"Role of Repetitive Transcranial Magnetic Stimulation on Drug Resistant Focal Epilepsy"

Thesis

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By

Ahmed Kamal Ahmed Hassan

M.B.B.Ch - Cairo University

Master of Neuropsychiatry- Ain Shams University

Supervisors

Prof. Samia Ashour Mohamed Helal

Professor of Neuropsychiatry
Faculty of Medicine - Ain Shams University

Prof. Ahmed Abd Elmonem Gaber

Professor of Neuropsychiatry
Faculty of Medicine - Ain Shams University

Assist. Prof. Tamer Hussien Fahmy

Assistant Professor of Neuropsychiatry
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
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لَا يُكَلِّفُ اللَّهُ نَفْسًا إِلَّا وُسْعَهَا ۚ لَهَا مَا كَسَبَتْ
وَعَلَيْهَا مَا اكْتَسَبَتْ ۗ رَبَّنَا لَا تُؤَاخِذْنَا إِن نَّسِينَا أَوْ
أَخْطَأْنَا ۚ رَبَّنَا وَلَا تَحْمِلْ عَلَيْنَا إِصْرًا كَمَا حَمَلْتَهُ
عَلَى الَّذِينَ مِن قَبْلِنَا ۚ رَبَّنَا وَلَا تُحَمِّلْنَا مَا لَا طَاقَةَ
لَنَا بِهِ ۖ وَاعْفُ عَنَّا وَاغْفِرْ لَنَا وَارْحَمْنَا ۚ أَنتَ مَوْلَانَا
فَانصُرْنَا عَلَى الْقَوْمِ الْكَافِرِينَ

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List of Abbreviations

ABC : ATP-binding cassette

AEDs : Antiepileptic drugs

BBB : Blood–brain barrier

EEG : Electroencephalogram

FLE : Frontal lobe epilepsy

GABA : Gamma-aminobutyric acid

GABAB : γ-aminobutyric acid type B

HS : Hippocampal sclerosis

IEDs : Interictal epileptiform discharges

ILAE : International league against epilepsy

LTD : Long-term depression

LTP : Long-term potentiation

MCD : Malformations of cortical development

MEP : Motor-evoked potential

MTS : Mesial temporal sclerosis

NMDA : N-methyl-d-aspartate

OLE : Occipital lobe epilepsy

PDS : Paroxysmal depolarization shift

PLE : Parietal lobe epilepsy

rTMS : Repetitive transcranial magnetic stimulation

SMA : Supplementary motor area

SMA : Supplementary motor area

TLE : Temporal lobe epilepsy

TMS : Transcranial magnetic stimulation

WHO : World Health Organization

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Introduction

Epilepsy is a chronic disorder of the brain that affects people of all ages, approximately 50 million people live with epilepsy worldwide **(WHO, 2018)**. It is the commonest neurological condition, with a prevalence of 0.5–1%. It can occur at any age, but is particularly likely to develop in the very young and the elderly **(Hart, 2012)**.

Epilepsy exists when someone has an epileptic seizure and their brain "demonstrates a pathologic and enduring tendency to have recurrent seizures". epilepsy is diagnosed when an individual has at least two unprovoked or reflex seizures>24 h apart, one unprovoked (or reflex) seizure and a probability of having another seizure similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years, and or diagnosis of an epilepsy syndrome**.** While an epileptic seizure is defined conceptually as: "a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain **(Fisher et al., 2014).** Evidence that increases the probability of having additional seizures includes epileptiform activity on electroencephalogram (EEG) or a potential abnormality on brain imaging **(Jessica et al., 2017).**

The previous definition considered the diagnosis of epilepsy only after two unprovoked seizures occurring at least 24 hours apart and was based on data demonstrating that the cumulative risk for a relapse after a first unprovoked seizure is about 40%, whereas the risk for further unprovoked seizures approaches 80% in those who have experienced at least two unprovoked seizures **(Beretta et al., 2017).**

Focal seizures also called partial, topographical, anatomicaland localized related seizures initially generate in and affect just one part of the brain or a whole hemisphere. Symptoms vary according to where the seizure occurs particularly at onset, are determined by localization and not etiology. However, specific anatomical localization is sometimes difficult, as when seizures originate from clinically silent epileptogenic regions **(Bradley and Daroff, 2012).**

Drug-resistant epilepsy is defined as failure of adequate trials of two tolerated, appropriately chosen and administered antiepileptic drugs (whether as monotherapy or in combination) to achieve sustained seizure freedom. And, about 20 to 40 percent of patients with epilepsy are refractory to medications **(Kwan et al., 2010).**This condition is also referred to as intractable, medically refractory, or pharmacoresistant epilepsy **(Kwan et al., 2011).**

A core feature of drug-resistant epilepsy (DRE) is hyperexcitability of the cortical areas **(Tassinari et al., 2003)**. These syndromes may benefit from repeated transcranial magnetic stimulation (rTMS) **(Theodore, 2003).**

The Frequency and severity of seizures vary among individuals with DRE and are important considerations when weighing treatment options. They have an impact in the context of the individual's life, job, and other psychosocial circumstances **(Benbadis et al., 2000).**

Neurostimulation based treatments for epilepsy is an alternative for the many patients who remain refractory to standard antiepileptic drugs (AEDs) **(Fisher, 2012)**.

The potential therapeutic effect of rTMS on focal epilepsy, however, has been much less clear. Controlled clinical trials of low-frequency rTMS in drug resistant epilepsy patients had yielded disparate outcomes, with seizures and interictal epileptiform discharges (IEDs) reduced in some studies but not in others. Differences in subject selection, location of rTMS target, and stimulation parameters could all potentially have played a role in the variability of outcomes **(Cantello et al., 2007).**

Aim of the Study

To assess the effectiveness of rTMS as adjunctive treatment in patients with drug resistant focal epilepsy.

Chapter (1)

Classification of Epileptic Seizures

The international league against epilepsy (ILAE) Commission 1989 classified focal epilepsies, according to their topographical/anatomical origin as: frontal lobe epilepsies, temporal lobe epilepsies, parietal lobe epilepsies and occipital lobe epilepsies. These epilepsies may be idiopathic, cryptogenic or symptomatic. The ILAE diagnostic scheme further classified focal epilepsies according to whether they were limbic or neocortical **(Engel, 2006)**. Simple and complex focal seizures may account for 60–70% of all epilepsies, and almost half originate from temporal lobe structures **(Banerjee and Hauser, 2008)**. There are numerous causes of symptomatic and cryptogenic focal epilepsies, such as: benign or malignant tumours, viral and other infectious and parasitic diseases, cerebrovascular disorders, malformations of cortical development, genetically determined brain and metabolic disorders and, or trauma and other injuries **(Sisodiya, 2004)**.