



# **Comparative study between transcranial direct current and repetitive transcranial electromagnetic stimulation in the rehabilitation of primary fibromyalgia**

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

# قَالَ

سَبَّحَانَكَ لَا إِلَهَ إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ  
الْعَلِيمُ الْعَظِيمُ

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# *List of Abbreviations*

Abb.	Full term
<b>1H-MRS</b> .....	Single-voxel proton magnetic resonance spectroscopy
<b>5-HT3</b> .....	Serotonin
<b>ACR</b> .....	American College of Rheumatology
<b>AMPA</b> .....	$\alpha$ amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
<b>BDI</b> .....	Beck depression inventory
<b>BDNF</b> .....	Brain-derived neurotrophic factor
<b>CBT</b> .....	Cognitive-behavioral therapy
<b>CCK</b> .....	Cholecystokinin
<b>CNS</b> .....	Central nervous system
<b>COMT</b> .....	Catechol-O-methyl transferase
<b>CSS</b> .....	Central sensitivity syndrome
<b>DLPFC</b> .....	Dorsolateral prefrontal cortex
<b>DNIC</b> .....	Diffuse noxious inhibitory control
<b>EAA</b> .....	Excitatory amino acids Treatment
<b>EEG</b> .....	Electroencephalogram
<b>FIQ</b> .....	Fibromyalgia Impact Questionnaire
<b>EMG</b> .....	Electromyography
<b>FDA</b> .....	Food and Drug Administration
<b>FM</b> .....	Fibromyalgia syndrome.
<b>fMRI</b> .....	Functional magnetic resonance imaging
<b>FMS</b> .....	Fibromyalgia syndrome
<b>GABA</b> .....	$\gamma$ -aminobutyric acid
<b>GH</b> .....	Growth hormone
<b>HBOT</b> .....	Hyperbaric Oxygen Therapy
<b>HD-tDCS</b> .....	High-density transcranial direct current stimulation
<b>HADS</b> .....	Hospital Anxiety and Depression Scale

# *List of Abbreviations Cont...*

<b>Abb.</b>	<b>Full term</b>
<b>HPA</b> .....	Hypothalamic-pituitary-adrenal
<b>IBS</b> .....	Irritable bowel syndrome
<b>ICD</b> .....	The International Classification of Diseases
<b>IGF</b> .....	Insulin-like Growth Factor
<b>LTD</b> .....	Long-term depression
<b>LTP</b> .....	Long term potentiation
<b>M1</b> .....	PRIMARY motor cortex
<b>MADD</b> .....	Myoadenylate deaminase deficiency
<b>MDD</b> .....	Major depressive disorder
<b>MEP</b> .....	Motor evoked potential
<b>NIBS</b> .....	Non-invasive stimulation
<b>NMDA</b> .....	N-methyl-D-aspartate
<b>NSAIDs</b> .....	Non-Steroidal Anti- Inflammatory Drugs
<b>rCBF</b> .....	Regional cerebral blood flow
<b>RCTs</b> .....	Randomized Controlled Trials
<b>rTMS</b> .....	Repetitive transcranial magnetic stimulation
<b>SNRIs</b> .....	Serotonin-norepinephrine reuptake inhibitors
<b>SPECT</b> .....	Single photon emission computed tomography
<b>SSRIs</b> .....	Selective serotonin reuptake inhibitors
<b>SSS</b> .....	Symptom severity scale
<b>tDCS</b> .....	Transcranial direct current stimulation
<b>TENS</b> .....	Transcutaneous electrical nerve stimulation
<b>tES</b> .....	Transcranial electric stimulation
<b>TMD</b> .....	Temporomandibular disorder
<b>TMS</b> .....	Transcranial magnetic stimulation
<b>tRNS</b> .....	Transcranial random noise stimulation
<b>VAS</b> .....	Visual Analogue Scale
<b>WPI</b> .....	Widespread pain index

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## INTRODUCTION

Fibromyalgia syndrome (FM) is a common chronic musculoskeletal disorder characterized by the presence of widespread pain and multiple tender points on physical examination. Other important accompanying symptoms of FM are fatigue, sleep disturbance, psychological distress, and cognitive disturbance (*Clauw, 2014*).

Several factors are associated with the pathophysiology of FMS, but the causal relationship is still unclear. This includes alterations of central pain pathways, hyporeactivity of the hypothalamus-pituitary-adrenal axis, increased systemic pro-inflammatory, and reduced anti-inflammatory cytokine profiles, and disturbance in the dopaminergic and serotonergic system (*McBeth et al., 2007*).

The treatment recommendations were classified as non-pharmacological therapies, pharmacological treatments, and complementary non-pharmacological therapies (*Macfarlane et al., 2017*).

Drug combinations may be administered in FM patients, who do not respond to monotherapy, under careful observation and with consideration of the adverse effects and majority of patients recommended to use combination of both pharmacological and non-pharmacological therapies (*Macfarlane et al., 2017*).

Non-pharmacological therapies include patient education, exercises, physical therapy modalities, hydrotherapy, and Cognitive-behavioral therapy (CBT) (*Nuesch et al., 2013*).

New alternative therapies have been advanced in latest years, one of these new treatments is noninvasive brain stimulation involving transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS) (*Castillo et al., 2016*).

Transcranial direct current stimulation (tDCS) is the application of weak electrical currents (1–2 mA) to modify the activity of neurons in the brain. Neuronal firing differs according to the pole located near the cell body and it increases when the positive pole (anode) is located near it and inhibited when cathode stimulation is applied (*Nitsche et al., 2008*).

The suggested mechanisms of neurophysiological effects induced by tDCS include improvements in regional cerebral blood flow (rCBF), facilitation of synaptic efficacy and expression of neurotrophic factors (*Fritsch et al., 2010*).

TMS is a non-invasive brain stimulation technique that uses changes in magnetic fields to increase or decrease neuronal activity and Its application is delivered through a magnetic coil placed over the head that transforms electrical current into a magnetic field, which can be focalized to different areas of the brain (*Lefaucheur et al., 2014*).

The rapidly changing magnetic field travels across the scalp and skull and induces an electric field within the brain

Therefore, induces current to flow in the brain by creating a transmembrane potential and depolarizes underlying superficial neurons, which then induces electrical currents in the brain (*Horvath et al., 2014*).

The effects of TMS can be acute, intermediate or prolonged depending on the mode of stimulation and area stimulated (*Amit et al., 2018*).

Repeated low frequency stimulation of a single neuron in culture produces long-lasting inhibition of cell communication while high frequency stimulation can improve communication so we can consider low frequencies ( $\leq 1$  Hz) can induce neuronal inhibitory function, whereas high frequencies ( $\geq 5$  Hz) are typically associated with increased cortical excitability (*Alberto et al., 2018*).

A systematic review of the transcranial electric stimulation (tES) studies on treatment of FM showed that anodal tDCS of motor cortex, that represent the most studied stimulation target, is able to induce significant therapeutic effects on pain measures and/or life quality in FMS patients, as compared to placebo sham tDCS (*Brighina et al., 2019*).

It was also found in a Systematic review which evaluated the pain reduction effect of rTMS in chronic pain a significant decrease in fibromyalgia pain (*Hamid et al., 2019*).

## **AIM OF THE WORK**

The aim of the study is to assess the effect of tDCS and rTMS stimulation as Non-invasive brain stimulation techniques in the rehabilitation of 1ry fibromyalgia in order to recommend the best line of rehabilitation.