THE VALUE OF BIOMARKERS, NEUROPHYSIOLOGY AND NEUROPSYCHOLOGY IN DIAGNOSIS AND PROGNOSIS OF MESIAL TEMPORAL SCLEROSIS

Thesis

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لجنة المناقشة و الحكم علي رسالة الدكتوراة المقدمة من الطبيبة هبة الله ساهر السيد هاشم توطئة للحصول علي درجة الدكتوراة في الامراض العصبية و المشكلة بقرار من مجلس الكلية و المعتمد من السيد الاستاذ الدكتور نائب رئيس الجامعة للدراسات العليا

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TO MY FAMILY

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ABBREVIATIONS

ACTH	Adrenocorticotrophic hormone
AED	Antiepileptic drug
AEDs	Antiepileptic Drugs
BBB	Blood Brain Barrier
BDNF	Brain-derived neurotrophic factor
bMTLE	Benign mesial temporal lobe epilepsy
CA	Cornu Ammonis
CNS	Central Nervous System
CRP	C-reactive Protein
CSD	Cortical spreading depression
DG	Dentate Gyrus
DTI	Diffusion tensor imaging
EC	Entorhinal cortex
ECM	Extracellular Matrix
EEG	Electoencephalogram
FCD	Focal cortical dysplasia
FMTLE	Familial mesial temporal lobe epilepsy
FS	Febrile Seizures
HS	Hippocampal Sclerosis
ILAE	International League Against Epilepsy
IPI	Initial Precipetating Incident
IVIG	Intravenous immunoglobulin
LTP	Long-term potentiation
MF	Mossy Fibers
MMP9	Matrix Metalloproteinase 9

MRI	Magnetic Resonance Imaging
MRS	Proton magnetic resonance spectroscopy
MTLE	Mesial Temporal Lobe Epilepsy
MTLE-HS	Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis
PTZ	Pentylenetetrazole
RAGE	Receptor for Advanced Glycation End products
S100b	S100 calcium binding protein B
SE	Status Epilepticus
TBI	Traumatic Brain Injury
TIMPs	Tissue inhibitors of metalloproteinases
TIRDA	Temporal intermittent rhythmic delta activity
TLE	Temporal Lobe Epilepsy
VBM	Voxel-based morphometry

ABSTRACT

Mesial temporal lobe epilepsy associated with hippocampal sclerosis is the most common form of partial epilepsy. **The aim of this work** is to find a suitable biomarker that can help with the diagnosis and prognosis of this intractable form of epilepsy. To achieve this aim, 30 patients with complex partial seizures and 30 controls with ages from 4-30 years were subjected to a battery of laboratory analysis including: S100B protein, Matrix Metalloproteinase 9, C-Reactive protein, prolactin, together with neurophysiological, radiological and psychometric assessments.

Results: A significant elevation was found in all the biomarkers between the cases and the controls. The performance of the epileptic patients in psychometric assessments were below average. MRI showed typical findings of MTS, EEG showed anterior temporal spikes. A significant negative correlation was found between MMP9 and psychometric test. Another significant negative correlation between seizure severity and biomarkers was found.

Conclusion: Serum biomarkers for neuronal injury are elevated with mesial temporal lobe epilepsy. Cognitive deficits are associated with mesial temporal lobe epilepsy.

KEYWORDS:

Mesial temporal lobe epilepsy, Hippocampal sclerosis, S100B, MMP9, CRP, Prolactin, psychometric assessments

INTRODUCTION

INTRODUCTION

Epilepsy has been recognized since antiquity. It is one of the most common serious neurological conditions, affecting 0.4%–1.0% of the world population **(Treiman, 2010)**.

Temporal lobe epilepsy (TLE) is the most common type of focal epilepsy syndromes in adults, representing approximately 60% of all partial epilepsies **(Téllez-Zenteno and Hernández-Ronquillo, 2012)**.

Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS) is the most common form of focal epilepsy with a distinct clinical presentation called "limbic seizure" resulting from epileptic activity within the limbic structures. MTLE-HS syndrome is restricted to patients in whom hippocampal atrophy and/or abnormal signal intensity on Magnetic Resonance Imaging (MRI), and additional evidence of temporal dysfunction on functional images and neuropsychological assessment are demonstrated. MTLE usually presents between 6–10 years of age but can present from infancy to the 30s and affects 10 to 20% of children undergoing surgical treatment of TLE in the second half of the first decade of life **(Engel** ***et al.,*** **2012).**

The association between Hippocampal Sclerosis (HS) and epilepsy has been known for almost two centuries. Mesial Temporal Sclerosis (MTS) is a progressive disorder and seizures initially controlled with antiepileptic drugs can later become intractable in 60–90%. Although surgery is a proven therapy, only 50% of cases have sustained postoperative seizure freedom and surgery can have important adverse consequences **(O'Dell** ***et al.,*** **2012)**.

Cases with intractable seizures due to unilateral MTLE are excellent candidates for surgical treatment and resective surgery achieves a short-term cure in up to 85% of cases and long-term cure in 57-66% of cases.

Unfortunately, up to 30% of temporal lobe epilepsy cases are unsuitable for surgery due to the bilateral nature of the disease or concerns for the risk of memory deficit, severe amnesia following the removal of the amygdalohippocampal complex and visual field defects, as well as cognitive impairment **(Min** *et al.,* **2013)**.

The discovery of damage extending beyond the hippocampus in cases with MTLE also highlighted that regional brain damage in MTLE is more likely to involve structures within the limbic system, particularly regions that are anatomically and functionally related to the hippocampus. This observation led to the hypothesis that MTLE is a disease affecting not only the hippocampus but also involving a network of interrelated structures, such as the entorhinal and perirhinal cortices, thalamus, anterior cingulate and cortical association areas **(Bocti** *et al.,* **2003)**.

AIM OF THE WORK