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

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By

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List of abbreviations

ACHE-I: Acetyl Choline Esterase- Inhibitor

AD: Alzheimer Disease

AD: Axial diffusivity

ADC: Apparent diffusion coefficient

AMPA: α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid

APCs: Antigen Presenting Cells

APOE : Apolipoprotien E

ATP: Adenosine Tri Phosphate

AWM: Abnormal White Matter

BAMA: Brief Assessment of Memory & Attention

BBB: Blood Brain Barrier

BDI: Beck Depression Inventory

BICAMS: Brief International Cognitive Assessment for Multiple sclerosis

BPF: Brain Parenchymal Fraction

BVMT-R: Brief Visuospatial Memory Test- Revised

BVRT: Benton Visual Retention Test

CC: Corpus Callosum

CCI: Corpus Callosum Index

CIS: Clinically Isolated Syndrome

CNS: Central Nervous System

COWAT: Controlled Oral Ward Association Test

CSF: Cerebro Spinal Fluid

CST: California Sorting Test

CTL: Cytotoxic T- Lymphocyte

CVLT: California Verbal Learning Test

DC: Dendritic Cells

DIR: Diffusion Inversion Recovery

DTI: Diffusion Tensor Imaging

DWI: Diffusion Weighted Imaging

EAA: Excitatory Amino Acids

EAE: Experimental Autoimmune Encephalitis

EBV: Epstein- Barr virus

EDSS: Extended Disability Survey Scale

FA: Fractional Anisotropy

fMRI: functional Magnetic Resonance Imaging

FOXP3: Fork head box P3f

FSS: Fatigue severity scale

GAP-43: Growth Associated Protien-43

GCA: Global Cortical Atrophy

GM-CSF: Granulocyte- Macrophage Colony Stimulating Factor

gWM: global White Matter

HDRS: Hamilton Depression Rating Scale

HLA: Human Leukocyte Antigen

ICAM: Intercellular Adhesion Molecule

ICR: Inter Caudate Ratio

ICV: Intracranial Volume

Ig: Immunoglobulin

iNO: inducible Nitrous Oxide synthase

INF: Interferon

IL: Interleukin

JLO: Judgment of Line Orientation test

Kir: inwardly rectifying potassium channel

MACFIMS: Minimal Assessment of Cognitive Function In Multiple Sclerosis

MAG: Myelin Associated Glycoprotein

MBP: Myelin Basic Protein

MCI: Mild Cognitive Impairment

MD: Mean Diffusivity

MHC: Major Histocompatiblity Complex

MLBV: Maximal Lifetime Brain Volume

MMP: Matrix Metalloproteinase

MMSE: Mini Mental State Examination

MMMS: Modified Mini Mental State Examination

MRI: Magnetic Resonance Imaging

MOG: Myelin Oligodendrocyte Glycoprotien

MS: Multiple Sclerosis

MSNQ: Multiple Sclerosis Neuropsychological Questionnaire

MTR: Magnetization Transfer Ratio

NAA: N-Acetyl Aspartate

NAWM: Normally Appearing White Matter

NK: Natural Killer

NMO: Neuromyelitis Optica

NO: Nitrous Oxide

NOs: Nitrous Oxide synthase

PALT: Paired Associate Learning Test

PASAT: Paced Auditory Serial Addition Test

PLP: Proteolipid Protein

PPMS: Primary Progressive Multiple Sclerosis

PRMS: Progressive Relapsing Multiple Sclerosis

RD: Radial Diffusivity

RIS: Radiologically Isolated Syndrome

ROI: Region of Interst

RRMS: Relapsing Remitting Multiple Sclerosis

SDMT: Symbol Digit Modality Test

SPMS: Secondary Progressive Multiple Sclerosis

TBSS: Tract Based Spatial Statistics

TCR: T- Cell Receptor

TGF: Transforming Growth Factor

Th: T –helper cells

TMT: Trail Making Test

TNF: Tumor Necrosis Factor

Treg: T- regulatory cells

TREM: Transmembrane Signaling Protein

VBM: Voxel Based Morphometry

VCAM: Vascular Cell Adhesion Molecule

VLA: Very Late Activating antigen

VZV: Varicella Zoster Virus

WCST: Wisconsian 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 impairement 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_1, T_2 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), poisteron emission tomography (PET), functional magnetic resonance imaging (f MRI) **(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.