Nitrous Oxide synthase
<b>PALT:</b>	Paired Associate Learning Test
<b>PASAT:</b>	Paced Auditory Serial Addition Test
<b>PLP:</b>	Proteolipid Protein
<b>PPMS:</b>	Primary Progressive Multiple Sclerosis
<b>PRMS:</b>	Progressive Relapsing Multiple Sclerosis
<b>RD:</b>	Radial Diffusivity

<b>RIS:</b>	Radiologically Isolated Syndrome
<b>ROI:</b>	Region of Interest
<b>RRMS:</b>	Relapsing Remitting Multiple Sclerosis
<b>SDMT:</b>	Symbol Digit Modality Test
<b>SPMS:</b>	Secondary Progressive Multiple Sclerosis
<b>TBSS:</b>	Tract Based Spatial Statistics
<b>TCR:</b>	T- Cell Receptor
<b>TGF:</b>	Transforming Growth Factor
<b>Th:</b>	T –helper cells
<b>TMT:</b>	Trail Making Test
<b>TNF:</b>	Tumor Necrosis Factor
<b>Treg:</b>	T- regulatory cells
<b>TREM:</b>	Transmembrane Signaling Protein
<b>VBM:</b>	Voxel Based Morphometry
<b>VCAM:</b>	Vascular Cell Adhesion Molecule
<b>VLA:</b>	Very Late Activating antigen
<b>VZV:</b>	Varicella Zoster Virus
<b>WCST:</b>	Wisconsin Card Sorting Test

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## Abstract

**Abstract: Background:** Cognitive impairment is a common concomitant of multiple sclerosis (MS) at both the earlier and later stages of the disease. **Objective:** to study the pattern of cognitive impairment in various types of MS and its correlation to the results of conventional MRI (c MRI) and diffusion tensor MRI (DTMRI) of the brain. **Methods:** this study done on 40 multiple sclerosis patients (MS) & 20 healthy control groups, patient group divided into two subgroups 20 RRMS, & 20 SPMS patients. Cognitive function tests have been done for both groups, c MRI & DTMRI of the brain have been done for MS group. **Results:** a significant difference was found between cases & control in most of cognitive function tests. Significant difference was found between RRMS & SPMS in cognitive function test & DTMRI brain results (for corpus callosum & temporal lobe) being severe in SPMS patients. Significant difference was found between RRMS & SPMS in c MRI results as regards to brain atrophy being severe in SPMS patients. **Conclusion:** cognitive dysfunction & brain atrophy occurs early in MS. Cognitive dysfunction was more severe in SPMS than in RRMS patients. DTI brain of NAWM was correlated with cognitive dysfunction in MS especially in regions of corpus callosum, temporal & prefrontal lobes.

**Keywords:** cognitive dysfunction, multiple sclerosis, diffusion tensor MRI

# Introduction

Cognitive decline is common in approximately 40–70% of patients with multiple sclerosis (MS). Cognitive symptoms are observed across all disease subtypes but they tend to be more significant in primary and secondary progressive MS. Cognitive deficits may precede the onset of MS in so far as 1.2 years. MS patients with early verbal deficits are more prone to cognitive impairment. Cognitive impairment is known to progress especially if it occurs early in MS and deterioration of cognitive dysfunction can be expected over a three year period (**Chiaravalloti & DeLuca, 2008; Amato et al., 2010; Bartko et al., 2012; Achiron et al., 2013; Viterbo et al., 2013**).

Cognitive dysfunction is closely associated with functional status in multiple sclerosis (MS). Individuals with MS who were cognitively impaired participated in fewer social and vocational activities. MS patients have a reduced ability to make decisions that could affect functioning during everyday life. The extent of cognitive decline has proven to be a significant & independent predictor of handicap in a patient's work & social activity more than the degree of physical impairment (measured by extended disability survey scan). MS is a disease of white matter & grey matter. Both white matter and grey matter affection are responsible for the cognitive impairment in MS (**Rao et al., 1991; Kessler et al., 1992; Beatty et al., 1995; Hoffmann et al., 2007; Benedict et al., 2008; Chelune et al., 2008; Shi et al., 2008**).

Conventional MRI has been known for several decades in diagnosis of MS. It has been used for diagnosis of cognitive impairment in MS by detection of brain atrophy & estimation of T<sub>1</sub>, T<sub>2</sub> lesion burden. Brain atrophy can occur early in MS even in the preclinical stage of MS

as clinically & radiologically isolated syndromes. Cognitive impairment can be presented early in MS (**Rao et al., 1989; Summers et al., 2008**).

Diffusion tensor imaging (DTI) is an effective means of quantifying parameters of demyelination and axonal loss. The assessment of the microstructural alterations of white and grey matter in MS by DTI may shed light on mechanisms responsible for irreversible disability accumulation including cognitive impairment. DTI is superior to conventional MRI in revealing tract injury responsible for cognitive dysfunction in MS patients (**Hoffmann et al., 2007; Roca et al., 2008; Sbardella et al., 2013**).

Other neuroimaging techniques is under investigation may be later used in early diagnosis of cognitive dysfunction in MS patients as magnetic resonance spectroscopy (MRS), positron emission tomography (PET), functional magnetic resonance imaging (fMRI) (**Chiaravalloti & DeLuca, 2008; Inglese et al., 2008**).

- **Aim of work:**

Aim of this study is:

- Comparing between relapsing remitting MS (RRMS) & secondary progressive MS (SPMS) in pattern of cognitive impairment.
- Correlation between the results of DTI with cognitive function tests in MS patients with comparison between RRMS & SPMS in results of DTI.
- Correlation between the findings of conventional MRI with cognitive function tests in MS patients with comparison between RRMS & SPMS in findings of conventional MRI.