Cognitive Assessment in Patients with Multiple Sclerosis

Thesis Submitted for Partial Fulfillment Of
Master Degree in **Neuropsychiatry**

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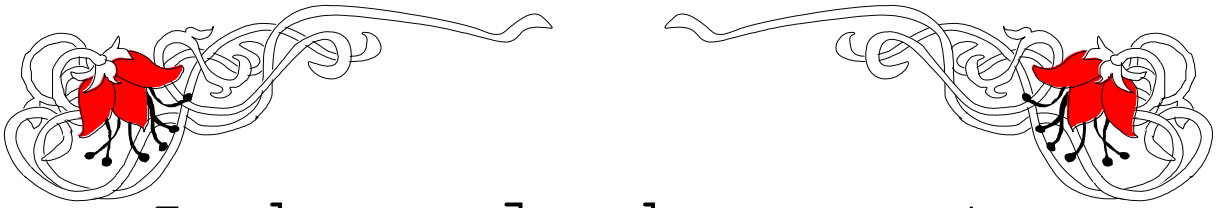

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Thank to Allah

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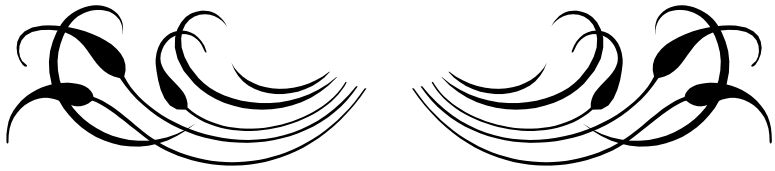

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LIST OF ABBREVIATIONS

ACH	Acetylcholine
AD	Alzheimer's Disease
ADEM	Acute Disseminated Encephalomyelitis
ANA	Antinuclear Antibody
ANCA	Antineutrophil Cytoplasmic Antibody
BP	Bodily Pain
BDI	Beck Depression Inventory
CADASIL	Cerebral Autosomal Dominant Arteriopathy With Subcortical And Leukoencephalopathy
CBT	Cognitive Behavioural Therapy
CIS	Clinical Isolated Syndrome
CNS	Central Nervous System
CSF	Crebro Spinal Fluid
CT	Computed Tomogrghy
EAE	Experimental Autoimmune Encephalomyelitis
ECT	Electroconvulsive Therapy
EDSS	Expanded Disability Status Scale
ESR	Erythrocyte Sedimentation Rate
FAMS	Functional Assessment Of Multiple Sclerosis Questionnaire
FDA	Food And Drug Adminstration
FS	Functional Systems
FSS	Functional System Sc

GH	General Health
IQ	Intelligent Quotient
HAQUAMS	Hamburg Quality Of Life Questionnaire In Multiple Sclerosis
HLA	Human Leukocyte Antigen
HPA	Hypothalamicpitutary-Adrenal
HRQOL	Health Related Quality Of Life
IEED	Involuntary Emotional Expression Disorder
IEF	Isoelectric Focusing
IFN	Interferon
IL	Interleukin
IV	Intravenous
LHON	Leber's Hereditary Optic Neuropathy
MACFIMS	Minimal Assessment Of Cognitive Dysfunction In Ms
MAO	Monoamine Oxidase
MDEM	Multiphasic Disseminated Encephalomyelitis
MDFI	Multidimensional Fatigue Inventoray
MH	Mental Health
MHC	Major Histocompatibility Complex
MRI	Magnetic Resonance Imaging
MS	Multiple Sclerosis
MSD	MS Depression
MSF	MS Fatigue
MSIS	Multiple Sclerosis Impact Scale

MSQLI	Multiple Sclerosis Quality Of Life
NAAG	N-Acetyl Aspartyl Glutamate
PAS	Pathognomic Period Acid-Schiff
PBA	Pseudo Bulbar Affect
PCR	Polymerase Chain Reaction
PF	Physical Functioning
PPMS	Primary Progressive Ms
PRISMS	Prevention Of Relapses And Disability By Interferon Beta 1-A Subcutaneously In Ms
OCBs	Oligo Clonal Bands
QOL	Quality Of Life
RE	Role Emotional
RIMAs	Reversible Inhibitors Of Mao-A
RRMS	Relapsing-Remitting Multiple Sclerosis
RP	Role Physical
RT	Relaxation Training
SBE	Subacute Bacterial Endocarditic
SF-36	Health Status Questionnaire
SNRIs	Serotonin Nor-Adrenaline Reuptake Inhibitors
SPMS	Secondary Progressive MS
SF	Social Functioning
SSRIs	Selective Serotonin Reuptake Inhibitors
TCA	Tricyclic Antidepressants
VI	Vitality Index

WAIS	Wechsler Adult Intelligence Scale
WMS	Wechsler Memory Scale
WCST	Wisconsin Card Sorting Test

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Introduction

Multiple sclerosis (MS) is an autoimmune disorder of the central nervous system (CNS) predominantly supported by a T helper 1 immune reaction **(Bagnato et al., 2003).** Although the etiology is predominantly unknown, MS is characterized pathologically by demyelination and subsequent axonal degeneration ***(Calabresi* 2004*)*.**

The clinical symptoms of the disease are varied, depending on the location of plaques or lesions within the CNS, but can include both physical difficulties (e.g. limb weakness, optic neuritis, incontinence, vertigo, ataxia, facial paralysis, seizures& fatigue) and also cognitive difficulties (e.g. aphasia, poor learning and memory, attention and concentration, mental speed, problem solving and word finding) **(Parmenter et al., 2007).**

Cognitive impairment occurs in about 50% of patients with MS **(Amato et al,.2006)** , even during the early stages of the disease **(Feuillet et al., 2007).** It is probably the most important determinant of employment status and associated societal costs, and also adversely affects driving safety, household task completion, social activity, physical independence, rehabilitation progress, coping, treatment adherence and mental health **(Langdon, 2011)**.

Cognitive dysfunction may subsequently result in reduced fulfillment in work life and social life as well as in a reduction in quality of life (QoL) **(Benedict et al., 2005).** Cognitive deficits typically involve

a few cognitive domains, spare language and are often undetected at consultation **(Langdon, 2010).**

Information processing speed is the most vulnerable cognitive ability, followed by episodic memory, and executive function **(Strober et al., 2009).** There is high interpatient variability, in part due to varying compensation capacities (cognitive reserve) **(Sumowski et al, 2010).**

Cognition is only loosely related to disease duration (**Amato et al., 2010),** and physical disability (in some instances clearly dissociated) **(Amato et al., 2008),** and is more strongly related to brain MRI parameters, especially atrophy **(Filippi et al., 2010).** The cognitive deficits seen in MS implicate a subcortical pathology similar to the subcortical dementias associated with other chronic diseases **(Turner et al., 2002).**

Patients may not be fully aware of their deficits, or may not report them reliably. Depression results in over-reporting **(Kinsinger et al.,2010)**, whilst metamemory impairment and insight loss lead to underestimation **(Sherman et al,. 2008).**

Aim of the Work

To investigate the cognitive dysfunctions in patients with MS, their related factors & their impact on quality of life.

Multiple sclerosis (MS)

Multiple sclerosis (MS), also known as disseminated sclerosis or encephalomyelitis disseminata, is an inflammatory disease in which the insulating covers of nerve cells in the brain and spinal cord are damaged. This damage disrupts the ability of parts of the nervous system to communicate, resulting in a wide range of signs and symptoms **(Compston and Coles, 2008),** including physical, mental, and sometimes psychiatric problems ***(Murray, et al., 2012).*** MS takes several forms, with new symptoms either occurring in isolated attacks (relapsing forms) or building up over time (progressive forms). Between attacks, symptoms may go away completely; however, permanent neurological problems often occur, especially as the disease advances ***(Murray, et al., 2012).***

While the cause is not clear, the underlying mechanism is thought to be either destruction by the immune system or failure of the myelin-producing cells ***(Reingold, et al., 1996).*** Proposed causes for this include genetics and environmental factors such as infections. MS is usually diagnosed based on the presenting signs and symptoms and the results of supporting medical tests ***(Nakahara, et al., 2012).***

There is no known cure for multiple sclerosis. Treatments attempt to improve function after an attack and prevent new attacks. Medications used to treat MS while modestly effective can have adverse effects and be poorly tolerated. Many people pursue alternative treatments, despite a lack of evidence. The long-term outcome is difficult to predict, with good outcomes more often seen in women; those who develop the disease early in life; those with a relapsing course; and those who initially experienced few attacks. Life expectancy is 5 to 10 years lower than that of an unaffected population ***(Weinshenker, 1994)***.