Computerized Dynamic Posturography findings in relapsing-remittent multiple sclerosis patients

Thesis submitted for partial fulfillment of the M.sc. Degree in Audiology

By:

Omnia Ismail Ahmed El-sayed

M.B.B.Ch

Supervisors:

Prof. Dr. Mostafa El khosht Mahmoud

Professor of Audiology

Faculty of medicine

Cairo University

Prof. Dr. Sherif Hamdy Abdel Maksoud

Professor of Neurology

Head of Neurology Department

Faculty of medicine

Cairo University

Dr. Mona Mohamed Hamdy

Lecturer of Audiology

Faculty of medicine

Cairo University

Faculty of Medicine

Cairo University

2015

نتائج اختبار الإتزان الحركي لمرضى التصلب المتعدد الإنتكاسي الترددي

بحث توطئة واستيفاء جزئيا للحصول على درجة الماجستير في أمراض السمع والصمم

أمنية إسماعيل أحمد السيد

بكالوريوس الطب والجراحة
جامعة قناة السويس

تحت إشراف

أ.د: مصطفى الخشت محمود
أستاذ أمراض السمع والصمم
كلية الطب
جامعة القاهرة

أ.د: شريف حمدي عبد المقصود
أستاذ الأمراض العصبية
رئيس قسم الأمراض العصبية
كلية الطب
جامعة القاهرة

د: منى محمد حمدي
مدرس أمراض السمع والصمم
كلية الطب
جامعة القاهرة

كلية الطب
جامعة القاهرة
٢٠١٥

Acknowledgment

First and for most, I feel always indebted to **ALLAH** *the kind and merciful.*

I wish to express my sincere thanks and appreciation to ***Prof. Dr. Mostafa El Khosht Mahmoud****, professor of* Audiology*, Faculty of Medicine, Cairo University for his continuous support, constant encouragement, unlimited help and fruitful guidance.*

I would like to express my sincere thanks and appreciation to ***Prof. Dr. Sherif Hamdy Abdelmaksoud*** *professor of neurology and head of neurology department, Faculty of Medicine, Cairo University, for his great effort, continuous encouragement, kind guidance and support throughout this work.*

My deepest gratitude and appreciation to ***Dr. Mona Mohamed Hamdy,*** *lecturer of Audiology, Faculty of Medicine, Cairo University for her continuous support, great help, meticulous supervision and valuable guidance.*

Last but not least, I want to thank my mother, my father & my whole family for their help and reassurance as without their help, this work could not have been completed.

Key words:

MULTIPLE SCLEROSIS_ POSTUROGRAPHY_ RELAPSING- REMITTENT_ EDSS_ BALANCE

ABSTRACT

Multiple sclerosis is an autoimmune demyelinating disease of the contral nervous system, and it is considered one of the commonest causes of non-traumatic neurological disabilitiy in young adults.
Impaired upright postural control and fratigue are considered the most common symptoms affecting people with MS, with reports of fatigue ranging from 50% to 85%, and impaired balance up to 87.9%.

INTRODUCTION AND RATIONALE

Multiple sclerosis (MS) is an autoimmune demyelinating disease of the central nervous system **(Kessler et al., 2011)**, and it is considered one of the commonest causes of non-traumatic neurological disability in young adults **(Yahia et al., 2011)**.

MS affects approximately 400,000 people in the United States **(National MS Society, 2011; Asche et al., 2010)** and about 2.3 million people worldwide **(MSIF, 2014)**, but unfortunately there are limited epidemiological data from the Middle Eastern countries regarding the prevalence, incidence or natural history of MS **(MSIF, 2014; Bohlega et al., 2013).**

Onset of MS usually occurs during the peak productive ages of 20 to 50 years **(NINDS, 2010)**, and affects women as twice as men according to MSIF report **(MSIF, 2014)**.

At the time of diagnosis, 85% of people had relapsing-remitting MS. It has been estimated that up to 80% of these people will go on to develop secondary progressive MS **(Holland et al., 2011).** And about 10% of people were diagnosed with primary progressive MS and 5% with progressive relapsing MS **(MSIF, 2014)**.

Fatigue and impaired upright postural control are considered the most common symptoms affecting people with MS **(Herbert et al., 2011)**, with reports of fatigue ranging from 50% to 85%, and impaired balance up to 87.9% **(Finlayson et al., 2010)** which strongly affect their physical activity and quality of life **(Motl et al., 2011)**.

MS can affect all areas of the central nervous system and cause such a wide range of impairments which may be thought to have multifactorial causes **(Alpini et al., 2012)**. A review by **Cameron et al.** in 2010 showed that changes in postural control in patients with MS are most likely to be the result of slowed somatosensory conduction as well as impaired central integration control.

Over the course of the disease, MS can lead to severe handicap. To evaluate the degree of neurologic impairment in MS, Kurtzke **(Kurtzke, 1983)** proposed the expanded disability status scale (EDSS), which is the most widely used scale. It is a 20-step scale of disease severity ranging from 0 (normal) to 10 (death due to MS).

The scale considers eight functional systems (FS): pyramidal, cerebellar, brainstem, sensory, bowel & bladder, visual, cerebral, and other. These FS represent eight different areas of the central nervous system and each ranges from 0 (normal) to 5 or 6 (maximal impairment). These FS scores plus indications of mobility and restrictions in daily life are used to rate the EDSS **(Kurtzke, 1983)**.

Computerized Dynamic Posturography (CDP) is a unique assessment technique used to objectively quantify and differentiate among the possible sensory, motor, and central adaptive impairments to balance control. CDP can identify and differentiate the functional impairments associated with the pathological processes. But by itself, CDP cannot diagnose pathology or site-of-lesion **(Clarke, 2010).**

Because of the complex interactions among sensory, motor, and central adapting processes, CDP requires separate protocols to adequately differentiate among impairments and quantify the failure of adaptive

mechanisms by exposing the patient to a variety of controlled visual and support surface conditions **(Duarte et al., 2010)**.

The Sensory Organization Test (SOT) protocol objectively identifies abnormalities in the patient's use of the three sensory systems that contribute to postural control which are: somatosensory, visual and vestibular **(Shepard et al., 2010).**

During the SOT, information delivered to the patient's eyes, feet and joints is effectively eliminated through calibrated "sway referencing" of the support surface and/or visual surround, which tilt to follow the patient's anteroposterior body sway **(Duarte et al., 2010)**.

By controlling the sensory (visual and proprioceptive) information through sway referencing and/or eyes open/closed conditions, the SOT protocol eliminates useful visual and/or support surface information and creates sensory conflict situations. These conditions isolate vestibular balance control, as well as stress the adaptive responses of the central nervous system. Consequently, patients may display either an inability to make effective use of individual sensory systems, or inappropriate adaptive responses, resulting in the use of inaccurate sense(s) **(Doumas et al., 2010)**.

As MS affects balance and postural control, and as it has been noted in many studies that this may be due to delayed somatosensory conduction, CDP testing will be our choice to investigate such issue using the SOT protocol.

AIMS OF THE WORK

1- Evaluation of balance control in patients with relapsing-remittent MS.

2- Comparison of SOT results between patient and control groups.

3- Comparison of CDP results with the EDSS.

CHAPTER (1)

MULTIPLE SCLEROSIS

Multiple sclerosis is a complex chronic immune mediated disease of the central nervous system (CNS) **(Lassmann et al., 2007)**, and is considered one of commonest chronic, non-traumatic neurological disorders among young adults **(Yahia et al., 2011)**. Onset usually occurs during the peak productive ages of 20 to 50 years **(NINDS, 2010)**.

Lifetime risk of MS in the general population is about one in 1,000. The risk increases to about 2% in children with one parent who has MS and is even higher in children whose parents are both affected. Siblings of an affected person have about 4% chance of developing the disease during the course of their lives. Lifetime risk of MS further increases to 5% in dizygotic twins and to 25% in monozygotic twins **(Compston et al., 2008; McElroy et al., 2008)**.

The cumulative prevalence of MS in the United States is currently about 400,000, or 135 cases per 100,000 **(Koch-Henriksen et al., 2010)**.

Globally, approximately 2.3 million persons suffer from this disease **(MSIF, 2014)**, but unfortunately there are limited epidemiological data from the Middle Eastern countries regarding the prevalence, incidence or natural history of MS **(MSIF, 2014; Bohlega et al., 2013)**.

In Egypt, there are no nationwide studies to define the exact status of multiple sclerosis. A study performed in three tertiary centers in Cairo however found MS to represent 1.41% of all neurological diseases **(Hashem et al., 2010)**. A door-to door study in Al-Qusair City, Egypt found the prevalence of MS to be 13.74/100,00 **(El Tallawy et al., 2010)**.

ETIOLOGY

Complex genetic traits as well as environmental factors determine the susceptibility to develop MS and the respective results indicate that immune mechanisms play an essential role in driving the disease process **(IMSGC, 2010)**.

GENETICS

Among first-degree relatives of an index case, the lifetime risk is 3% to 5%; for a monozygotic twin, which represents 25%. The identification of specific risk alleles, and the expression of their related gene products, is still a subject of much interest and ongoing research **(Sawcer et al., 2011)**.

ENVIRONMENTAL FACTORS

Environmental factors are thought to play an important role in the development of MS **(Sawcer et al., 2011)**. Studies have shown an association between latitude and risk, with the lowest risk in found among persons living near the equator **(Simpson et al., 2011)**. Thus, the prevalence of MS is higher in geographic locales having less sunlight exposure (and hence diminished production of vitamin D), suggesting that low levels of vitamin D may be a risk factor **(Ascherio et al., 2010)**.

Also, it was found that persons who smoke have an increased relative risk of developing MS compared to those who do not **(Wingerchuk, 2012)**.

Certain infections acquired at a young age, and characterized by chronic latency and CNS trophism, have been implicated as risk factors **(Ascherio et al., 2007)**.

These include mumps, rubella, Epstein-Barr virus (EBV) **(Handel et al., 2010)**, human herpes virus 6 (HHV-6) **(Voumvourakis et al., 2010)**, and Chlamydia pneumonia **(Contini et al., 2010)**.

Although genetic material and proteins specific to microbial agents have been identified in MS brain lesions, and specific T-cell or antibody responses in blood and CSF have been found in some MS patients, the significance of these findings is uncertain, and the role of infection remains unclear **(Pawate et al., 2010)**.

PATHOPHYSIOLOGY

It was for long time believed and is still postulated in many recent publications that MS is an autoimmune disease, in which the immune reaction is directed against one or more myelin antigens. This simplistic view, however, is misleading. Autoimmunity, mediated by Class II restricted T-cells, shows very similar patterns of inflammation and tissue injury in the CNS, regardless whether it is directed against myelin, neuronal or astrocytic antigens, although the distribution of the lesions within the CNS may vary in an antigen specific manner **(Krishnamoorthy et al., 2009)**.

The mechanism by which autoreactive T-lymphocytes traverse the blood brain barrier to initiate inflammation is poorly understood (**Goverman, 2009)**. There is some evidence that early in the disease process there is an increase in adhesion molecules, particularly intercellular adhesion molecule-1 (ICAM-1), on the vascular endothelium of brain and spinal cord. These molecules increase the permeability of the blood-brain barrier and could permit the entry of lymphocytes **(Lebedeva et al., 2005)**.

Upon entry into the CNS compartment, previously activated T-lymphocytes proliferate and engage myelin-based antigens, triggering the autoimmune inflammatory cascade leading to demyelination. The release of cytokines activates microglial cells (CNS macrophages) which in turn promotes the expression of class II major histocompatibility complex (MHC) molecules and the accumulation of additional cytokines and other inflammatory mediators, such as nitric oxide, free radicals, and superoxide. The net result is a sustained proinflammatory state that destroys myelin, disrupts oligodendrocyte integrity and function, and damages axons **(Frohman et al, 2011)**.

Demyelination impairs nerve impulse transmission and leads to abnormal patterns of nerve conduction, which accounts in large part for the various clinical symptoms and signs of MS **(Agamanolis, 2015)**.

The B-lymphocyte arm of the immune system may play a role in certain aspects of MS during the late stages of disease when inflammatory changes are more marked in the gray matter of the brain. In contrast to T-cell mediated inflammation of white matter, myelin-reactive B-lymphocytes and the secretion of myelin-specific antibodies appear to play a significant role in the pathogenesis of gray matter inflammatory injury **(Lisak et al., 2012)**.

PATHOLOGY

The characteristic MS plaque is formed as follows: in the acute phase, activated mononuclear cells, including lymphocytes, microglia, and macrophages destroy myelin and to a variable degree, oligodendrocytes. Myelin debris are picked up by macrophages and degraded. At an early stage, macrophages contain myelin fragments;

later, myelin proteins, and, at the end, lipids from chemical degradation of myelin proteins **(Agamanolis, 2015)**.

This evolution takes a few weeks. With time, gliosis develops, and plaques reach a burned-out stage consisting of demyelinated axons traversing glial scar tissue. Remaining oligodendrocytes attempt to make new myelin. If the inflammatory process is arrested at an early phase, plaques are partially remyelinated. In more advanced lesions, remyelination is ineffective because gliosis creates a barrier between the myelin producing cells and their axonal targets **(Agamanolis, 2015)**.

In most cases, the inflammatory reaction subsides only to appear at another location or at another time. Some lesions expand at their periphery while activity in their center dies down **(Agamanolis, 2015)**.

SYMPTOMS

MS symptoms can be categorized into three categories: primary, secondary, and tertiary.

PRIMARY SYMPTOMS:

Primary symptoms of MS are caused by the demyelination of the CNS and spinal cord **(National MS Society, 2010)**. The most common primary symptoms in patients with MS are:

Fatigue

Fatigue is a characteristic finding in patients with MS, seen in as many as 78 % of patients, and is usually described as physical exhaustion that is unrelated to the amount of activity performed **(Braley et al., 2010)**.

Primary MS-related fatigue typically occurs daily and worsens as the day goes on thus so far interferes with daily activities, also, it is often aggravated by heat and humidity **(Olek et al., 2015)**.

However, there is a poor correlation between fatigue and the overall severity of disease or with the presence of any particular symptom or sign (**Krupp et al., 2010)**.

Heat Sensitivity

Heat sensitivity (also known as Uhthoff phenomenon) is common in most individuals with MS. This occurs when the body becomes overheated due to fever, physical exercise, or exposure to a hot environment. It is suspected that the increase in body temperature results in nerve conduction block in central pathways (**Frohman et al., 2013)**.

Patients with MS reach this stage earlier and at comparatively lower temperatures than healthy individuals because nerves are demyelinated. Also, a small increase in body temperature can temporarily result in worsening of neurologic signs and symptoms (**Frohman et al., 2013)**.

Spasticity

The majority of patients with MS report some level of spasticity. Painful muscle spasm is experienced by approximately 15% and is often a source of debilitation (**Foley et al., 2013)**.

Dizziness and Vertigo

Approximately 49% to 59% of MS patients suffer from dizziness or vertigo, and this condition is usually associated with impairment of cranial nerves (**Marrie et al., 2013)**.

Pain

Up to 80% of patients with MS experience varying degrees of pain, and an estimated 50% experience chronic pain (**Piwko et al., 2007)**.One study found that 63% of patients with MS reported one or more painful symptoms (**Foley et al., 2013)**.

Impaired Cognition

Approximately 40% to 70% of patients with MS experience varying degrees of cognitive impairment (**Siengsukon, 2013)**.

Vision Problems

Impaired vision is frequently present in patients with MS, most commonly unilateral optic neuritis, which is present in approximately in 66% of cases. It can also lead to blurring of vision or blindness in one eye. Approximately 90% of those patients regain normal vision over a period of 2 to 6 months after an acute episode of optic neuritis **(National MS Society, 2013)**.

Patients may also present with internuclear ophthalmoplegia (INO), a condition characterized by impaired nystagmus and defective horizontal ocular movements of the abducting eye. When present in young patients, bilateral internuclear ophthalmoplegia is suggestive of MS **(National MS Society, 2013)**.

Sensory Symptoms

Sensory disturbances are often one of the earliest symptoms of MS and occur in 20 to 40% of individuals with the disease. These disturbances may include one or more of the following: numbness, unpleasant feelings or paresthesias, and Lhermitte's sign **(MSIF, 2014)**.