

# Versatility of Repetitive Transcranial Magnetic Stimulation in the Treatment of Poststroke Dysphagia

Soultana L. Papadopoulou, Avraam Ploumis<sup>1</sup>, G. Exarchakos<sup>2</sup>, S. J. Theodorou<sup>3</sup>, A. Beris, A. D. Fotopoulos<sup>4</sup>

Departments of Orthopedic Surgery and <sup>1</sup>Physical Medicine and Rehabilitation and <sup>2</sup>Otorhinolaryngology, Departments of <sup>4</sup>Nuclear Medicine and <sup>3</sup>Radiology, University of Ioannina Medical School, University Hospital of Ioannina, Greece

**ABSTRACT**

Various techniques and courses of treatment have been researched, proposed, and implemented to evaluate and treat poststroke dysphagia (PSD) which is one of the main medical conditions affecting not only elderly people, as previously assumed, but also in recent years younger populations as well. The effectiveness of therapeutic methods depends mainly on the expertise of an interdisciplinary team of therapists, as well as on the timely application of the treatment. The present review discusses the therapeutic benefits of repetitive transcranial magnetic stimulation (rTMS) in patients suffering from PSD regardless of the location of the lesion. The use of rTMS directly manipulates cortical brain stimulation to restore neuroplasticity in the affected brain areas. This review presents a synopsis of the available literature on the patient along with a discussion on the effectiveness of rTMS as a safe and easy to use promising technique in the rehabilitation of dysphagic patients. Although the results from the studies so far have been largely positive in that direction, the question still remains whether larger scale and longitudinal studies will be able to corroborate the aspiring future of rTMS. Therefore, research questions to advance further investigation on the application and future of this technique are much in need.

**KEYWORDS:** *Dysphagia, rehabilitation, repetitive transcranial magnetic stimulation, stroke*

## INTRODUCTION

Stroke is a common medical complication and among the most frequent causes of neurological disability in adults<sup>[1]</sup> and can be differentiated into unilateral, bilateral lesions of the cerebral hemisphere, brainstem lesions, and combined lesions.<sup>[2]</sup> Increased mortality is evident and even though most of the patient's swallowing capacity is restored within a few weeks<sup>[1]</sup> in some cases, dysphagic symptoms continue to be present even a year after stroke. It is a major cause of prolonged neurological disability in adults occurring up to 76% of patients with acute stroke,<sup>[3]</sup> and it inflicts a heavy burden on the patients and their immediate environment.

Swallowing is a complex sensory motor process, in which 75 muscles, 7 cervical nerves, and 5 cranial nerves are involved. Any structural and anatomical dysfunction in the above-mentioned structures will cause malnutrition, dehydration, and in severe

cases mortality due to pneumonia aspiration, which is the most common complication of poststroke dysphagia (PSD). In any case, the quality of life is heavily compromised and inhibits social integration for the patients.<sup>[4]</sup>

Deglutition is generated in the medulla oblongata<sup>[2]</sup> which commences with the desire to eat, the intake, manipulation, propulsion and safe swallowing of food of every consistency (solid, semi-liquid, and liquid), saliva, and medicine from the oral cavity to the stomach.

**Address for correspondence:** Dr. Soultana L. Papadopoulou, Department of Orthopedic Surgery and Physical Medicine and Rehabilitation, University of Ioannina Medical School, Panepistimiou Avenue, P. O. Box: 45110, Greece. E-mail: soultpap@yahoo.gr

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Oropharyngeal dysphagia (OD) is commonly observed in the case of degenerative disorders after surgery, chemoradiation, structural and functional abnormalities, osteophytes, or neurological disorders.<sup>[5]</sup> OD also often occurs after traumatic brain injury and neurological disorders such as a stroke with a reported incidence up to 78% and is bound to be connected with dehydration, malnutrition, aspiration pneumonia, and mortality among other<sup>[6]</sup> side-effects.

Even though the majority of the patients recover from dysphagia after therapeutic intervention, the risk of aspiration pneumonia, asphyxia, dehydration, and malnutrition remains.<sup>[7]</sup>

Speech-language pathologists have reportedly used a variety of compensatory strategies and therapeutic techniques to improve swallowing function in individuals with swallowing impairment, which appears as a secondary complication after stroke. Swallowing exercises, alterations in dietary habits, and medication among others<sup>[7]</sup> have shown to reduce dysphagic symptoms. The effect of OD after a stroke can vary in severity from minor difficulty to utter loss in the ability to swallow.<sup>[2]</sup>

There are various noninvasive techniques currently applied in the rehabilitation of dysphagia, resulting in remarkable progress in speech, language, and swallowing disorders. Repetitive transcranial magnetic stimulation (rTMS) is a form of brain stimulation therapy initially used to treat depression and anxiety. It has been in use by psychiatrists since 1985. The therapy involves using a magnet to target and stimulate certain areas of the brain, thus conducting targeted neuromodulation shaping the plasticity of brain cortexes to assist specific processes.

The use of rTMS, transcranial direct current stimulation (tDCS), and neuromuscular electrical stimulation among others have proven quite efficacious in that area of pathology, given the new studies that have shed light to improved and fuller consideration of the plasticity and remodeling attributes of the brain.<sup>[8]</sup> rTMS as an innovative neuromodulatory technique is effective by causing direct modulation of certain brain pathways, such as intrahemispheric and interhemispheric cortical areas,<sup>[9]</sup> which may have long-term effects.

## METHODS

### Search strategy

A comprehensive literature search in the database of PubMed was conducted for English language articles published in December 2016. This search was completed following the standards outlined in the preferred reporting items for systematic reviews. The search

strategy included the following keywords: deglutition, deglutition disorders, dysphagia, swallow, rTMS, stroke therapy, and noninvasive therapeutic methods. References cited in the originally retrieved publications were searched to identify additional potentially relevant studies. Only studies in which a valid tool (namely, video fluoroscopy swallowing study) was used for the assessment of dysphagia were included in the review.

### Implementation of repetitive transcranial magnetic stimulation

The use of rTMS involves the transmission of a magnetic pulse of short duration by means of an insulated coil placed over the affected brain area. There are two types of TMS, the single pulse or the repetitive train of pulses (rTMS).<sup>[10]</sup> There is a variation of frequency in the studies compiled, ranging from 1 to 5 Hz. Barwood and Murdoch found that high-frequency rTMS has been shown to have excitatory effects while low frequency inhibits cortical neurons.<sup>[10]</sup> It is a noninvasive stimulation technique which changes the magnetic field below the skull, thus allowing for the focal depolarization of the neurons in specific cortical areas.<sup>[4]</sup>

rTMS is growing in popularity as it helps develop causative links between specific brain regions and measurable behavioral responses and can be used alongside mainstream therapeutic techniques.<sup>[10]</sup>

Two different strategies have been suggested for the recovery after unilateral hemispheric stroke, the alteration of ipsilesional cortical areas and as proposed by Lefaucheur<sup>[11]</sup> the increase in the excitability of intralesional homotopic areas.

rTMS uses surface electrodes to apply electrical stimulation of the anterior neck muscles making the muscles contract by depolarizing the nerve fibers<sup>[3]</sup> controlling in that way the imbalance between the hemispheres. Several parameters influence the effectiveness of the method, among those coil orientation and type, selection of targeted area, and distance from the target. Specific parameters such as intratrain interval, pulse width, frequency of the pulses as well as duration, and intensity of the stimulation play a key part.<sup>[12]</sup>

Patients with cognitive impairment, anosognosia, head injury, dysrhythmia, fever, infection, hyperglycemia,<sup>[13]</sup> epilepsy, radiotherapy in the head and neck, unstable medical condition, and contraindication to magnetic or electrical stimulation were excluded from the application of this method.<sup>[14]</sup>

There are also a number of patients who should not get rTMS such as those who have aneurysm clips or coils,

bullet fragments or shrapnel near the head, cardiac pacemakers or implantable cardioverter defibrillators, facial tattoos that have magnetic ink or ink that is sensitive to magnets, implanted stimulators, metal implants in the ears or eyes, and stents in the neck or brain.<sup>[11]</sup>

We conducted a systematic review on the effectiveness of the use of rTMS, as a noninvasive therapeutic method for poststroke dysphagic patients by reviewing the evidence on the use of rTMS for the treatment of swallowing problems in stroke patients.

## RESULTS

The original search retrieved 26 articles. A study by Khedr *et al.*<sup>[15]</sup> found that five daily sessions of rTMS in the esophageal motor cortex of the stroke hemisphere can help patients recover from dysphagia and it is connected with an increase in the excitability of the corticobulbar projection.<sup>[14]</sup>

In the study by Yang *et al.*,<sup>[7]</sup> there was significant difference between the ipsilesional or contralesional stimulation, although most of the patients restore swallowing capacity within a few weeks<sup>[4]</sup> while Rofes *et al.* found that lack of coordination between laryngeal vestibule cohorts and upper esophageal sphincter opening time causes swallowing disorders which leads to a retention of the bolus in the hypopharynx, overflowing the airway.<sup>[2]</sup> In rTMS, the magnetic stimulus is applied to the pharyngeal motor cortex.<sup>[2]</sup> They also proposed that after rTMS, the pharyngeal phase of swallow response was improved and the risk of aspiration and penetration was reduced immediately, after treatment and 2 weeks after that.<sup>[2]</sup> Swallowing recovery is achieved in two ways as follows: by the disinhibition of neighboring ipsilesional cortical areas or as Park *et al.* suggested by increasing the excitability of the contralesional homotopic areas.

Recovering from dysphagia depends on the reorganization of the noninjured motor cortex.<sup>[3]</sup>

There is a difference in the intensity of the used Lim *et al.* applied 1 Hz magnetic stimulation of the 100% intensity and applied for 20 min five times a week for 2 weeks.<sup>[16]</sup>

High-intensity rTMS (130%) can spread as much as 2–3 cm from the coil, thereby targeting a much bigger area within a 5-day period over the esophageal motor cortex of both hemispheres. Khedr *et al.* reported a significant improvement after the application of 3-Hz rTMS that maintained for up to 2 months, which is mainly related to the fact control of swallowing, is bilateral while the lesion is usually unilateral.

A growing number of case investigations by Lim *et al.* and Kim *et al.* conducted 5 Hz stimulation in the affected hemisphere. As a result high-frequency magnetic stimulation increases the excitability of the cortex, whereas low frequency lowers cortical excitability.<sup>[16]</sup> On the basis of these results, Momosaki *et al.* studied the implementation of rTMS over a 6-day period during hospitalization. They used the MAGPRO R30 magnetic simulator and 70-mm radius figure-of-eight coil with a daily application of 3 Hz for 10s in both hemispheres. They found that rTMS alongside swallowing rehabilitation improved PSD regardless of the locality of the lesion.<sup>[17]</sup>

In a study by Barwood<sup>[10]</sup> using rTMS to stimulate the mylohyoid cortical area a noticeable improvement in swallowing was shown using videofluoroscopic swallowing study. Whereas, the implementation of rTMS has shown to be a valuable tool in the rehabilitation of dysphagia, there are still many issues that need to be dealt with as Barwood<sup>[10]</sup> pointed out, namely, the induction of seizures in the pathological brain.<sup>[10]</sup>

Barwood and Murdoch suggested further research in larger scale populations and randomized, placebo-controlled clinical trials to accurately pinpoint the effectiveness of rTMS.<sup>[10]</sup> In addition, a study by Michou *et al.*<sup>[18]</sup> found that rTMS did not achieve significant increases in brain excitability of the unaffected pharyngeal projection. By preceding investigations, Kim and Han noted that when the suprahyoid muscle is stimulated, then the hyoid bone is elevated thereby enabling better deglutition.<sup>[19]</sup>

Du *et al.* applied single-pulse TMS to both hemispheres to measure cortical excitability. The coil was first placed at the vertex of the cranium, then positioned 2–4 cm anteriorly and 4–6 cm laterally, and moved around in the area to ensure higher motor evoked potential. They established the cumulative effects of rTMS that lasted for at least 3 months after stroke rehabilitation.<sup>[14]</sup>

Compared to this, Verin *et al.* studied how rTMS can reduce the prevalence of swallowing disorders as active stimulation of the oropharyngeal motor cortex were shown to decrease oropharyngeal transit time,<sup>[20]</sup> whereas Khedr *et al.* researched the use of 10 trains of 3 Hz stimulation for 10 s each time repeated every minute with the coil placed over the provisional esophageal cortical area of both hemispheres provisional esophageal cortical area of both hemispheres for 5 days and found significant improvement in dysphagia in comparison with the sham group.<sup>[3]</sup> Through the use of five daily sessions of 1-Hz rTMS for 2 weeks on the esophageal motor area of the affected hemisphere they

found that patients who underwent real rTMS on the motor area of the affected hemisphere presented no changes in the unaffected hemisphere while there was an increase in the excitability of the stroke hemisphere.<sup>[15]</sup> Recently, Jefferson *et al.* found that 250 pulses of 5-Hz rTMS showed an increase in the pharyngeal motor cortex excitability, which lasted for over 2 h. Active contralateral 5-Hz rTMS completely abolished the cortical suppression caused by the virtual lesion. Active rTMS also reversed the changes in the swallowing behavior, restoring function to prelesional levels.<sup>[13]</sup>

rTMS studies have shown that the pharyngeal motor cortex reorganizes following acute unilateral stroke and that an increase in cortical excitability in the unaffected hemisphere is associated with the recovery of swallowing function.<sup>[18]</sup>

Relative low-cost and safety focal target ability make rTMS techniques widely tested in the treatment of dysphagia,<sup>[8]</sup> although more research should be conducted to further investigate the rehabilitation advantages.<sup>[8]</sup>

Vasant *et al.* studied the effects of 10-Hz cerebellar rTMS and found that it can produce physiologically relevant effects on the excitability of corticobulbar projections to the pharynx, enabling physicians in the way to understand the role of cerebellum in swallowing, and the possible role of cerebellar conditioning in poststroke dysphagia rehabilitation.<sup>[21]</sup>

Lee *et al.* used the magnetic instrument to deliver stimulatory trains through the figure-eight coil on the ipsilesional hemisphere at 10 Hz for 10 s and repeated very minute for 10 min. It was performed once a day for 10 min and for 10 consecutive days. They found that dysphagia scores started to improve immediately after rTMS and proceeded to do so up to 4 weeks. The results showed that performing rTMS over the cortical area in the suprahyoid muscle was more effective than rTMS over the cortical area.<sup>[19]</sup>

In the study by Michou *et al.*, focal rTMS was performed using a figure-eight magnetic coil connected to a Magstim BiStim magnetic stimulator. The results outlined that a single application increases cortical excitability and is associated with reductions in aspiration, while 5-Hz rTMS was less effective. rTMS did not show a significant increase in brain excitability when applied to the unaffected pharyngeal projection. Intriguingly, while there was a visible increase in the brain excitation following real rTMS, there was also an increase with sham rTMS suggesting some kind of biological effects on sham stimulation on cortical function.<sup>[18]</sup>

Sebastianelli *et al.* found that ten sessions of inhibitory rTMS over the right posterior inferior frontal gyrus in combination with speech and language therapy improved language recovery in early ischemic stroke patients and the effect lasted for at least 3 months. Moreover, 1-Hz rTMS improved cortical excitability of the affected hemisphere and decreased that of the contralesional hemisphere, while 3-Hz rTMS only increased cortical excitability of the affected hemisphere.<sup>[22]</sup>

In the study by Vasant *et al.*, the coil handle was held in anteroposterior direction at an angle of 45° tangential to the scalp. Optimized parameters of tDCS over the unconditioned hemisphere reverses the brain and behavioral consequences of inhibitory preconditioning.<sup>[23]</sup>

## DISCUSSION

Evidence suggests that following a stroke, the cortex maintains the ability for reorganization.<sup>[13]</sup> Physiological and functional neuroimaging studies have shown that the effects of rTMS affect not only the stimulated area but also the connected structures, probably through the activation of synapses.<sup>[13]</sup>

This review discusses the therapeutic benefits of a relatively new and promising method, rTMS, which is based on the principle that magnetic stimulation can increase excitability in the affected brain areas following a stroke in dysphagic patients. Moreover, the aim of the reviewer was to investigate the available literature on the patient and highlight the necessity to apply rTMS on a larger population using longitudinal studies in collaboration with other existing therapeutic regimes.

The use of rTMS has shown to be appealing, mainly because it is easy and safe to use and carries minimum potential counter indications. Current research outlines the right frequency (1–5 Hz), while the majority seems to opt for 1 Hz of repetitive train pulses to achieve optimum results. It is important to determine exclusion criteria at the beginning of the program, as in all other protocols, and proceed with patients whose conditions allow them to participate in magnetic stimulation sessions.

Further research in the patient will enable physicians to use rTMS in a more frequent way, primarily in an effort to make this promising method the mainstream technique in the rehabilitation of poststroke dysphagic patients. To that effect, emphasis should be given on the long-term effects, the burden of cost that will be inflicted and equipping medical, and rehabilitation centers with the necessary infrastructure to allow physicians with time and space to implement rTMS.

## CONCLUSION

This review study aims to designate rTMS as a novel and innovative therapeutic technique to be used in combination with other standard forms of therapy. Existing studies so far have shown that its implementation is instrumental in assisting physicians in their efforts to counter the symptoms that stroke patients present. In the majority of the population, the results seem utterly promising, pinpointing to the need for further long-scale studies, which will transform rTMS into a reliable and mainstream tool at the physician's disposal.

However, such progress can only be reliant on longitudinal studies on larger populations, in particular, randomized, placebo-controlled clinical trials to identify rTMS as a neurorehabilitatory treatment for speech, language, and swallowing disorders. The technology needed to administer rTMS should further be advanced so that more specific areas are targeted in a more consistent way. It is important to note that such therapeutic techniques should be used alongside conventional regimes to ensure the optimum result for each individual regardless of the locality of the lesion. Moreover, rTMS can potentially be developed to provide improvement in other field as well.

Overall, the results warrant rTMS as an instrumental, noninvasive method for the rehabilitation of dysphagic patients, and further studies in the future may solidify its usefulness as well as its long-term and far-reaching effects.

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## Conflicts of interest

There are no conflicts of interest.

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