Schizophrenia. Addressing these gaps is critical to improving the management of patients.
Funding. Medscape Education, Cerevel Therapeutics

52-Week Open-Label Safety and Tolerability Trial of Centanafadine Sustained Release in Adults With Attention Deficit Hyperactivity Disorder (ADHD)

Osman Turkoglu, MD, Taisa Skubiak and Jessica McDonough, MD

Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ

Introduction. Centanafadine (CTN) is a potential first-in-class norepinephrine/dopamine/serotonin triple reuptake inhibitor (NDSRI) in development for ADHD. In 2 pivotal adult ADHD trials, CTN sustained-release (SR) 200 mg/d and 400 mg/d, administered twice daily (BID), significantly reduced Adult ADHD Investigator Symptom Rating Scale (AISRS) total score vs placebo, with favorable safety and tolerability. Long-term effects of CTN SR 400 mg/d in adult ADHD are reported here.
Methods. Adults meeting *DSM-5* criteria for ADHD who completed a pivotal trial or enrolled de novo were eligible for the 52-week, phase 3, open-label trial. Uncontrolled comorbid psychiatric disorder, undifferentiated diagnosis of ADHD, prohibited medicines, or positive alcohol or drug screen were exclusionary. All patients (pts) received CTN SR BID, titrated to 400 mg/d by day 8, and fixed thereafter. Safety was primarily assessed by adverse events (AEs); laboratory results, physical examinations, vital signs, ECG, Study Medication Withdrawal Questionnaire (SMWQ), and Columbia-Suicide Severity Rating Scale (C-SSRS) were also assessed. Efficacy was assessed by AISRS, Clinical Global Impression-Severity (CGI-S) and ADHD Impact Module-Adult (AIM-A). Analyses were based on observed results using descriptive statistics. Baseline was relative to the first CTN dose in the open-label trial.
Results. Of 662 pts enrolled (mean [SD] age 36.7 [10.1] years; 51.1% female; 82.9% White), 653 received CTN SR; 345 pts completed the trial. Common discontinuation reasons were pt withdrawal (119; 18%), AEs (81; 12.2%), and lost to follow-up (41; 6.2%); 22 (3.4%) pts discontinued for lack of efficacy. Treatment-emergent AEs (TEAEs) occurred in 401 pts (61.4%); 16 (2.5%) had severe TEAEs. Common TEAEs were insomnia (8.0%), nausea (7.7%), diarrhea, and headache (7.0% each). Serious TEAEs occurred in 12 pts (1.8%); none were CTN related. AEs of special interest (n=18; 2.8%) included rash (n=5; 1 severe), papule, rash erythematous, rash maculopapular, rash papular, and urticaria (n=1 each); 3 discontinued. Abuse potential–related AEs occurred in 31 pts (4.7%). No deaths occurred. SMWQ scores were low throughout. Suicidal ideation/behavior occurred in 13 pts (2.0%) per C-SSRS. There were no trends in laboratory, vital sign, or ECG changes. Baseline mean (SD) AISRS Total, Inattentive, and Hyperactive-Impulsive scores were 34.4 [10.3], 19.2 [5.6], and 15.2 [6.0], respectively; mean (SD) changes at week 52 were −20.4 (11.9), −11.2 (6.6), and −9.2 (6.2). Baseline mean (SD) CGI-S score was 4.2 (0.9); mean (SD) change at week 52 was −1.5 (1.1). Baseline mean (SD) AIM-A score was 6.5 (1.8); mean change at week 52 was 1.23 (2.0).
Conclusions. Safety, tolerability, and exploratory efficacy results from this trial demonstrate that CTN SR 400 mg is a safe and effective long-term treatment for ADHD in adults.
Study Registration: NCT03605849
Previous presentation: APA Annual Meeting, May 20–24, 2023, San Francisco, CA
Funding. Otsuka

A Review and Comparison of FDA-Approved Transcranial Magnetic Stimulation (TMS) Protocols for Depression

Paula Gomes, MD, Ayyub Imtiaz, MD, Menachem Groden, MD and Muhammad Zaidi, MD

Saint Elizabeths Hospital, Department of Behavioral Health, Washington, DC

Introduction. Transcranial Magnetic Stimulation (TMS) is a Food and Drug Administration (FDA) approved treatment that induces neuronal activity in the left dorsolateral prefrontal cortex. TMS was initially developed to treat major depression after studies of patients with depression revealed hypometabolism in this brain region. Since it was first FDA approved in 2008, several types of TMS have been developed and its clinical indications expanded. Given the dearth of literature guiding clinicians in understanding different forms of TMS and their protocols, this poster will review the common and unique aspects of several forms of TMS in an effort to aid clinicians in appropriately utilizing this safe and effective neuromodulatory treatment.
Methods. Specific keywords were used to conduct a thorough but nonsystematic review of multiple databases, including PubMed, Google Scholar, and PsychInfo. Articles describing protocols rather than direct comparisons were selected. The outcomes regarding protocol guidelines, advantages, disadvantages, safety, and side effects were included in the review.
Results. The FDA approved types of TMS include repetitive TMS (rTMS), deep TMS (dTMS), intermittent theta burst stimulation (iTBS), and accelerated TMS (aTMS). While rTMS is limited to cortical tissue, other forms of TMS reach subcortical neurons with aTMS using functional magnetic resonance imaging (fMRI) to specifically locate the target area. dTMS was approved in 2013 and its session time is half that of rTMS. Subsequently developed TMS types have even shorter sessions; iTBS sessions are only 3 minutes and aTMS is 9 minutes per session. Most TMS protocols require 8-9 weeks for full treatment, but aTMS only needs 5 days. All TMS protocols stimulate at 120% of resting motor thresholds except for aTMS which adjusts based on the patient using fMRI results. Efficacy is mostly similar with rTMS, dTMS, and iTBS

https://doi.org/10.1017/S1092852924001767 Published online by Cambridge University Press

demonstrating remission rates up to 30%, but aTMS had remission rates up to 90.5%. aTMS can also be used for suicidality, patients with severe or refractory depression, as well as those with comorbid anxiety, which have historically shown lower rates of success with other treatments. Overall, all forms of TMS produce minimal and temporary side effects with patients being able to return to normal activities the same day as treatment, although aTMS may cause side effects of greater intensity resulting in sleep dysregulation. Cost remains a barrier, with many insurances covering rTMS but not iTBS or aTMS.
Conclusion. TMS is an evidence based, efficacious, and safe treatment for depression. Most FDA-approved TMS protocols for depression have similar number of sessions, duration of treatment, common side effects, and remission rates, besides aTMS, which has dramatically greater remission rates and shorter treatment duration, making it a potentially rapid and effective treatment modality for acute and more severe cases of depression.
Funding. No Funding

Repetitive Transcranial Magnetic Stimulation (rTMS) versus Transcranial Direct Current Stimulation (tDCS) for Depression: a review

Paula Gomes, MD, Ayyub Imtiaz, MD, Menachem Groden, MD and Muhammad Zaidi, MD

Saint Elizabeths Hospital - Department of Behavioral Health, Washington, DC

Introduction. The World Health Organization estimates depression affects 5% of the adult population and is the leading cause of disability and the 3rd cause of disease burden worldwide. Despite progress in therapies and pharmacology, 30% of patients have refractory symptoms. Patients with partial response and patients who do not want or are intolerant to medication can benefit from alternative treatment modalities such as repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS). However, there is scant literature comparing these two neuromodulatory techniques. The authors provide an overview of rTMS and tDCS to guide clinicians.
Methods. A review of MEDLINE, Google Scholar, and EBSCOHost databases was conducted. Keywords used included "rTMS," "tDCS," and "depression." All types of articles discussing or comparing the modalities were selected. The unique characteristics, indications, and side effects of rTMS and tDCS were included.
Results. rTMS is a neurostimulator used in-clinic that induces depolarization and neuronal activity in the dorsolateral prefrontal cortex, where hypofunction has historically been associated with depressive symptoms. The treatment is Food and Drug Administration (FDA) approved, and the most common protocol consists of 36 sessions over 8-9 weeks. Side effects are mild and temporary, and patients can resume daily activities after sessions. Its absolute contraindications are limited to metallic objects or implanted stimulator devices in or near the head. The total cost varies from $6,000-$11,000 but is covered by most insurance.

In contrast, tDCS is a cost-effective, small, and portable neuromodulator self-administered by patients at home that either increases or decreases intrinsic neural firing in the primary motor cortex and dorsolateral prefrontal cortex. Multi-session tDCS is thought to promote or regulate information processing efficiency. The most common protocol uses a constant low current for 20-30 minutes applied daily for 10 to 15 days. Common side effects are mild and temporary, and there is no absolute contraindication. Some meta-analyses have found its efficacy comparable to rTMS or antidepressants. However, due to uncertainties about the specific mode of administration, number of treatments, and duration of effect, its status remains investigational by the FDA.
Conclusions. The efficacy and safety of rTMS for the treatment of depression have been demonstrated in numerous studies. However, the lack of adequately equipped clinics and large cost limits its availability in spite of FDA approval. In contrast, tDCS has some advantages, including safety, tolerability, ease of administration at home, and cost-effectiveness, but requires further research and more rigorous evidence.
Funding. No Funding

Impact of Progressive Muscle Relaxation on Psychological Symptoms on an Inpatient Psychiatric Unit

Penelope C. Farris, BS[1], Sean T. Lynch, MD[1,2], Emily Groenendaal, MD[1,3], Lidia Klepacz, MD[1,3], Bambina Meyers, LCSW[3] and Stephen J. Ferrando, MD[1,3]

[1]New York Medical College, Department of Psychiatry and Behavioral Sciences, Valhalla, NY; [2]Icahn School of Medicine at Mount Sinai, Mount Sinai Beth Israel, Department of Psychiatry, New York, NY and [3]Westchester Medical Center Health Network, Department of Psychiatry, Valhalla, NY

Objectives. To examine the effectiveness of short-term progressive muscle relaxation therapy in reducing symptoms of depression, anxiety, and aggression/agitation, in patients on an inpatient psychiatric unit. Additionally, to determine the impact of clinical and sociodemographic factors on its effectiveness.
Methods. Psychiatric inpatients at a private, community-based psychiatric hospital were invited to participate in a progressive muscle relaxation activity and filled out pre- and post-activity surveys querying symptoms of depression, anxiety, and aggression/agitation, using a created Likert scale.
Results. The 57 participants in this study showed an average decrease in every symptom domain, including -0.93 in agitation/aggressive symptoms ($p<0.001$), -2.14 in depressive symptoms ($p<0.001$), and -1.81 in anxiety symptoms ($p<0.001$). While diagnosis did not appear to be significantly related to change in score, patients with different primary diagnoses had changes in different symptom domains, with patients with Bipolar Disorder

https://doi.org/10.1017/S1092852924001767 Published online by Cambridge University Press