بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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شبكة المعلومات الجامعية

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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MONA MAGHRABY

A clinical trial to assess the role of repetitive Transcranial Magnetic Stimulation (rTMS) in Smoking Cessation in an Egyptian Sample

Thesis
Submitted for the partial fulfilment of the Doctoral degree in Psychiatry

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List of Abbreviations

5 As	Ask-Advise-Assess-Assist-Arrange
AAC	Ask-Advise-Connect
AAR	Ask-Advice-Refer
ACC	Anterior Cingulate Cortex
Ach	Acetyl Choline
AMPAR	α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor
ANOVA	Analysis of variance
AP	Action Potential
APA	American Psychiatric Association
APB	Abductor Pollicis Brevis
app	Application
ATCQ-12	Arabic Tobacco Craving Questionnaire
BCE	Before the Current Era
BDNF	Brain-Derived Neurotrophic Factor
BEN	Brain Entropy
Ca2+	Calcium ion
cAMP	Cyclic Adenosine Monophosphate
CBF	Cerebral Blood Flow
CBT	Cognitive behavioral therapy
CI	Confidence Interval
CNDS	Competing Neurobehavioral Decision System
CO	Carbon Monoxide
COHb	Carboxyhemoglobin
COPD	Chronic Obstructive Pulmonary Disease
CPD	Cigarettes Per Day
CQR	Continuous Quit Rate
DA	Dopamine
DLPFC	Dorsolateral Prefrontal Cortex
D-mechanism	Direct mechanism
DSM-5	Diagnostic and Statistical Manual of mental disorders (5th edition)
DSM-IV	Diagnositic and Statistical Manual (4th edition)
DTMS	Deep Transcranial Magnetic Stimulation
EEG	Electroencephalography

E-field	Electric field
ENDS	Electronic nicotine delivery systems
FDA	Food and Drug Administration
fMRI	Functional Magnetic Resonance Imaging
FTND	Fagerstrom Test For Nicotine Dependence
GABA	Gamma Amino Butyric Acid
Glu	Glutamate
Gs	G=protein coupled stimulatory receptor
h	hour
HB-IPN	habenula–interpeduncular system
HF	High frequency
Hx	History
Hz	Hertz
ICD-10	International Classification of Diseases (10th revision)
ICH	International Council on Harmonization
I-mechanism	Indirect mechanism
IOMS	Islamic Organization for Medical Sciences
IPN	Interpeduncular Nucleus
K+	Potassium ion
Ka	Acid dissociation constant
kA	kilo Ampere
LDTg	laterodorsal tegmental nucleus
LF	Low Frequency
LTD	Long-term Depression
LTP	Long-term Potentiation
LWDS-11	:ebanese Waterpipe Dependence Scale
M1	Primary Motor Area
MAO	Monoamine oxidase
MDD	Major Depressive Disorder
MEP	Motor Endplate Potential
Mg2+	Magnesium ion
MHb	Medial Habenula
MINI	Mini International Neuropsychiatric Interview
MPFC	Medial Prefrontal cortex
MRI	Magnetic Resonance Imaging
ms	millisecond

List of Abbreviations

MT	Motor Threshold
MTP	Motor Threshold Potential
N	number
Na+	Sodium ion
NAc	Nucleus Accumbens
nAChR	nicotinic Acetyl Choline Receptor
NCD	Non-communicable diseases
NCI	National Cancer Institute
NIBS	Non-invasive Brain Stimulation
NMDAR	N-methyl D-aspartate receptors
NO	Nitric Oxide[i]
NRT	Nicotine Replacement Therapy
NUI	Nicotine Use Inventory
OCD	Obsessive Compulsive Disorder
OFC	Orbitofrontal cortex
OR	Odds Ratio
PFC	Prefrontal Cortex
PKA	Protein Kinase A
pKa	pH acid dissociation constant
ppm	Parts Per Million
PPTg	pedunculopontine tegmental nucleus
ppTMS	Paired-pulse Transcranial Magnetic Stimulation
QPS	Quadripulse Stimulation
REC	Research Ethics Committee
rMT	Resting Motor Threshold
rppTMS	repetitive paired pulse Transcranial Magnetic Stimulation
RR	Relative Risk
rTMS	repetitive Transcranial Magnetic Stimulation
SFG	Superior Frontal Gyrus
SMFC	Superomedial Frontal Cortex
SN	Spiny Neurons
SNpc	substantia nigra pars compacta
SPSS	Statistical Package for the Social Sciences
spTMS	Single Pulse Transcranial Magnetic Stimulation
sTCQ	Short form of Tobacco Craving Questionnaire
SUD	Substance Use Disorder
TBS	Theta Burst Stimulation

List of Abbreviations

tDCS	Transcranial Direct Current Stimulation
TMS	Transcranial Magnetic Stimulation
TQD	Target Quit Date
Trk-B	Tropomycin Receptor Kinase B
U.S.	United States
VTA	Ventral Tegmental Area
WHO	World Health Organization

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Introduction

Background

The World Health Organization (WHO) reported that tobacco use continues to be the leading global cause of preventable death with almost 6 million deaths each year (World Health Organization, 2019). Although the prevalence is declining worldwide, it still seems to be increasing in the Eastern Mediterranean region. Despite the well-documented morbidity and mortality, estimated prevalence of smoking any tobacco product among males aged >= 15 years in Egypt has been rising from 43.9% in 2010 to 49.9% in 2015 and is predicted to continue rising until 2025 (World Health Organization, n.d.).

Research indicates that most smokers endorse a desire to quit, but few (only about 4–7%) will actually quit in a given year without treatment. A striking discrepancy exists between early success rates and long-term outcomes. In most studies, more than 50% of smokers achieve abstinence for at least a few initial weeks. Of initially successful quitters, 50% to 60% go on to relapse within a year (Tonstad et al., 2006). Currently used medications for tobacco dependence include nicotine replacement therapy, varenicline HCl, bupropion HCl, and group and/or individual psychotherapy. These treatments show around 20–25% abstinence rates in smokers at 6 months or more after treatment

initiation and are therefore considerably better than attempting abstinence without treatment. Research also shows that a high percentage of smokers who initiate treatment will relapse within the first year (Brody & Cook, 2011).

The major addictive component of tobacco, Nicotine, activates the mesolimbic dopamine system originating in the ventral tegmental area and projecting to reward-related brain areas including the prefrontal cortex (PFC), nucleus accumbens (NAc), amygdala and hippocampus (Di Chiara, 2000). A decreased activity of the brain reward system during nicotine withdrawal has been shown to be closely associated with craving, relapse and continued nicotine consumption (Epping-jordan et al., 1998). Additional support for this hypothesis comes from studies with the atypical antidepressant bupropion that blocks neuronal uptake of dopamine which is currently approved as a treatment for smoking cessation (Holm & Spencer, 2000). For these reasons, modulation of dopaminergic neurotransmission might serve as a potential target for treating tobacco addiction.

Repetitive transcranial magnetic stimulation (rTMS) is a tool that can potentially induce dopamine release and long-lasting changes in neural excitability (Dinur-Klein et al., 2014). High frequency rTMS at the left dorsolateral prefrontal cortex (LDPFC) has been shown to modulate cigarette cue-induced