Effect of Trans Cranial Magnetic Stimulation in Management of Dysphasia, A Systematic Review

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By

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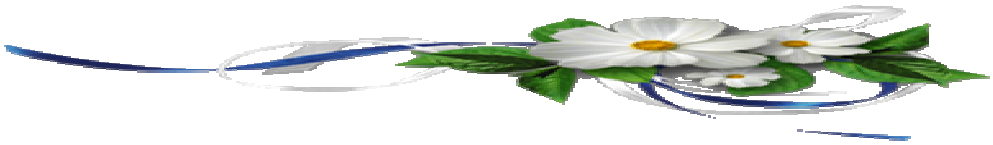

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List of Contents

List of Figures

List of Tables

INTRODUCTION

Aphasia is the most disabling functional defect after ischemic stroke, it affects more than a third of all stroke victims. It improves during the first 4 weeks in one-third of patients and during the first 6 months in approximately half of them. Effective therapeutic strategies are needed to treat aphasic patients, treatments which can benefit people with aphasia include: intensive speech and language therapy (SLT), medications such as piracetam, bifemelane and piribedil, Stem cell transplantation and Transcranial Magnetic Stimulation. Early and intensive speech and language therapy (SLT) is the only effective treatment to date but usually is limited in duration and intensity. Therefore, improved and additional treatment strategies are required to improve recovery of language functions **(Tippett et al., 2014)**. Recent advances in neuroimaging contribute to a new insights regarding brain-behavior relationships and expand understanding of the functional neuroanatomy of language. Increasingly, aphasia is seen as a disruption of cognitive processes underlying language. Rehabilitation of aphasia incorporates evidence based and person-centered approaches. Novel techniques, such as methods of delivering cortical brain stimulation to modulate cortical excitability, such as transcranial magnetic stimulation (TMS) and transcranial

direct current stimulation (tDCS), are just beginning to be explored **(Platz, 2015)**. Post-stroke aphasia results from the lesion of cortical areas involved in the motor production of speech (Broca's aphasia) or in the semantic aspects of language comprehension (Wernicke's aphasia). Such lesions induce an important reorganization of speech/language-specific brain networks due to an imbalance between cortical facilitation and inhibition. The purpose of rTMS and tDCS application in the neuro-rehabilitation of aphasic patients is to act on specific networks involved in the pathophysiology of language processing and to promote adaptive cortical reorganization after stroke **(Platz, 2015).**

The first studies of Transcranial Magnetic Stimulation (TMS) were performed in 1985 by Anthony Barker and his colleagues at the Royal Hallamshire Hospital in Sheffield, England. These studies demonstrated that TMS could induce muscle movements in the hand when applied to the cortical motor strip **(Barker et al., 1985)**. These early studies provided support for a noninvasive method that could focally stimulate underlying cortical pathways and were the foundation for research into the stimulation of cortical pathways involved in a number of disease processes. Barker's original research was based on single-pulse TMS where a single stimulus was delivered to a specific brain region. Expanding on this, the technology developed to allow a device to deliver multiple stimuli over a short period of

time, that is, repetitive TMS (rTMS). rTMS was shown to have lasting effects on cortical excitability that persisted beyond the actual stimulus delivery **(Maeda et al., 2000)**. Given the ability of this treatment to modulate cortical activity in a focal way, focus was soon placed on the use of this technique to in various neurological and psychiatric diseases such as aphasia. Although numerous clinical trials of TMS for the treatment of aphasia have been conducted **(Platz, 2015)**, there is a deficient good quality evidence for its role that support its use in a day to day practice. This study is an attempt to provide clinicians with such an evidence for an evidence-based practice of this technique.

TRANSCRANIAL MAGNETIC STIMULATION

I. Types of Transcranial Magnetic Stimulation:

Fitzgerald et al. (2006) divided the effects of TMS, depending on the mode of stimulation, into:

-Single or paired pulse TMS, where the pulse(s) causes neurons in the neocortex under the site of stimulation to depolarize and discharge an action potential. In single-pulse TMS, one pulse is applied no faster than once every few seconds. In paired pulse, 2 pulses applied out of phase to inhibit or excite neurons within the same hemisphere or to inhibit neurons in one hemisphere while exciting them in the other hemisphere **(Galletta et al., 2011)**. If used in the primary motor cortex, it produces muscle activity referred to as a motor-evoked potential (MEP) which can be recorded on electromyography (EMG). If used on the occipital cortex, 'phosphenes' (flashes of light) might be detected by the subject. In most other areas of the cortex, the participant does not consciously experience any effect, but his or her behavior may be slightly altered (e.g. slower reaction time on a cognitive task), or changes in brain activity may be detected using Positron Emission Tomography (PET) or functional

Magnetic Resonance Images (fMRI). Effects resulting from single or paired pulses do not outlast the period of stimulation (**Fitzgerald et al., 2006)**.

-Repetitive TMS (rTMS) produces effects that last longer than the period of stimulation. Multiple stimuli (called ‘‘trains’’) of rTMS of appropriate frequency, intensity, and duration can lead to transient increases or decreases in the excitability of corticospinal or cortico-cortical pathways depending on the intensity of stimulation, coil orientation and frequency of stimulation. For example, **slow rTMS** (1Hz), where one magnetic pulse is applied every second, delivered to the motor cortex can give rise to a lasting decrease in corticospinal excitability primarily by affecting intra-cortical facilitation. Applied to other cortical regions, slow rTMS appears to similarly decrease excitability in the targeted cortical region leading to measurable behavioral effects. Conversely, **fast rTMS** (5, 10, or 20 Hz) can induce a transient increase in cortical excitability (**Fitzgerald et al., 2006)**.

Intermittent Theta burst stimulation **(iTBS)** is a patterned form of rTMS**. Huang et al. (2005)** were the first to describe this very rapid method of conditioning the human motor cortex that yield controllable modulatory effects on motor cortical and corticospinal excitability physiology and impact on several types of behavior **(Bulteau et al., 2017)**.

iTBS are delivered in short intervals to produce a rapid facilitation of synaptic transmission in the stimulated cortex that may persist for over an hour after the initial stimulation session. In addition to facilitating changes in local synaptic transmission and evoked potential amplitude, iTBS can lead to changes in ongoing neural dynamics at larger spatial scales that reflect changes in the functional organization of distributed functional networks **(Griffis et al., 2016).** In contrast with traditional rTMS patterns (such as 5 Hz, 10 Hz or 20 Hz) that induce significant but weak, variable and short-lasting modulatory effects on motor and non-motor cortical excitability and behaviors, TBS induces longer-lasting and powerful effects after a short period of 20–190 seconds of stimulation **(Bulteau et al., 2017)**.

It is thus important to discriminate TMS from rTMS as they are used in different ways for different purposes.

II. Basic component description of TMS equipment:

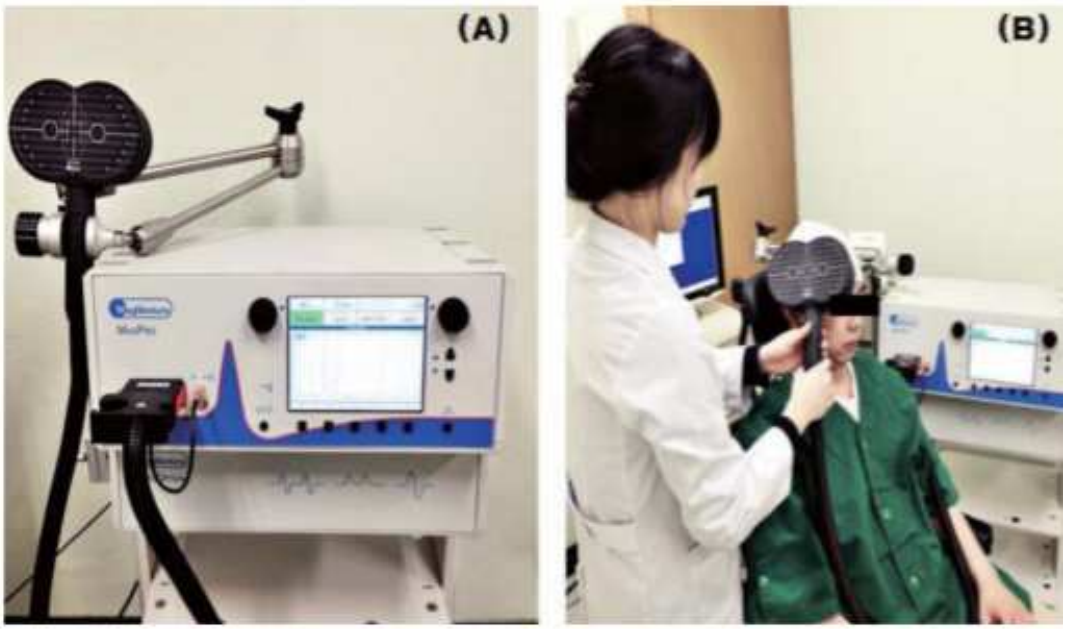

Figure (1): (A) rTMS was conducted using a MagPro® (MagVenture Company, Farum, Denmark). (B) After tying a cap tightly to the head of the patient, magnetic stimulation using a circular coil was performed (**Yoon et al., 2015)**

TMS equipment is made of:

(1) A stimulation coil containing the loops of copper wire to generate the magnetic field, (2) A central unit to set up the amount of current and synchronize its release at a given time, and (3) A group of capacitors to accumulate high loads of electric charge drawn from power supply lines. When a pulse is triggered, an electrical switch is activated

and a given amount of charge stored in the capacitors is sent to the coil, circulates through the wire loops to produce the magnetic field and different stimulation parameters can be set **(Valero-Cabré et al., 2017).** The participant feels a ‘‘light tap’’ on the scalp, may feel a twitch of the face muscles, and hears a brief, loud click as the current passing through the coil tightens the copper wire. Participants report that this is not unpleasant. The stimulation of the brain itself is painless **(Rossini et al., 2007) (Figure 1).**

The electrical current circulating at high speed in the stimulation coil’s wire loops produces with each pulse some abrupt contraction of conducting wire thus generating high-pitched, dry and brief sound called click as well as slight deformation of the coil plastic case surface. Depending on intensity level, the loops diffuse heat over time, which progressively increases coil temperature. Stimulation coils are manufactured from different materials in several sizes, shapes, and designs. These features determine the magnetic field penetration and distribution capabilities, the focality of the magnetic field in the brain (determining to the spatial resolution of its effects or its ability to discriminate between two adjacent cortical locations), the ability to induce weaker or higher intensity intracortical currents, brain area localization, and thus potential motor, sensory or behavioral effects **(Valero-Cabré et al., 2017).**

For example, flat circular coils are made with single high-density circular wire windings covered by a plastic sheath, so that the maximal induced current distributes like a doughnut under its perimeter. Such coils have high penetration power, but as trade-off they lack spatial selectivity i.e. less focal (> 4–5 cm^2), as their induced current is highest at the circumference of the coil with no current induced in the center **(Hallett, 2007)**, unless only the edge of the coil is used as stimulation surface (around 1.2–1.5 cm^2) **(Valero-Cabré et al., 2017).**

Figure (2): Different stimulation coils used for TMS interventions which differ in field shape, size and depth: (first line left to right); 40-mm diameter figure-of-eight, butterfly or double coil, 70-mm circular coil, 70-mm butterfly coil, 50-mm circular coil; (second line) 45- mm butterfly coil, bell-shaped coil, 50-mm butterfly coil, 50-mm butterfly coil with an integrated 0.7-mm thick heat-resistant card to be used in combination with intracranial recordings in animal models **(Valero-Cabré et al., 2017)**.