

Transcranial Magnetic Stimulation in Post-Stroke Rehabilitation

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<p>Abstract: A stroke occurs when blood vessels that carry blood to the brain become blocked or ruptured, causing paralysis of the area of the brain that has lost blood circulation. It is a disease that affects men more and is one of the leading causes of death, disability, and hospitalizations worldwide. The faster a stroke is diagnosed and treated, the greater the chances of a full recovery. Therefore, it is essential to be aware of the signs and symptoms and seek immediate medical attention. The objective of the article is to verify whether Transcranial Magnetic Stimulation (TMS) can contribute to improving the health conditions of individuals after stroke. This study is an integrative literature review. A literature review is a study based on collecting selected materials and bibliographies, through a precise search in the databases made available by the scientific community. To collect the material in the databases, keywords related to the subject of the study are used, so that the use of Boolean operators (and, or and not) allows for further refinement of the results and, consequently, the corpus of the research.</p> <p>Keywords: Blood, Hemorrhagic stroke, Ischemic stroke, Risk factors, Thrombus.</p>	<p style="text-align: center;">Research Paper</p>
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1. INTRODUCTION

A stroke occurs when blood vessels that carry blood to the brain become blocked or rupture, causing paralysis of the area of the brain that has lost blood circulation. It is a disease that affects men more and is one of the leading causes of death, disability, and hospitalizations worldwide. The faster a stroke is diagnosed and treated, the greater the chances of a full recovery. Therefore, it is essential to be aware of the signs and symptoms and seek immediate medical attention (Gov.br, 2022).

1.1 There are two types of strokes, which occur for different reasons, symptoms, risk factors, and rehabilitation

Hemorrhagic stroke:

Occurs when a cerebral vessel ruptures, causing hemorrhage. This hemorrhage can occur within the brain tissue or on the surface between the brain and the meninges. It is responsible for 15% of all stroke cases but can cause death more frequently than ischemic stroke (Figure 1) (Gov.br, 2022).

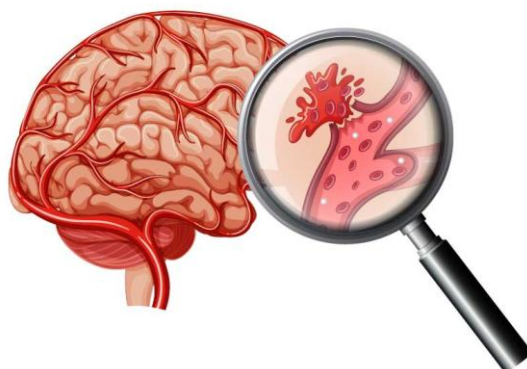


Figure 1: Hemorrhagic stroke

Source: <https://atlanticbrainandspine.org/understanding-hemorrhagic-strokes/>

Ischemic stroke:

Occurs when an artery becomes blocked, preventing the passage of oxygen to brain cells, which die. This obstruction can occur due to a thrombus

(thrombosis) or an embolus embolism. Ischemic stroke is the most common and accounts for 85% of all cases (Figure 2) (Pigott, 2015; Carpenter *et al.*, 2021; Gros *et al.*, 2021; Gov.br, 2022).

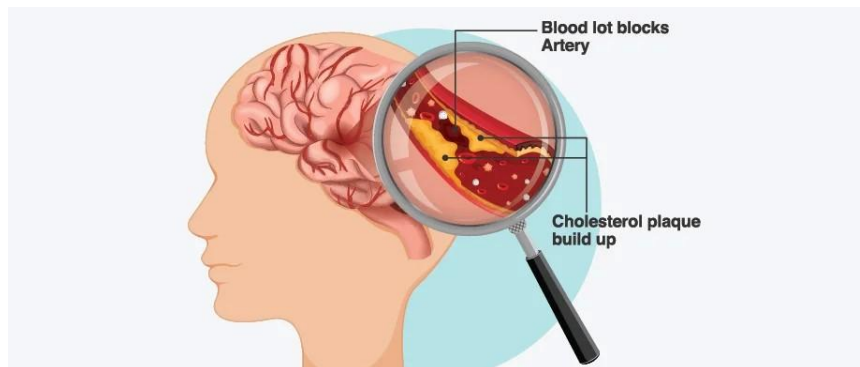


Figure 2: Ischemic stroke

Source: <https://www.ibshospitals.com/blog/understanding-ischemic-stroke>

Many symptoms:

Very severe headache, with sudden onset, especially if accompanied by vomiting; weakness or numbness in the face, arms, or legs, usually affecting one side of the body; paralysis, difficulty or inability to move; sudden loss of speech or difficulty communicating and understanding what is being said; loss of vision or difficulty seeing with one or both eyes. Other symptoms of ischemic stroke are dizziness and loss of balance or

coordination. Ischemic attacks can also manifest changes in memory and in the ability to plan daily activities, as well as negligence. In this case, the patient ignores objects placed on the affected side, tending to divert visual and auditory attention to the normal side, to the detriment of the affected one (Figure 3) (Brazilian Academy of Neurology, 2015; Santana and Chun, 2017; Gov.br, 2022; Winckler, 2024).

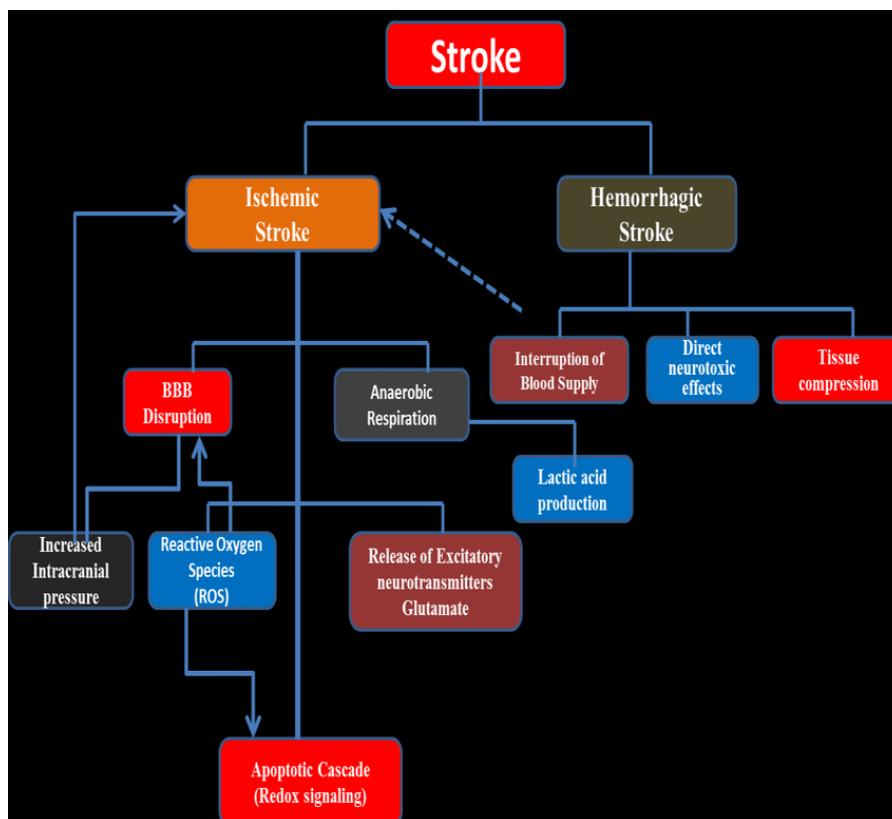


Figure 3: Schematic showing different types of strokes and the cascade of events following ischemia

Source: https://www.researchgate.net/figure/Schematic-showing-different-types-of-stroke-and-cascade-of-events-following-ischemia_fig3_348554347

The symptoms of intracerebral hemorrhagic stroke may include nausea, vomiting, mental confusion, and even loss of consciousness. Hemorrhagic strokes, in turn, are commonly accompanied by drowsiness, changes in heart rate and respiratory rate, and, occasionally, seizures. Strokes are a medical emergency. If you think you or someone else have one, you should go to the nearest hospital emergency room immediately for a complete diagnosis:

Risk factors: hypertension; diabetes; smoking; frequent consumption of alcohol and drugs; stress; high cholesterol; cardiovascular diseases, especially those that cause arrhythmias; sedentary lifestyle; blood diseases; aging; people over 55; genetic characteristics;

black race; family history of cardiovascular diseases (Santana and Chun, 2017; Gov.br, 2022).

Rehabilitation: An important part of treatment, the rehabilitation process often begins in the hospital itself, so that the patient can adapt more easily to their new situation and reestablish their mobility, functional abilities, and physical and mental independence. This process occurs when blood pressure, pulse, and breathing stabilize, often one or two days after the stroke, and is conducted by a multidisciplinary team consisting of neurologists, nurses, physiotherapists, and occupational therapists (Figure 4) (Brazilian Academy of Neurology, 2015; Winckler, 2024).

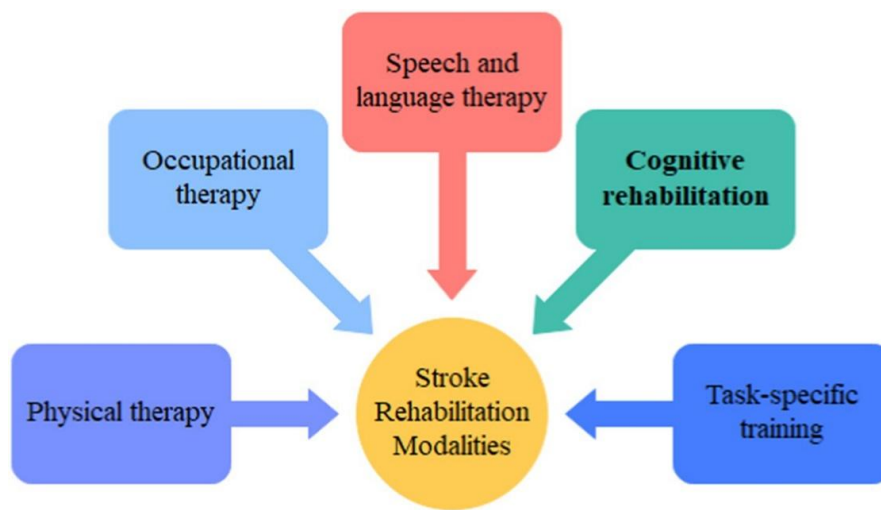


Figure 4: Different stroke rehabilitation modalities

Source: Doi: 10.3389/fneur.2024.1402729

The relearning process requires patience and determination from the patient and also from their caregiver, who plays an extremely important role throughout the rehabilitation. Another aspect of considerable importance is the reintroduction of the individual to social life, whether through light walks, shopping in stores, or any activities common to their normal routine (Brazilian Academy of Neurology, 2015; Santana and Chun, 2017; Li *et al.*, 2024; Winckler, 2024).

1.2. OBJECTIVE

The objective of the project is to verify whether Transcranial Magnetic Stimulation (TMS) can contribute to improving the health conditions of individuals after stroke.

2.0. METHODS

This study is an integrative literature review. A literature review is a study based on collecting selected materials and bibliographies, through a precise search in the databases made available by the scientific community. To collect the material in the databases, keywords related to the subject of the study are used, so that the use of Boolean operators (and, or and not) allows

for further refinement of the results and, consequently, the corpus of the research. To ensure a more comprehensive search, the descriptors were combined using different strategies. For this review, 14 articles were selected, whose inclusion criteria were defined for selection: (1) publication in English; (2) related to the objective of this work; (3) publication between 2016 and 2021. Regarding the exclusion criteria, we used: (1) repeated records on different platforms; (2) articles incompatible with the objective of this review; and (3) literature reviews.

3.0. SELECTED STUDIES

The consequences of a stroke are varied, with the most common being weakness, difficulty speaking, and imbalance. Transcranial Magnetic Stimulation (TMS) has been used in clinical research for stroke rehabilitation with encouraging results. The results are best in the first 6 months after the stroke. Suppose you have the opportunity to undergo stimulation treatment. In that case, it may be appropriate, but be aware that the results are not guaranteed, especially if the stroke occurred more than 6 months ago (Figure 5) (Fitzgerald *et al.*, 2008; Santana and Chun, 2017; Sheng *et al.*, 2023; Winckler, 2024).



Figure 5: rTMS stands for Repetitive Transcranial Magnetic Stimulation

Source: <https://brain-nm.com/treatment/repetitive-transcranial-magnetic-stimulation-rtms/>

It is worth remembering that all rehabilitation must include the work of other professionals in addition to the doctor, such as a physiotherapist, speech therapist, and occupational therapist, among others. Current research conducted at Universidade de São Paulo is obtaining improvements in balance with the use of stimulation (Casanova *et al.*, 2014; Refkes and Fink, 2016; Santana and Chun, 2017; Winckler, 2024).

The treatment is a non-invasive technique and can be applied to people who have suffered a stroke, after a neurological medical evaluation. There is an activation

of the functional areas of the injured limb which, combined with occupational therapy, increases the patient's chance of recovery. Transcranial magnetic stimulation (TMS) has been recognized as an effective technique in the treatment of depression since 2012 in Brazil and since 2008 in the United States. This approach is considered a non-invasive form of brain stimulation, using a magnetic field to generate an electric field in neurons, with the ability to stimulate or inhibit them (Figure 6) (George *et al.*, 2010; Almeida, 2012; Santana and Chun, 2017; Winckler, 2024).

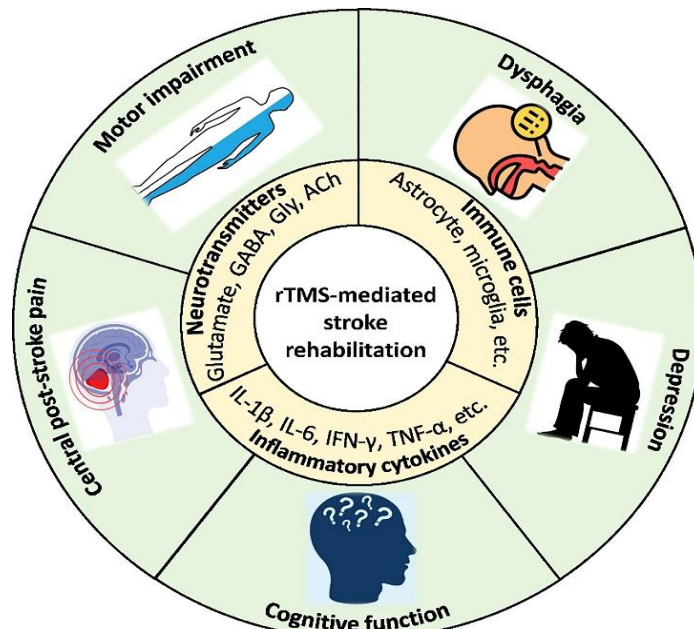


Figure 6: Scheme of neuroinflammation mechanisms of rTMS-mediated stroke rehabilitation

Source: Doi: 10.3389/fimmu.2023.119742

Repetitive Transcranial Magnetic Stimulation (rTMS) is increasingly being discovered to treat various diseases that affect the brain with this type of

neurological technology known as non-invasive brain neuromodulation. Patients who have suffered a stroke can count on this ally in the treatment and recovery of

injured brain areas through neurorehabilitation (Almeida, 2012; Bensenor, 2015; Winckler, 2024).

When a stroke occurs, the blood vessel that carries oxygen and nutrients to the brain is blocked by a clot ischemic stroke or ruptures hemorrhagic stroke, depriving part of the brain of blood and oxygen. This

leads to the death of brain cells and lasting deficits, such as speech disorders, vision and memory problems, and motor problems. There is decreased neuronal activity in the affected area and an imbalance in the recovery of the injured side (Figure 7) (Ovando *et al.*, 2010; Xiao *et al.*, 2020; Satisht *et al.*, 2021; Winckler, 2024).

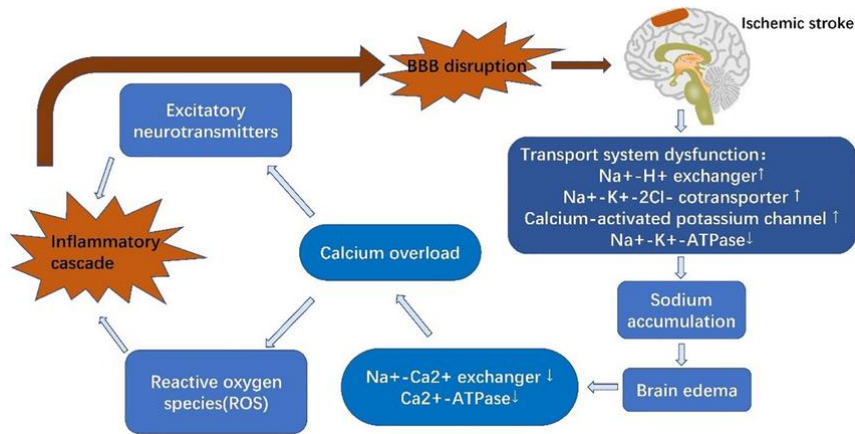


Figure 7: Schematic diagram of blood-brain barrier alterations in acute ischemic stroke. Reduced levels of glucose and oxygen result in dysfunction of EC ion transporters, inducing calcium overload and triggering inflammatory cascades. These inflammatory cascades further degrade tight junctions, thus aggravating brain edema and increasing infarct size

Sources: https://www.researchgate.net/figure/Schematic-diagram-of-blood-brain-barrier-alterations-in-acute-ischemic-stroke-Reduced_fig2_343643605 and Doi: 10.3389/fnins.2020.00764

Noninvasive transcranial magnetic stimulation (rTMS) may help post-stroke patients regain language and speech dominance. This is a major advance in the treatment of stroke sequelae because 20% to 30% of stroke patients suffer from aphasia, a neurological medical term for patients who have difficulty understanding and formulating language after a stroke. The study demonstrated significant efficacy in restoring language, which highly benefits the patient's quality of life [Professor Alexander Thiel - McGill University - Montreal] (Carrington *et al.*, 2014; Pigott, 2015; Carpenter *et al.*, 2021; Gros *et al.*, 2021).

The technique called neural stimulation, which performs treatments through the conscious touch of specific points on the hand, strengthens the three basic pillars of the human body, the nervous, immune, and blood systems, benefiting them. A TMS can act by modulating cortical excitability in the human brain. Therefore, this technique can be used in the treatment of brain pathologies that involve changes in cortical excitability, such as epilepsy, stroke, dystonia, Parkinson's disease, depression, and schizophrenia. psychostimulants, such as methylphenidate, are the first choice for treatment (Ovando *et al.*, 2010; Almeida,

2012; Bensenor, 2015; Satisht *et al.*, 2021; Winckler, 2024).

Neuromodulation is useful in treating imbalance between the cerebral hemispheres and facilitating neuronal plasticity, with rehabilitation. Forms of neuromodulation in the aftermath of a stroke include transcranial magnetic or electrical stimulation. A coil is positioned over the head, usually while the patient is seated in an armchair. Pulses of magnetic stimulation are applied to the head at rest or while performing a task. These pulses can be applied to the side of the brain affected by the stroke, the opposite side, or both sides (George *et al.*, 2010; Carrington *et al.*, 2014; Bensenor, 2015; Barbosa, 2019).

Electrodes Fixed to The Skull (tDCS) promotes an increase or decrease in cortical excitability according to the type of stimulation used, anodic or cathodic, respectively, and is capable of producing synaptic plasticity. Its effects are related to long-term potential or long-term depression depending on the established objective (Figure 8) (Fagundes *et al.*, 2015; Goh *et al.*, 2015; Andrade, 2019; Azevedo and Marques, 2020).

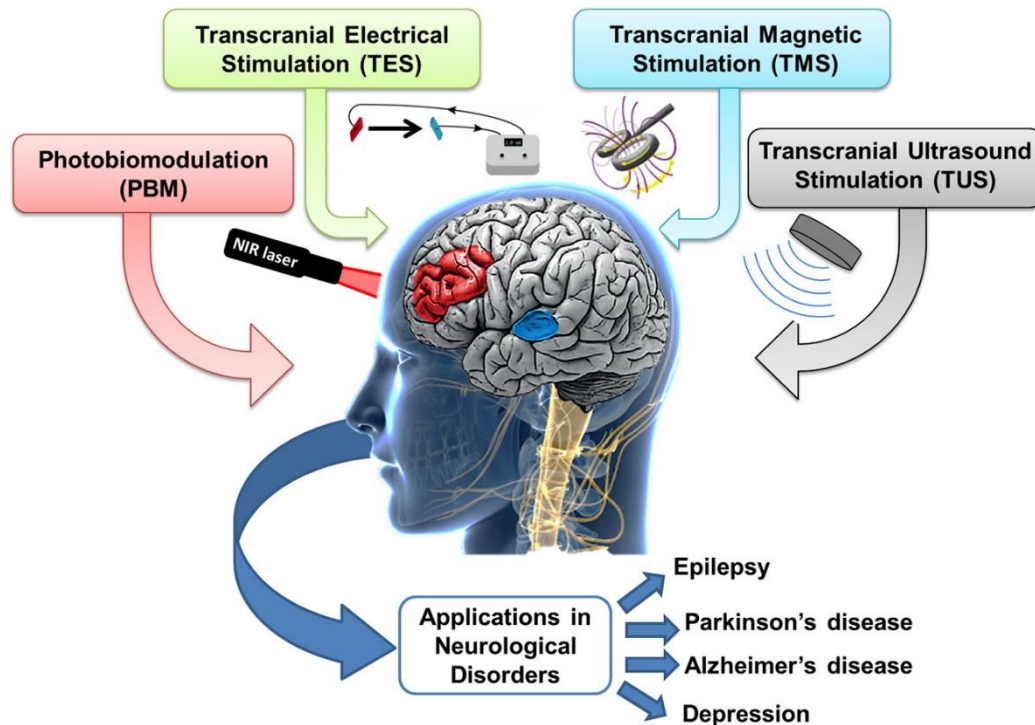


Figure 8: The main reasons behind the rapid emergence of physical brain stimulation techniques in the treatment of neurological disorders are the non-invasive nature of targeting brain sites of interest, minimal side effects, high efficacy, quick results, easy handling, and they are also therapeutic tools for various neurological disorders

Source: Doi: <https://doi.org/10.1016/j.lfs.2022.120869>

The rTMS works by applying pulses of the same intensity to a cortical area at a specific frequency/time through a coil interface. Depending on the type of pulse chosen, the current can cause impairment or activation of cortical areas. Lower frequencies are responsible for decreasing the excitability of the motor cortex, while higher frequencies have the opposite effect. Recent studies have demonstrated the effectiveness of rTMS in the rehabilitation of individuals with stroke sequelae due to the improvement in the reorganization of their cortical activity (Machado *et al.*, 2011; Adachi *et al.*, 2012; Goh *et al.*, 2015; Azevedo and Marques, 2020).

Cortical stimulation electrode implantation: A surgical procedure to implant a device that stimulates the surface of the brain, either just below the skull or within the brain, to influence the function of neural circuits that affect the condition; Implantation of an intracanal drug infusion pump, a delivery system that delivers baclofen; A muscle relaxant medication commonly used to reduce

spasticity directly into the spinal cord (Machado *et al.*, 2011; Adachi *et al.*, 2012; Marques, 2020).

The principle of action in pain is to increase the function of the pathways that block pain. Its effect on motor skills loss of strength and spasticity occurs by inhibiting the healthy side and stimulating the diseased side, so that the healthy side stops blocking the diseased side and the latter can better develop its residual functions (Conforto and Ferreira, 2009; Adachi *et al.*, 2012; Huang *et al.*, 2017).

The neuromodulation sessions were preceded by local abdominal treatment using tecar therapy, a 448KHz radiofrequency. After two weeks, the treatment frequency was three times a week, with an increase in the therapeutic resources of respiratory endurance exercises. During this period, the patient was instructed to use an auricular vagal electrostimulation at home in the late afternoon, when symptoms were exacerbated, or during times of increased symptoms (Figure 9) (Rao *et al.*, 2014; Celnik, 2015; Zhao *et al.*, 2016).

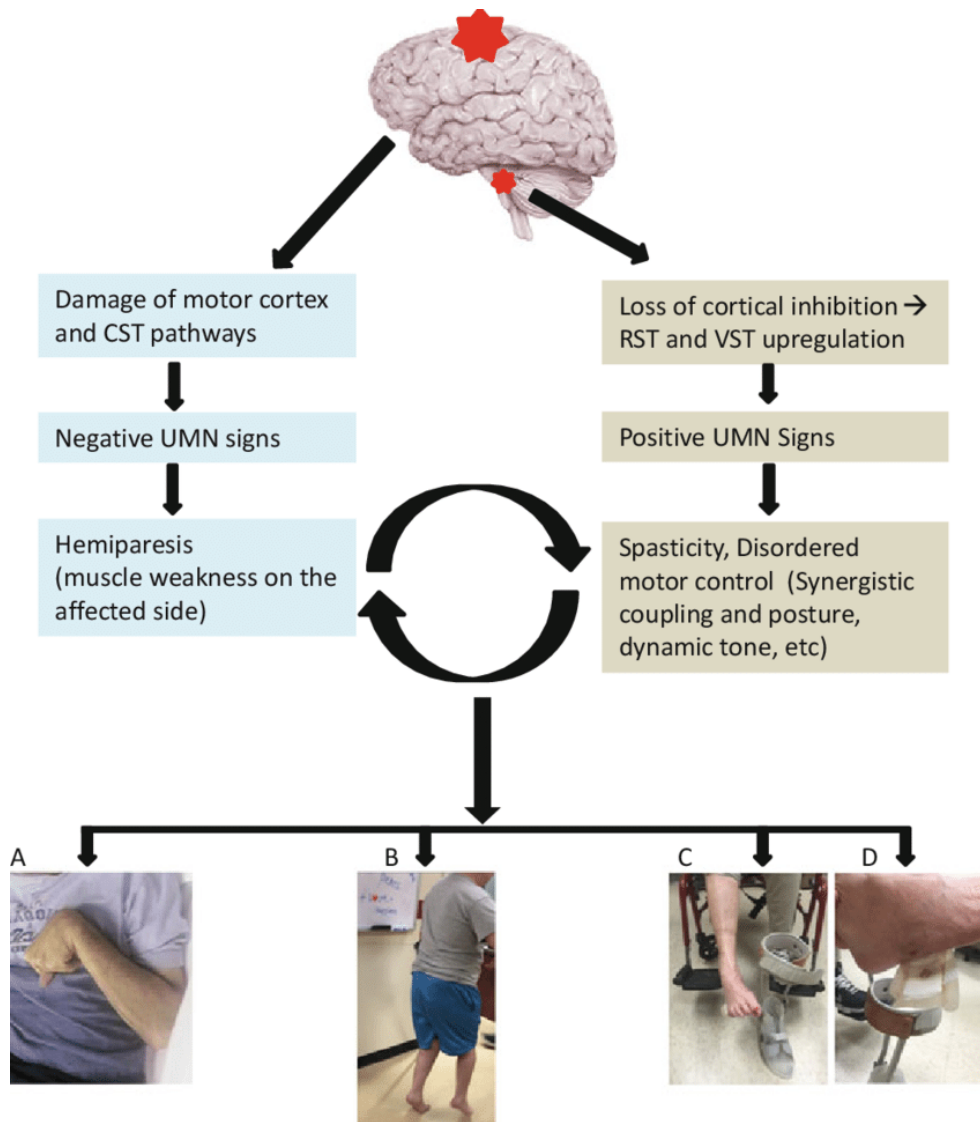


Figure 9: Pathophysiology of spasticity and its reticulospinal tract, relations to clinical problems. (UMN) Upper Motor Neuron, (CST) Corticospinal Tract, (RST) (VST) Vestibulospinal Tract, (MN) Motor Neuron (a) Abnormal posture leading to difficulty with hygiene and dressing; (b) Abnormal gait; (c) Spastic equinovarus; (d) Pressure sore

Source: https://www.researchgate.net/figure/Pathophysiology-of-spasticity-and-its-relations-to-clinical-problems-UMN-upper-motor_fig1_347527543

Neuromodulator resources, such as intraoperative vagal stimulation, have proven effective in regulating intestinal transit when frequencies in the 5 Hz or 20 Hz band are used for just 2 minutes, before and after colorectal resection, using implantable electrodes. The reduction of pro-inflammatory cytokines is the likely therapeutic mechanism of the technique. New clinical and surgical approaches have allowed for greater survival and quality of life for these patients. Low anterior resection is currently standard surgery, which allows preservation of the sphincter without the need for permanent colostomy (Rao *et al.*, 2014; Celnik, 2015; Asseldonk and Boonstra, 2016; Zhao *et al.*, 2016).

However, it is associated with Ultra-Low Rectal Resection Syndrome (LARS), a severe, extremely

limiting bowel dysfunction that affects 60-90% of patients, with symptoms of fecal incontinence of gas and/or feces, fecal urgency inability to avoid a bowel movement for 15 minutes, clustering of new fecal evacuation within 15 minutes after the last bowel movement, and frequent bowel movements increased bowel movement frequency (Rao *et al.*, 2014; Celnik, 2015; Asseldonk and Boonstra, 2016; Zhao *et al.*, 2016; Askinn *et al.*, 2017).

3.1. Application of low-frequency TMS

The inhibitory frequency is 1 Hz applied to the motor cortex of the hand in the unaffected region to reduce interhemispheric damage. Interhemispheric prevention is an interference associated with the lack of improvement in the thermometer affected by the stroke,

that is, the non-diseased side of the stroke creates a certain dominance, preventing the diseased side from recovering. TMS helps prevent this phenomenon, thus

freeing the diseased side for motor improvement (Figure 10) (Li *et al.*, 2022; Rocha, 2022; Vicente, 2022; Sousa *et al.*, 2023; Moraes *et al.*, 2024).

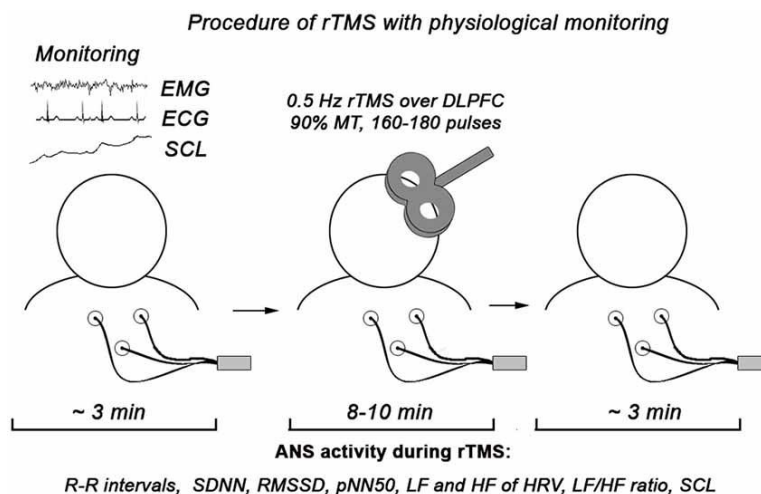


Figure 10: Procedure of physiological monitoring during rTMS session. In the statistical analysis, we used only autonomic data recorded during rTMS (approximately 10 min)

Source: <https://doi.org/10.3389/fnhum.2014.00851>

3.2. Application for High-Frequency (TMS)

The application of high-frequency TMS (5-20 Hz) to the affected motor cortex can directly improve plasticity, learning, and the acquisition of motor skills in stroke patients. Currently, Brazil ranks sixth in the world in cases of stroke, behind the USA, China, Japan, India, and Russia, standing out as the country with the highest mortality rate due to stroke in Latin America and the leading cause of death from cardiovascular diseases in Brazil. As it is one of the main causes of disability and mortality, stroke is one of the main diseases that burden the public health system (SUS) (Emara *et al.*, 2010; Avenanti *et al.*, 2012; Eldaief *et al.*, 2013; Higashi Clinic, 2018; Bakulin *et al.*, 2020).

4. CONCLUSION

In an integrative review, they concluded that TMS has other indications, still little addressed, such as in the treatment of chronic pain, such as fibromyalgia, chronic tinnitus, degenerative joint diseases such as osteoarthritis, as well as in the treatment of addictions and in improving the physical performance of athletes. TMS usage protocols require further research so that solid evidence can emerge about its application and so that the technique can be widely used, respecting the indications, contraindications, and therapeutic effects.

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