

Neurodevelopmental Disorders: Role of Non-invasive Neuromodulation Therapies

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Introduction

The term neurodevelopmental disorders (NDDs) refers to a broad category of illnesses that usually occur in childhood and are related to brain disruptions that result in developmental deficits, such as autism spectrum disorder (ASD) and intellectual disability (ID). NDDs are complex conditions where abnormalities in brain development lead to impairments in behaviour, motor skills, cognition and/or communication. These impairments manifest as multifaceted challenges within individuals affected by NDDs. NDDs include a range of complex disorders that arise from atypical brain development, leading to difficulties in cognitive abilities, motor skills, behaviour and/or communication. NDDs are multi-faceted diseases defined by impairments in behaviour, communication, cognition and/or motor skills that result from abnormal brain development. NDDs are classified into six overarching groups such as ID, Communication disorders, ASD, SLD (specific learning disorders) neurodevelopmental motor disorders and ADHD (attention-deficit/hyperactivity disorder). These disorders usually occur in early childhood, typically before starting school¹ or at least some symptoms and impairment, persist well into adult life for many individuals. NDDs impact a substantial portion of the world's population and have a major global social and economic impact.² Based on statistics from the 2011 Census of India, 1.1% of the population in the 0–4 age group had any disability. Additionally, for children aged five to nine years, the prevalence of disabilities was reported at 1.5%³ Understanding the pathology of NDDs is indeed a complex endeavour yet unknown. Owing to the difficult and intricate nature of NDDs and their common or distinct aetiologies, many of the neural mechanisms behind them are still unknown. There is no cure and limited effective treatment options are available, majority focusing on symptomatic management. Usually, pharmacological treatment options are not preferred by physicians and parents as well. Nonetheless, some non-pharmacotherapies can assist children in controlling their symptoms. Combinations of medicine, behaviour therapy,

speech therapy, physiotherapy, sensory integration therapy and non-invasive neuromodulation are frequently used.

The Role of Non-invasive Neuromodulation Therapies Treating NDDs

Neuromodulation involves a wide range of invasive and non-invasive approaches aimed at modifying neuronal activity or excitability. Neuromodulation techniques can be defined as 'the alteration of nerve activity through targeted delivery of a stimulus, such as electrical stimulation or chemical agents, to specific neurological sites in the body's.⁴ Repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS), photo-bio-modulation (PBM) and neurofeedback are examples of frequently used non-invasive neuromodulation methods that were widely used in nervous system illness and their different secondary symptoms. New scientific discoveries have led to the development of promising treatments for a range of NDDs, including ASD and ADHD. These groundbreaking treatment approaches do not rely on pharmaceutical interventions or invasive procedures. Instead, they harness the power of specialised devices capable of modulating nervous system activity through various means, such as light, magnetic or electrical impulses. The results obtained thus far have shown considerable effectiveness, offering hope for individuals grappling with these conditions. Further, we would like to elucidate the role of non-invasive neuromodulation techniques for NDDs.

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Transcranial magnetic stimulation (TMS): The TMS is a non-invasive method that stimulates brain nerve cells using magnetic fields, aiming to alleviate symptoms. Unlike surgical procedures or electrode implantation, TMS does not require invasive interventions. Typically, single-pulse TMS, which like paired-pulse TMS, is utilised to investigate brain functioning. While rTMS is employed to generate enduring alterations in brain activity beyond the stimulation period. rTMS has garnered growing attention as a potential treatment approach for individuals with ASD.⁵ Further, low-frequency rTMS improved symptom severity in patients with tic disorder,⁶ improved sustained attention and processing speed in ADHD,⁷ and improved cognition in mild cognitive impairment.⁸ A review finding indicates that the effects of rTMS may not vary amongst individuals according to intellect or illness; however, the particular application process such as the targeted area of stimulation and the frequency utilised has a significant impact on TMS effectiveness.⁹

Transcranial direct current stimulation (tDCS): It is a non-invasive method that enables the reversible modulation of activity in specific regions of the brain. This has proven to be a valuable tool for exploring the relationship between brain function and various cognitive, motor, social and affective domains. By acting on the balance between excitatory and inhibitory neural activity, TDCS can modify the functioning of neural circuits. As a result, it holds promise as a potential therapy for NDDs, offering the ability to modulate activity within these circuits. Clinical studies have demonstrated encouraging outcomes in the use of tDCS for alleviating symptoms in conditions such as ASD, schizophrenia and ADHD.¹⁰ In a systematic study of randomised controlled trials, tDCS was observed to be both safe and applied in NDDs, particularly in the context of ADHD, ASD and dyslexia.¹¹

Photobiomodulation (PBM): It is also referred to as low-level laser therapy, has recently gained attention as a treatment approach involving the application of laser or light-emitting diode light for various disorders. PBM has shown promise as a treatment for NDDs like Alzheimer's disease, Parkinson's disease and other neurological conditions like stroke and traumatic brain injury.¹² PBM assisted children with ASD with their behaviour, sleep quality, attention span and cognitive rigidity.¹³ Recent research has demonstrated that 635 nm wavelength reduces ASD-related hypersensitivity, among other symptoms.¹⁴ Nevertheless, the specific therapeutic mechanism through which PBM affects children with ASD remains unclear. PBM's potential uses have been investigated in a variety of disorders, including neuropsychiatric disorders, neurodegeneration and neurotrauma. PBM is a novel possible therapy approach for neurological disorders since it can modulate both human and animal brain function.¹⁵

Neurofeedback therapy (NFT): A non-invasive method called neurofeedback therapy monitors a patient's brainwaves and provides them real-time feedback on how their brain is functioning. NFT can treat a variety of conditions that arise from abnormal brainwave patterns. Additionally, it has been

found that NFT can aid in alleviating symptoms associated with these conditions. A systematic report by Saif and Sushkova¹⁶ highlighted that TBR (theta/beta ratio), SCPs (slow cortical potentials) and SMR (sensorimotor rhythm) neurofeedback protocols are most widely used for treating ADHD. NFT is a well-examined treatment for ADHD. This has been demonstrated by multiple meta-analyses.¹⁷ NFT has drawn a lot of interest as a substitute treatment for ADHD.¹⁸ A case study by Rauter et al.,¹⁹ demonstrates that infra-low frequency NFT is a practical and effective therapeutic tool for treating ASD children.

Conclusion

Although neuromodulation interventions are not approved as first-line treatment for NDDs, considering the clinical effectiveness in adult populations and limited options available for the treatment of NDDs, it is important to explore the role of neuromodulation in NDDs. Recent studies show that non-invasive neuromodulation therapies like TMS, tDCS, PBM and NFT hold potential as adjunctive treatments for NDDs. However, more study is required to fully comprehend their effectiveness and establish standardised protocols for their use.

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