Correlation between the effect of rTMS on gait & cognition In patients with parkinson's disease

Thesis

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العلاقة بين تأثير جلسات التنبيه المغناطيسى على المخ عبر الجمجمة على المشية والقدرات المعرفية فى مرضى الشلل الرعاش (باركنسون).

رسالة

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List of Abbreviations

APA	:	Anticipatory Postural Adjustment
APB	:	Abductor Pollicis Brevis
DBS	:	Deep Brain Stimulation
EEG	:	ElectroEncephaloGram
ERP	:	Event Related Potential
FOG	:	Freezing Of Gait
FOG-Q	:	Freezing Of Gait Questionnaire
GARS	:	Gait Assessment Rating Scale
Ham-DS	:	Hamilton Depression Scale
ICA	:	Independent Component Analysis
MEP	:	Motor Evoked Potential
MMSE	:	Mini-Mental State Examination
PD	:	Parkinson's Disease
QOL	:	Quality Of Life
r-TMS	:	Repeated Trans-cranial Magnetic Stimulation
SMA	:	Somato-Motor Area
t-DCS	:	Transcranial Direct-Current Simulation

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Abstract

Introduction: Parkinson's disease is aneuro-degenerative disorder that results from dopaminergic fibers degeneration in the substantia nigra and ventral mid-brain tegmentum, it is characterized by motor symptoms (bradykinesia, tremors, rigidity and gait disorders) and non-motor symptoms (cognitive, mood, psychotic, ……) these symptoms may affect the Quality Of Life (QOL) of PD patients. The relationship between higher-level cognitive function and gait disturbances has received considerable attention in recent years. Studies on cognitive function and gait now include many areas of research, ranging from physiology and biomechanics to brain mapping, physics and neuropsychology. For example, imaging studies have demonstrated frontal and parietal activity during locomotion. After application rTMS the cortex may be repeatedly stimulated and modulate its activity, for PD patients high frequency r TMS were applied on the motor areas showed marked improvement as regard motor and gait symptom. rTMS over the DLPF cortex improves depression, cognition and may motor function as well. While the number of studies investigating the role of the PFC in motor function in PD is limited, it is possible that stimulating the PFC increases endogenous dopamine production from the basal ganglia via corticostriatal pathways.

Aim of the Work: To assess the efficacy of motor (M1, M2) areas stimulation using high frequency r TMS in improving the gait and motor symptoms in PD patients and its correlation to cognitive function.

Patients and Methods: Study design: Cross- over clinical trial. Sample selection: A total of 15 patients were recruited with the diagnosis of idiopathic Parkinson's disease according to UK Parkinson's disease (PD) Society Brain Bank Clinical Diagnostic Criteria. Procedure: Each patient received 6 sessions of SHAM TMS with wash-out period of 2 weeks then the same patient received 6 sessions of Active r-TMS. Patients were assessed using motor and cognitive scales before starting the sessions (T0) then after receiving 6 sessions (T1), and 2 weeks after the end of sessions (T2). Motor assessment, Fast Ten meters walk test (10MWT). Unified Parkinson's Disease Rating Scale (UPDRS): New freezing of gait questionnaire, Freezing of Gait (FOG) questionnaire, Gait Abnormality Rating Scale GARS-modified. Cognitive scales: The Wisconsin Card Sorting Test (WCST), ERP: p300.

Keyword: Parkinson disease, Wisconsin Card Sorting Test, rTMS, freezing of Gait.

Introduction

Until very recently, the adult brain was considered immutable, and the notion of neurogenesis in the adult brain was regarded as far-fetched. In the last 2 decades, it is clear that the central nervous system is plastic that, it changes as a result of experience, and that neurogenesis occurs in the adult brain at discrete locations. These paradigm shifts have fueled the notion that brain function can be modulated to improve neurologic recovery and aid in rehabilitation ***(Ming and Song, 2005).***

Because neuromodulators can transform the intrinsic firing properties of circuit neurons and alter effective synaptic strength, neuromodulatory techniques (as transcranial direct current stimulation tDCS & rTMS) reconfigure neuronal circuits often massively, altering their output ***(Eva Marder, 2012).***

Most reports in the 1950s focused on positive phenomena that were elicited by brain stimulation **(Hassler et al., 1960).** And so, the idea of treating neurologic disorders with chronic stimulation began to emerge in the 1960s, but stimulation was largely used for targeting surgical lesions rather than neurological degenerative lesions ***(Bergstrom et al., 1966).***

Since the discovery of transcranial direct current stimulation (tDCS) - a non-invasive brain stimulator - years ago, interest in tDCS has grown exponentially. A

noninvasive stimulation technique that induces robust excitability changes within the stimulated cortex, tDCS is increasingly being used in a wide range of neurological and psychiatric disorders ***(Stagg and Nitsche, 2011).***

Nearly 20 years ago repetitive transcranial magnetic stimulation(rTMS) was recommended for the treatment of Parkinson's disease ***(Málly and Stone, 1999).***

Gait disturbance are universal features of advanced disease in PD.

Gait dysfunction in PD patients is usually multifactorial in origin and requires a comprehensive assessment to determine contributing factors and targeted interventions.

Early identification of gait and balance disorders and appropriate intervention may prevent dysfunction and loss of independence.

The motor loop originates from the motor cortices, namely, the primary motor cortex, supplementary motor area (SMA), and lateral premotor cortex, and projects to the somatomotor region of the basal ganglia, thereby controlling voluntary movement.

Dysfunction of the basal ganglia-thalamo-SMA loop results in gait disturbance in Parkinson's disease and vascular Parkinsonism.

The dysfunction of the SMA loop could be compensated for by the activation of the lateral premotor cortex, the function of which appears to be preserved under appropriate external stimuli in such patients ***(Iseki and Hanakawa, 2010).***

Several studies have shown the therapeutic benefits of rTMS therapy for control of motor symptoms in PD.

The relationship between higher-level cognitive function and gait disturbances has received considerable attention in recent years.

Gait is no longer considered as merely an automated motor activity that utilizes minimal higher-level cognitive input. Instead, the multi-faceted neuropsychological influences on walking and the interactions between the control of mobility and related behaviors are increasingly appreciated. This is manifest in part by an individual's awareness of a destination, the ability to appropriately control the limb movements that produce gait, and the ability to navigate within often complex environs in order to successfully reach the desired location. Studies on cognitive function and gait now include many areas of research, ranging from physiology and biomechanics to brain mapping, physics and neuropsychology. For example, imaging studies have demonstrated frontal and parietal activity during locomotion ***(Sheridan, Hausdorff, 2007)***.

AIM OF THE WORK

So we aim to investigate the effect of rTMS on gait of patients with Parkinson ’s disease & its relation to cognitive effect.