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REVIEW

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Effects of primary motor cortex noninvasive brain stimulation on post-stroke aphasia: a narrative review

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Abstract

Aphasia is one of the most debilitating impairments after stroke, significantly affecting patients' comprehension, communication, functional recovery, and overall quality of life. There are numerous strategies for treating aphasia in post-stroke patients. Noninvasive brain stimulation (NIBS) technologies, particularly transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS) have demonstrated promising improvements in post-stroke aphasia when used as an adjunct therapy. However, previous studies have stimulated language-related areas only. This literature review examined the effect of primary motor cortex (M1) stimulation on language function and aphasia following stroke. Applying tDCS or TMS to the primary motor cortex has been shown to improve language recovery following stroke, suggesting a combination with other forms of speech-language rehabilitation has the potential to improve aphasia.

Keywords Stroke, Aphasia, Primary motor cortex, Transcranial direct current stimulation, Transcranial magnetic stimulation

Introduction

Aphasia is a language impairment with varying degrees of severity on comprehension, spontaneous speech fluency, repetition, naming, and written language [1]. Post-stroke aphasia (PSA) impedes social interaction and overall quality of life and is often associated with several comorbid impairments including upper extremity, cognitive, and mood dysfunction [2]. Among the various types of language impairments including Wernicke's (receptive), Broca's (expressive), transcortical, conduction, anomic, and global aphasia that can occur after a stroke, anomia or word-finding difficulty is common in all types of aphasia. Anomia usually occurs following a left hemisphere stroke and is considered the most recalcitrant type of aphasia, requiring special management strategies such as lexical-semantic therapy [3, 4]. Anomia results in errors of both commission and omission [5]. Commission occurs when a patient produces the wrong word, while omission is when a patient fails to produce a word. Often complicating a PSA patient's attempt to communicate is a co-occurrence of apraxia of speech (AOS), a motor speech disturbance whereby is hard to move the mouth, lip, tongue, and jaw to make appropriate sounds and words. According to the same neuroanatomical involvement, individuals with non-fluent or expressive aphasia usually have AOS [6, 7].

Speech production pathways in the brain work by activating multiple different parts of the motor cortex, followed by sending signals to the corresponding organs including the laryngeal and oropharyngeal muscles [8].

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Among the various requirements for accurate speech production, phonation and articulation are two critical components activated in the larynx-associated area of the primary motor cortex [9, 10]. Coordination between speech muscles is required during articulation, whereas vocal cords play an important role during phonation.

Distinct regions of the primary motor cortex, most notably the lower part of M1, are activated during speech production [11, 12]. The primary motor cortex's prominent functional role in the dominant hemisphere compared to the non-dominant hemisphere demonstrates the lateralization toward the left side indicating the left hemisphere's remarkable role in language production, particularly phonation and articulation [13].

Numerous studies indicate a link between motor and linguistic abilities following stroke, implying a synergistic recovery pattern between language and motor involvement in patients with these concomitant impairments. For instance, improvement in motor skills ameliorates speech and vice versa [14–18]. According to previous research, activating the motor network aids in language recuperation. One possible explanation for this connection is the mirror neuron system (MNS), a multimodal group of neurons in the brain that activates in response to various stimuli. For instance, when a person observes or performs a particular task, the cortical region related to that action is activated. Neuroimaging methods such as functional magnetic resonance imaging (fMRI) are used to detect MNS in humans [19]. Language mirror neurons lateralize to the left hemisphere, which contains the right-hand motor cortex, and this region's excitability increases as a result of reading and spontaneous speech [20]. Studies also show that hand movement observation or training activates the mirror neuron system to a greater extent and can improve language function. In terms of its unique capacity to facilitate the recovery process, mirror neuron-based therapy can be employed to rehabilitate motor and language impairment following stroke [21–23].

There are various strategies for managing post-stroke aphasia [24]. While speech-language therapy is the cornerstone of aphasia treatment [25], intensive therapy is necessary to achieve the best outcomes, with research suggesting that approximately 9 h of speech therapy per week is required for optimal recovery. However, these intensive sessions seldom occur, with patients receiving only an average of only 1–5 h per week [26].

To compensate for the lack of intensive hours of traditional speech therapy treatments, other techniques such as noninvasive brain stimulation (NIBS), can be used to enhance the effect of conventional therapy. NIBS technologies such as transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS) are frequently employed and have promising results in treating post-stroke aphasia. Intermittent theta-burst stimulation (iTBS) is a newer form of TMS that delivers magnetic pulses in a specific pattern (intermittent bursts of theta frequency) to the motor cortex of the brain. On the other hand, TMS can be delivered in a variety of patterns and frequencies to different brain regions. This pattern of iTBS has been shown to enhance cortical excitability and promote long-term potentiation (LTP), a process by which the strength of synaptic connections between neurons is increased [27, 28]. Although TMS is more expensive and targeted than tDCS [29], in terms of safety issues, both are well-tolerated, and while TMS can cause seizures in rare cases, tDCS induces minimal side effects. NIBS are generally safe but there are some contraindications that need to be considered before applying them. The absolute contraindications are metal implants in the skull, eye, or any serious skin lesions on the scalp. There are also relative contraindications, such as a previous history of seizures or the use of medication that may increase the risk of it. Additionally, it is important to note that the effects of NIBS have not been studied on pregnant or breastfeeding women and should be avoided in those cases [30–32].

A systematic review of the efficacy of tDCS on PSA has shown promising results in terms of naming ability in the chronic post-stroke stage (after 6 months). However, the area stimulated was associated with language, including the left and right inferior frontal gyrus, the left superior temporal gyrus, and the dorsolateral prefrontal cortex [33]. In addition to the language-related areas, anodal stimulation of the primary motor cortex with an excitatory effect has also been shown to improve speech following stroke [34–39]. M1 or primary motor cortex stimulation may also influence distant neural areas via neural network connectivity, and the accompanied language task produces a better functional outcome [38]. Additionally, high-frequency TMS over the M1 region, such as iTBS, can also improve language function [39].

The aim of this study is to investigate the effects of noninvasive brain stimulation targeted primary motor cortex and explore language outcomes in individuals with post-stroke aphasia.

Methods

For this qualitative review, relevant published articles indexed in Google Scholar and PubMed between January 2014 and March 2022 were searched. The search words were (((((“electrical stimulation of the brain” [Mesh Terms] OR (“noninvasive brain stimulation” [Text Word] OR (“transcranial direct current stimulation” [Mesh Terms]) OR (“transcranial magnetic stimulation” [Mesh Terms] OR (“repetitive transcranial magnetic stimulation" [Mesh Terms] AND ("motor cortex" [Mesh Terms] OR ("primary motor cortex" [Text Word]) AND ("stroke" [Mesh Terms]) OR ("cerebrovascular disorder" [Mesh Terms]) AND ("aphasia" [Mesh Terms]) OR ("Broca aphasia" [Mesh Terms]) OR ("Wernicke aphasia" [Mesh Terms]) OR ("anomic aphasia" [Mesh Terms]) OR ("global aphasia" [Mesh Terms]).

Inclusion criteria were adult participants with a confirmed diagnosis of stroke and subsequent aphasia, studies that reported language outcomes, such as naming ability, speech fluency or comprehension following NIBS of the primary motor cortex, and studies that used randomized controlled trials (RCTs), quasi-experimental, or single-case experimental designs. Studies that investigated the effects of invasive brain stimulation, such as deep brain stimulation (DBS), or target brain regions other than the primary motor cortex were excluded. In addition, associated psychological or other neurological conditions were not included in this study.

Discussion

Neuroplasticity, the ability of the brain to change or modify neural networks, occurs after stroke and follows a non-linear pattern, with reorganization primarily happening during the acute and sub-acute phase (within the first 90 days) with continued recovery into the chronic stage. The reactivation of intact cortical areas is one of the mechanisms important in this PSA recovery process [40, 41]. Thus, rehabilitation using NIBS changes cortical excitability and is advantageous at various stages of recovery.

NIBS are neuromodulator tools capable of promoting plasticity in the brain's neural networks. tDCS delivers a weak electrical impulse through the scalp, altering cellular excitability and amplified by the associated task. TMS also modifies neural connectivity though has a more focal effect and is not task-dependent [24]. Numerous studies have established the efficacy of NIBS in neurorehabilitation, particularly after a stroke [42].

M1 and other brain regions are interregional, whereby increased activity in the primary motor cortex spreads to other regions, including the premotor area, posterior supplementary motor area, cerebellum, thalamus, putamen, and the cingulate motor area [43, 44]. As a result, tDCS and TMS change motor cortex excitability affecting remote fields of the brain [45–47]. M1 activation with TMS enhances abstract word processing through a selected mechanism which decreases undesirable processing in other parts of the language comprehension system [48, 49].

The current review establishes stimulating the primary motor cortex affects language, remarkably naming performance, and articulation (Table 1).

There are some methodological similarities among the various studies, including the placement of the anode electrode and using tDCS in conjunction with a language task. Regardless of the severity of the symptom, tDCS can be effective in post-stroke aphasia. Additionally, multiple sessions, greater than five, are more effective at promoting language function than just a single session [50, 51]. In addition, coupling tDCS with a language task can increase the efficacy of the stimulation [52]. Language-related tasks include word retrieval training, lexical decision tasks, reading, and the articulatory–kinematic method. Apart from anodal tDCS over the language areas, TMS applied over M1 improves language as well. However, there is a lack of data in terms of TMS application over the M1 region in PSA.

Initially, Meinzer et al. [34] utilized M1-tDCS combined with intensive computer-based naming therapy over two weeks (twice a day for 4 days). The outcome measures were assessed before and after the intervention, followed by 6 months later. Naming and communication abilities improved after the intervention and maintained over 6 months. They emphasized the efficacy of multiple sessions of tDCS associated with a task-related activity. Moreover, functional MRI during the stimulation concomitant with a task showed increased activity in the bilateral prefrontal regions, and they concluded that, apart from the effect of direct stimulation, activation in the adjacent area can also play an important role.

A study by Stahl et al. [38] also demonstrated the positive effects of anodal tDCS over M1 coupled with intensive speech-language therapy (SLT) on communication and naming abilities in PSA.

Anodal tDCS was located based on 10–20 international EEG systems, and they stated that this montage is easily accessible and not required pre-treatment mapping.

Branscheidt et al. [35] employed M1-tDCS concomitant with a lexical decision task (LDT). Anodal tDCS was located regarding TMS as guidance and lasted 20 min in each session, and LDT took about 22 min. Participants should differentiate between pseudowords from existing German words through a computer. Action-like words, such as typing, and different objects from action verbs were chosen. The test lasted 22 min and consisted of four blocks (each block contains 40 words), and there was a 2-min pause between each block. Results showed that M1-tDCS has more influence on action-related verbs in comparison to object words. They assumed that stimulation of the motor cortex might be responsible for better action word understanding. Moreover, motor excitability could facilitate lexico-semantic networks.

Darkow et al. [36] used an MRI-compatible tDCS to observe the activity patterns while stimulating the M1. Functional MRI showed higher activation in the

Table 1 Summary of M1 stimulation studies in post-stroke aphasia

Authors	Study design	Subject	Type of intervention	Session	Aphasia severity	Type of aphasia	Outcome measure	Main result
Meinzer et al. (2016) [34]	RCT	26 Chronic	Anodal tDCS (1 mA) over the left motor cortex	16	Mild	Wernicke Broca Amnestic Global	AAT	M1 tDCS enhances language recovery after stroke
Branscheidt et al. (2017) [35]	RCT	16 Chronic	Anodal tDCS (2 mA) over the left motor cortex	1	Mild	Broca Amnestic Global	AAT	Motor cortex stimulation improves lexico-semantic retrieval
Darkow et al. (2017) [36]	RCT	16 Chronic	Anodal tDCS (1 mA) over the left motor cortex	1	Mild	Amnestic	AAT	M1-tDCS enhances activity and connectivity within a naming network
Wang et al. (2018) [37]	RCT	52 Sub-acute	M1-tDCS (1.2 mA) Broca's area	10	Moderate–severe	Broca Mixed Global	PACA BDAE	M1-tDCS improves the speech function
Stahl et al. (2019) [38]	RCT	130 Chronic	Anodal tDCS (1 mA) over the left motor cortex	15	Mild–moderate Severe	Wernicke Broca Amnestic	AAT ANELT	M1-tDCS enhances naming ability
Xu et al. (2021) [39]	Pilot	16 Sub-acute Chronic	TMS (iTBS 50 Hz, 800 pulses) over the primary motor cortex	1	Mild moderate Severe Very severe	Not applicable	WAB-AQ	M1-iTBS enhances language function and neural connectivity

AAT Aachen Aphasia Test, PACA Psycholinguistic Assessment in Chinese Aphasia, BDAE Boston Diagnostic Aphasia Examination, ANELT Amsterdam Nijmegen Everyday Language Test, WAB-AQ Western Aphasia Battery Aphasia Quotient, iTBS intermittent theta-burst stimulation, TMS transcranial magnetic stimulation, M1 primary motor cortex, tDCS transcranial direct current stimulation, RCT randomized controlled trial

language-related regions (bilateral prefrontal cortices) after applying anodal tDCS compared to the motor and visual components, and the difference was statistically significant ($P=0.011$). They demonstrated the favorable outcome of anodal tDCS on language network connectivity, particularly coupling with a specific task (naming a picture). The most activity was in the language-related areas; however, the source of stimulation was the primary motor cortex. Thus, the associated task performed during the stimulation affects the tDCS rather than the stimulation's site.

The aforementioned studies aimed to investigate the effects of real and sham tDCS over M1 on different outcome measures. However, Wang et al. [37] carried out comparative research among M1-tDCS, sham-tDCS, and tDCS over Broca's region groups. The M1-tDCS group revealed promising results, particularly in word repetition and articulation compared to the other groups. AOS also improved following the application of M1-tDCS. Based on neuroanatomical models, the premotor cortex is most affected in patients with apraxia. On the other hand, an anodal electrode located over M1 is large enough to affect adjacent regions, and this could justify the motor speech improvement in these patients. Their explanation for the lesser impact of Broca's stimulation was the larger size of the ischemic brain lesion in that area.

Few studies have determined brain functional changes following iTBS in patients with PSA. However, Xu et al. [39] designed a preliminary study to assess the immediate effects of M1-iTBS on brain activities and connectivity. FMRI exhibited increased ipsilesional cortical excitability and altered connectivity in different regions, which facilitates language-related networks. Right frontal lobe activation was prominent after the intervention. This area is located close to the mirror part of Broca, which accounts for language recovery in patients.

According to the current literature review, stimulating the primary motor cortex has several advantages. First, this area is not required for brain mapping to determine the presence of intact neural connections before initiating treatment, and localization is simple. Thus, this is a cost-effective and time-saving method. Second, activating preserved language segments improves the region's connectivity, which aids in the recovery process.

Conclusion

In conclusion, whether through direct stimulation of M1 or network connections to other regions of the brain, M1 stimulation can improve aphasia and is recommended as a complementary technique for post-stroke aphasia management. However, motor cortex stimulation in conjunction with various language tasks should be considered when applying tDCS to assess the various characteristics of language recovery. Moreover, additional research is required regarding the application of TMS.

Abbreviations

AAT	Aachen Aphasia Test
ANELT	Amsterdam Nijmegen Everyday Language Test
AOS	Apraxia of speech
BDAE	Boston Diagnostic Aphasia Examination
DBS	Deep brain stimulation
FMRI	Functional magnetic resonance imaging
ITBS	Intermittent theta-burst stimulation
LDT	Lexical decision task
LTP	Long-term potentiation
M1	Primary motor cortex
MNS	Mirror neuron system
NIBS	Noninvasive brain stimulation
PSA	Post-stroke aphasia
PACA	Psycholinguistic Assessment in Chinese Aphasia
RCT	Randomized controlled trial
SLT	Speech-language therapy
TMS	Transcranial magnetic stimulation
TDCS	Transcranial direct current stimulation
WAB-AQ	Western Aphasia Battery Aphasia Quotient

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SR designed the work. SR and SG collected the data. SR, VB, and HF interpreted data. SR and VB wrote the main manuscript. SR, SG, and HF prepared Table 1. All authors reviewed the manuscript. All authors read and approved the final manuscript.

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