Rebooting the Brain: Non Invasive Brain Stimulation and the Future of Neurorehabilitation

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Abstract

Non-Invasive Brain Stimulation (NIBS) is an emerging technology in neurorehabilitation with potential benefits to promote the neuroplasticity and functional recovery. This mini-review aims to summarize the recent clinical evidence evaluating the role of NIBS modalities- including repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS), theta burst stimulation (TBS) - in neurorehabilitation settings. We explore the application of NIBS in major neurological conditions including spasticity and motor recovery in post-stroke, spinal cord injury and cerebral palsy, gait in Parkinson's disease and, cognitive improvement in traumatic brain injury. Recent evidence suggests that integrating NIBS with traditional therapies and with advanced technologies like virtual reality, robotic assisted therapies can further improve the functional outcome. Despite promising results, clinical heterogeneity, lack of standardized safety and treatment protocol and financial constraints limit its widespread use. There is a need for better clinical trials to guide its clinical application. NIBS has the potential to become an important component of evidence based neurorehabilitation interventions in the future.

Keywords: Repetitive Transcranial Magnetic Stimulation (rTMS), Transcranial Direct Current Stimulation (tDCS), theta burst stimulation (TBS), Stroke Rehabilitation, Neuroplasticity, Electrical stimulation transcranial

DOI: https://doi.org/10.47391/JPMA.26-33

Introduction

Neurological disorders are one of the leading causes of long-term disability around the globe. They place a significant burden on healthcare systems and community resources.[1] Most traditional neuro-rehabilitation strategies result in functional improvements in patients but recently Non-invasive brain stimulation (NIBS) has also gained popularity as an adjunct to conventional rehabilitation in improving functional outcome.[2] It includes repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS), theta burst stimulation (TBS) and transcutaneous auricular Vagus nerve stimulation (taVNS). TMS was first described by Dr. Barker at Sheffield University, UK in 1985 and since then clinical research on NIBS is increasing.[2]

NIBS works on the principle of targetted neural stimulation of brain area by applying an electrical current directly or indirectly by creating an electrical field with magnetic induction on the scalp. The main goal of NIBS in neuro-rehabilitative setting is to create neuromodulation either by inhibiting or activating the neural activity in the target cortical area to induce neuroplasticity. All forms of NIBS have a potential to enhance motor, cognitive, and language domain as well as to reduce tone in carefully selected patients.[2]

There is growing evidence to support the role of NIBS role in various neurological disorders. For example, in case of stroke rehabilitation both tDCS and rTMS have shown to improve upper limb motor function, gait performance, and reduce spasticity.[3] Similar preliminary result have been reported in spinal cord injury and Cerebral palsy patients.[4,5] Moreover, in post-stroke patients with dysphasia and aphasia, NIBS also shows significant functional improvement.[3,6] In cases of traumatic brain injury (TBI) application of NIBS improves attention, executive function, motor recovery, and working memory.[7] NIBS has shown to be of benefit in patients with Parkinson disease by providing postural stability, gait improvement and overall motor recovery.[8]

Despite the emerging evidence, there are significant knowledge gaps, in creating clinical protocols for the optimal application of NIBS in rehabilitation settings. Many studies have shown mixed outcomes. This is likely due to different stimulation protocols, patient selection criteria, and different outcome measures. This results in a lack of consensus upon a protocol for clinical practice.[9] In addition, the mechanisms underlying NIBS induced neuroplasticity are not fully understood, resulting in difficulty for its usage to maximize functional gains.[10] The data on long-term

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sustainable benefits and the effect of NIBS when used along other rehabilitation therapies, such as task-specific training and occupational therapy is also limited.[11] Similarly, data regarding safety and feasibility in frail and comorbid populations are insufficient. These knowledge gaps highlight the need for well-designed, clinical trials with long term follow-ups.

Considering these development and limitations, a focussed synthesis of recent research findings in neuro-rehabilitative settings is required to guide future research and its implications.

NIBS is uniquely placed at the intersection of neuroscience, engineering and rehabilitation, and research in this domain could potentially play a pivotal role in transforming rehabilitation outcomes. We critically review the application of NIBS as supplement to traditional rehabilitation therapies for various neurological diseases such as stroke, spinal cord injury (SCI), traumatic brain injury (TBI), cerebral palsy, multiple sclerosis, and Parkinson disease.

Application of NIBS in Specific Neurological Disorders

The following section summarizes the current evidence for various neurological diseases with emphasis on rehabilitation outcomes, limitations in existing studies, and future direction for implications.

Stroke:

Stroke is one of the most widely studied conditions in NIBS. Neural recovery in stroke is often disrupted by maladaptation in cortical reorganization, which results in hyperexcitability in the contralesional hemisphere. This causes inhibition of affected part of brain. NIBS techniques such as rTMS and tDCS can correct this imbalance by either inhibition of contralesional hyperexcitability or stimulation of ipsilesional excitability.[3]

Kelin et. al in a subgroup analyses of a meta-analysis showed that bilateral and high intensity stimulation with tDCS resulted in improvement on post-stroke dysphagia and also enhanced deglutition function in these patients.[6] tDCS has also shown better results in motor recovery and aphasia rehabilitation.[3] However, combination approaches-such as task specific training, combined-induced movement therapy when used along with NIBS resulted in significant functional improvements than either modality alone.[11]

Despite these promising results, there is heterogeneity in stimulation parameters, and shorter follow up period. There is a need for future studies with patient-personalized stimulation protocol guided by neuroimaging biomarkers and incorporation of digital rehabilitation platform to maximize sustained recovery.

Spinal Cord Injury

Recovery after an SCI is hampered by disconnected corticospinal tract, inadequate plasticity, and spasticity. NIBS technique modulates excitability in spared cortical and spinal circuits.[4] A recent meta-analysis showed that rTMS has a potential role in improving the lower extremity strength and modest improvement in gait speed in comparison to sham-control group.[4] Another meta-analysis by Kuwahara et. al suggested that rTMS combined with robotic assisted gait training had better outcome than sham treatment alone.[12] It is important to note that the effect of tDCS in both the meta-analysis were modest.[4,12] Management of spasticity is of particular importance in SCI. NIBS decreases spasticity and improves functional outcome which can lead to improve the quality of life of SCI patients and also compliment pharmacological interventions.[4]

Despite all these benefits, the evidence is still heterogeneous as trials are of short duration with small sample sizes. Larger clinical trials are required to validate the role of NIBS in SCI rehabilitation, especially combining the NIBS with task specific training, and also evaluating the effects of NIBS with neuromodulatory drugs.

Traumatic Brain Injury

TBI is a major healthcare burden and cause of long term disability. It often results in persistent and/or residual motor, cognitive and behavioural impairments. This limits long-term recovery. Conventional rehabilitation provides some benefits but they can be sometimes partial. New research identifies tDCS as a promising new avenue. Stimulation by tDCS causes improved working memory, executive function, and attention by modulating cortical excitability.[7] Similarly, tDCS is also associated with improvements in motor recovery and reduction of post-TBI depression.[7] NIBS is generally safe and well tolerated, although optimal stimulation protocols are yet to be standardized. Large multicenter studies with standardized stimulation parameters and long-term follow-up are required to establish efficacy and integration into clinical guidelines.[7]

Cerebral Palsy:

Cerebral palsy (CP) results in lifelong disabilities in children. It can result in spasticity, impaired balance, and reduced motor coordination. Recent studies have explored NIBS as an adjunct to traditional rehabilitation techniques. Both tDCS and rTMS have demonstrated potential in improving motor function and learning, mobility, balance and enhance cortical reorganization.[5] A recent meta-analysis reported that tDCS combined with conventional rehabilitation significantly improved gross motor function,

gait patterns and reduced spasticity in children with CP.[5] rTMS has been investigated as well, particularly for upper limb motor recovery, with preliminary evidence of increased cortical excitability in motor regions.[5] NIBS is proven to be generally safe and feasible in paediatric populations. However long-term safety data remains limited. NIBS integrated with task-specific training, occupational therapy, and robotics-assisted rehabilitation holds promise in maximizing outcomes but data on these domain in paediatric population is scarce. Future large-scale paediatric trials are necessary to standardize stimulation parameters and identify optimal candidates for therapy.[5]

Multiple Sclerosis and Parkinson's Disease:

TMS and tDCS, or non-invasive brain stimulation (NIBS), has grown as a clinically significant tool to complement the rehabilitation of Multiple Sclerosis (MS) and Parkinson's disease (PD). Its main utility is in modifying cortical excitability and augmenting neuroplasticity and thus potentiating the efficacy of physical, occupational, and cognitive therapies.[9]

In MS, the rehabilitation aims to improve mobility, reduce cognitive impairment, and fatigue. Anodal tDCS over the dorsolateral prefrontal cortex (DLPFC) significantly decreases self-reported fatigue-one of the most disabling and treatment-resistant symptoms. Motor cortex stimulation also provides some benefits in motor functions enhancement and reduces spasticity, leading to independence in functioning.[13]

In PD, NIBS provides focal treatment for important motor impairment like freezing of gait, bradykinesia, and postural instability. rTMS at high frequency in the primary motor cortex is associated with clinically significant improvement in UPDRS motor scores, and the effect is larger than the stimulation session.[8]

Relevance to Pakistan and other Low- and Middle income Countries (LMICs)

NIBS like rTMS and tDCS is gaining popularity across South Asia. In Pakistan, knowledge and awareness among healthcare professionals for the application of NIBS in neurological and psychiatric disorders is limited. This was highlighted by a cross sectional study conducted to assess the awareness of speech language pathologists and neurologist about aphasia rehabilitation through NIBS. The study emphasizes the need for structured education and training of doctors about NIBS.[14] The Pakistan Institute of Mental Health in Rawalpindi is the one that is providing rTMS services for depression, and other neuropsychiatric conditions, providing a foundation for extension it into rehabilitation domain.[15] In Bangladesh, Ashiyana Medical College Hospital, Dhaka, has also established clinical rTMS services for psychiatric and neurological disease, showing regional feasibility and gaining clinical research interest.[16] All India Institute of Medical Science, New Delhi, India has conducted a clinical trial on NIBS to devise the optimal protocol of NIBS to implement it into post stroke rehabilitation for motor recovery.[17] These developments suggest increasing interest in adopting NIBS as a safe, feasible, portable and modestly cost effective rehabilitation adjunct in the LMIC. Considering the current evidence in support of NIBS for neurorehabilitation, we need to conduct local research, improve training and create disease and demographic specific protocol for its implementation in our region and other LMICs.

Conclusion

NIBS has evolved from an experimental procedure to a translational modality in neurorehabilitation. It supplements traditional therapies through central nervous system priming for adaptive change, to optimize recovery. Future research must aim at individualizing stimulation parameters and developing home-based NIBS solutions to allow optimizing maximal accessibility, compliance, and long-term outcomes.

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