Therapeutic Applications of Noninvasive Neuromodulation in Children and Adolescents

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KEYWORDS

• Neuromodulation • Noninvasive brain stimulation
• Transcranial magnetic stimulation • TMS • Transcranial direct current stimulation
• tDCS • Adolescent depression • Autism spectrum disorder

KEY POINTS

- Neuromodulation is a rapidly developing field that will provide opportunities to develop new therapeutic modalities in child and adolescent psychiatry.
- Recent research has examined the feasibility and safety of transcranial direct current stimulation and transcranial magnetic stimulation in child and adolescent neuropsychiatric disorders.
- Enthusiasm for applying neuromodulatory tools in childhood and adolescent neuropsychiatric disorders must be moderated with systematic study, neurodevelopmental considerations, and rigorous ethical analyses.

INTRODUCTION

Noninvasive brain stimulation (NIBS) techniques have emerged as alternatives to invasive modalities given the ease of application, safety, tolerability, and reversibility. The

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2 most well-studied forms of NIBS are transcranial magnetic stimulation (TMS) and transcranial electrical stimulation. Research protocols began applying brain stimulation techniques to children and adolescents in the early 1990s. Progress has been slow due to practical limitations and safety concerns.[1] As of 2017, there is no Food and Drug Administration–approved therapeutic use of NIBS techniques in children. Current evidence suggests potential use of NIBS techniques in children with depression, attention-deficit hyperactivity disorder (ADHD), epilepsy, autism, schizophrenia, dystonia, dyslexia, cerebral palsy, and Tourette syndrome (**Table 1**).[2–4]

TRANSCRANIAL MAGNETIC STIMULATION

The applications of TMS in children first started in the early 2000s and included both diagnostic and therapeutic approaches. Potential therapeutic applications of TMS in children include epilepsy, ADHD, autism spectrum disorder (ASD), depression, schizophrenia, and Tourette syndrome.[2] Single-pulse TMS is also used for presurgical mapping of the motor cortex and language areas.[5]

Safety and application guidelines for TMS were published in 2009 but focused on adults.[1]

In children and adolescents, recent systematic reviews suggest that both single-pulse and repetitive TMS have similar adverse effect profiles to adult populations.[3,6,7] The most commonly reported side effects are headache (11.5%), scalp discomfort (2.5%), twitching (1.2%), mood changes (1.2%), fatigue (0.9%), and tinnitus (0.6%).[3] The most serious side effect is seizure and to date there are 3 reported seizures in adolescents receiving TMS. These events occurred in the context of epileptogenic medication use,[8,9] alcohol consumption before the TMS session,[9] and application of deep TMS.[10] There are 2 reported instances of TMS-induced hypomania[8,11] and 2 reported cases of neurocardiogenic syncope, which were associated with preexisting circumstances.[12] No changes in cognitive functioning have been reported (**Fig. 1**).[13]

Major Depressive Disorder

Major depressive disorder is one of the most common psychiatric illnesses in children and adolescents. Suboptimal outcomes in the treatment of depression in children and adolescents have sparked interest focused on the study of novel, brain-based approaches such as TMS. Prior therapeutic TMS studies included 73 participants between the ages of 7 to 21 years in open trials, case studies, case series, and small sham-controlled trials. In a systematic review, Donaldson and colleagues[14] suggested that TMS may be an effective and well-tolerated treatment for treatment-resistant depression in adolescents. The most common TMS application was high-frequency TMS (10 Hz) over the left dorsolateral prefrontal cortex (L-DLPFC). TMS parameters varied in terms of number of sessions (10–30), session duration (10–37.5 min), and intensity (80%–120% of motor threshold [MT]). Among these studies, 2 open trials by Bloch and colleagues[11] (2008) and Wall and colleagues[15] (2011) showed statistically significant improvement in depressive symptoms measured by CDRS-R as well as the significant improvement in the Clinical Global Impression Severity of Illness Scales (CGI-S) with high-frequency TMS applied over the DLPFC. The study by Wall and colleagues differed from the study by Bloch and colleagues based on MT intensity (120% vs 80%), total number of pulses per session (3000 vs 400) and number of total TMS sessions (30 vs 14). A follow-up study by Bloch and colleagues[11] showed sustained improvement after 3 years.[13] Another open-label study by Wall and colleagues[16] in 2016 (n = 10) showed significant improvement (60% of participants) in depressive symptoms measured by CDRS-R, the Quick Inventory for Depressive