PSYCHIATRY ALERTS NOS

Volume XI / December 2019 / Number 12 www.alertpubs.com

Vagus Nerve Stimulator Recall

The LivaNova VNS Therapy SenTiva Generator System has been voluntarily recalled due to reports of reset errors that cause the system to stop delivering stimulation.

VNS systems consist of an implantable generator that delivers electrical pulses to the brain through leads and electrodes around the vagus nerve, along with an external programming device. VNS is approved for use in patients aged ≥18 years experiencing major depression that has not responded to pharmacotherapy. LivaNova has received 14 reports of unexpected generator resets, 4 of which required early revision surgeries. All malfunctions occurred within 60 days of implantation. Screening procedures have been put in place by the manufacturer to detect devices susceptible to the reset, but patients should be alerted to the possibility of the malfunction and counseled to notify a healthcare professional immediately if there is a change in depressive symptoms. If the VNS generator is determined to have reset unexpectedly, patients should be offered alternate therapy.

FDA MedWatch Alerts: LivaNova recalls VNS therapy SenTiva Generator due to reset error. Available at www.fda.gov/medical-devices/medical-device-recalls/livanova-recalls-vns-therapy-sentiva-generator-due-reset-error.

Maintenance DBS in Resistant Depression

According to the results of a follow-up study, response to deep brain stimulation appears to be relatively stable over time in patients with treatment-resistant depression.

Methods: Study subjects were adults with unipolar major depression and a Hamilton Rating Scale for Depression (HAM-D) score of ≥18 who had participated in a sham-controlled trial of deep brain stimulation. To be eligible for the initial trial, patients were required to have undergone unsuccessful trials of ≥2 second-generation antidepressants, ≥1 TCA with subsequent lithium augmentation, ≥1 MAOI, and ≥6 sessions of bilateral ECT, or to have experienced a relapsed after discontinuation of maintenance ECT. Following DBS electrode implantation, patients underwent a 1-year optimization phase followed by a double-blind, sham-controlled, crossover phase. The present report describes outcomes after an additional year of maintenance

PSYCHIATRY ALERTS NOT OTHERWISE SPECIFIED (ISSN 1559-5641) is published monthly by M.J. Powers & Co. Publishers, 45 Carey Ave. Ste 111, Butler, NJ 07405. Telephone 973-898-1200. E-mail: psychnos@alertpubs.com.

Subscription $105 a year in the U.S.; $113.50 Canada; $123.50 elsewhere; $157.00 institutional. Subscribers may enroll in the 12-month CME program for $83.00 per year. M.J. Powers & Co. Publishers is fully independent and accepts no commercial support of any kind.

treatment, during which DBS parameters and medication could be adjusted as needed. Response was defined as ≥50% decrease in HAM-D score compared with presurgical baseline, and remission as HAM-D score of ≤7.

Results: Of 25 patients enrolled in the acute-phase study, 21 (mean age, 53 years; 15 women) received maintenance treatment and 18 completed the full protocol. Mean total follow-up duration after surgery was 99 weeks, including an average maintenance phase of 62 weeks.

Of the patients who began maintenance treatment, 10 (40%) met criteria for acute response; 6 maintained response throughout the maintenance phase. Overall, 8 of the 18 patients (32%) who completed the maintenance phase met response criteria at the last assessment, including 5 who achieved depression remission. An additional 4 patients met criteria for partial response (i.e., 25–50% HAM-D reduction). A single patient who met response criteria experienced relapse during the maintenance phase due to stimulator battery depletion, but regained full response several months after battery replacement.

During maintenance treatment, there was little change in HAM-D score; however, scores on the self-reported Inventory of Depressive Symptomatology showed small additional improvement over time. Despite continued efforts to optimize DBS parameters, none of the patients who experienced minimal or no improvement during the 1-year acute phase improved during the maintenance phase.

Treatment was well tolerated, and few adverse effects were attributed to DBS. Those that did occur (e.g., agitation, nausea, headache, fatigue) were transient. A total of 3 patients experienced a serious adverse event: the patient in whom the battery failed experienced increased depression and suicidal ideation; an additional 2 patients self-administered medication overdoses, 1 with and 1 without suicidal intent.

Discussion: These results suggest that response to DBS in patients with treatment-resistant depression is fairly stable over time. While several patients did lose responder status during maintenance treatment, actual changes in their HAM-D scores were small. Although it was judged unlikely, medication adjustments in 8 patients could have affected outcomes. Future research should control for these changes and compare maintenance DBS with other long-term modalities such as ECT.

Van der Wal J, Bergfeld I, Lok A, Mantione M, et al: Long-term deep brain stimulation of the ventral anterior limb of the internal capsule for treatment-resistant depression. *Journal of Neurology Neurosurgery and Psychiatry* 2019; doi 10.1136/jnnp-201-321758. From Amsterdam Universitair Medische Centra, The Netherlands; and other institutions. **Funded by Medtronic; and The Netherlands Organisation for Health Research and Development. Three of 11 study authors disclosed potentially relevant financial relationships; the remaining authors declared no competing interests.**

EEG Traits and Suicide Risk

Results of a preliminary study suggest electroencephalogram resting state power characteristics may be a clinically useful biomarker to predict suicide risk in patients with depression. Observations in this study were anatomically consistent with those of neuroimaging studies using functional magnetic resonance imaging (fMRI), single-photon emission computed tomography (SPECT), and positron emission tomography (PET). Unlike these technologies, EEG is routinely available, inexpensive, and time-efficient. There has been little research on EEG-based prediction of suicidality; instead EEG research has been focused on markers for depression not unique to suicidal behavior.

Methods: Study subjects were 78 women with DSM-IV major depressive disorder who were seeking treatment with repetitive transcranial magnetic stimulation (rTMS). Men were excluded because they were markedly underrepresented in the study population. Suicide risk

was assessed using the Mini International Neuropsychiatric Interview. EEGs were obtained in a standard manner and the data were transformed to identify larger-than-predicted clusters. The data were also analyzed using a technique that facilitated comparison among the study groups.

Results: Among the 78 participants, 19 had attempted suicide within the past 30 days, 36 were experiencing suicidal ideation, and 23 were not suicidal. Patients with a recent suicide attempt had higher Beck Depression Inventory (BDI) scores than those with suicidal ideation and nonsuicidal patients; scores were similar in the latter groups. The EEG analysis revealed differing patterns of activity in suicide attempters, ideators, and nonsuicidal controls. After adjustment for BDI scores, significant differences in EEG power were found between suicide attempters and low-risk controls (effect size,* 0.85), those with suicidal ideation and controls (effect size, 0.75), and suicide attempters and ideators (effect size, 0.61). Compared with nonsuicidal patients, both ideators and attempters had less resting-state beta and low gamma activation in the frontal regions of the brain. Power differences for attempters and ideators were localized within the orbito-, medial, middle, superior, and inferior frontal areas and the anterior cingulated cortex. Compared with ideators, suicide attempters showed gamma I hypoactivity in several right hemisphere areas.

Discussion: Results of this analysis are consistent with a previous meta-analysis of structural and functional MRI studies showing differences between suicide attempters and psychiatric controls. According to the study authors, applying machine-learning techniques to EEG data could help develop a reliable biomarker for suicide risk in the clinical setting. This research could also help identify anatomic targets for brain stimulation. Future research should extend to men and should take medication use into account.

Benschop L, Baeken C, Vanderhasselt M, Van de Steen F, et al: Electroencephalographic resting state frequency power characteristics of suicidal behavior in female patients with major depressive disorder. *Journal of Clinical Psychiatry* 2019; doi 10.4088/JCP.18m.12661. From Ghent University, Belgium; and other institutions. **Funded by Brain Resource, Sydney, Australia; NeuroCare Group, Munich, Germany; and other sources. One of 6 study authors disclosed a potentially relevant financial relationship; the remaining authors declared no competing interests.**

***See Reference Guide.**

Artificial Intelligence in Psychiatry

According to a review, although many research questions are yet to be investigated, conversational artificial intelligence (AI) could alter the way mental health care is delivered by gathering diagnostic information, facilitating treatment, and reviewing clinician behavior. Use of AI could also have a positive impact on access to care.

Traditionally, psychotherapy involves a single patient and a clinician. However, limited access to mental health treatment—a major barrier to care—is based in part on a decreasing number of clinicians available to provide services. Additionally, use of talk therapy by available practitioners has been steadily declining, meaning fewer patients are receiving talk therapy during psychiatric visits. Conversational AI has the potential to help address insufficient clinician availability. While conversational AI is not likely to have sufficient technical sophistication to replace human therapists, software programs that speak like people (e.g., chatbots, digital assistants) are now being embedded into health care services. Many clinicians are already using telehealth, social media, mobile, and text-based services to deliver mental health care, which demonstrates a willingness by both patients and clinicians to try new approaches to care.

Human-delivered, AI-informed therapy introduces a listening device connected to software programmed to detect clinically relevant information such as symptoms or intervention and relay the information back to the patient or clinician. Another option—AI-delivered, human-supervised therapy—allows patients to speak directly to a conversational AI that can manage

routine tasks such as structured diagnostic interviews. Clinician can then review the conversation and potentially hand off specific tasks to conversational AI or supervise conversations between AI and patients. Therapeutic alliance, which is consistently associated with symptom improvement in psychotherapy, may be a concern with AI. However, users have reported experiencing a sense of alliance when speaking directly with conversational AI, suggesting this bond may not necessarily be restricted to human–human relationships. If conversational AI is permitted to take over repetitive, time-consuming tasks such as such as reviewing symptoms or taking patient history, clinicians' attention and expertise could potentially be employed more judiciously.

Other areas of medicine have used AI successfully to build diagnostic and prognostic models. Although early findings point to potential benefits in psychiatric practice, uncertainty remains about patients' willingness to disclose personal and clinical information to AI and there is a lack of rigorous clinical trial data. Collaboration between mental health specialists and the software industry could facilitate the development and deployment of AI systems with the capacity to improve patient outcomes.

Miner A, Shah N, Bullock K, Arnow B, et al: Key considerations for incorporating conversational AI in psychotherapy. *Frontiers in Psychiatry* 2019;10 (October):Art 746. doi 10.3389/fpsyt.2019.00746. From Stanford University School of Medicine, CA; and other institutions. **Funded by the NIH; and other sources. The authors declared no competing interests.**

Smartphone Apps for Depression/Anxiety

A review of mental health apps in the Apple App and Google Play stores suggests that while the majority of available apps are free, few are backed by scientific research or affiliated with government, healthcare, or educational institutions.

A search of the 2 popular app stores identified a total of 293 mobile apps that claimed to address symptoms of depression and/or anxiety. Of these, only 10 (see table) have a published evidence-base supporting their efficacy, and the majority of the research was undertaken by individuals involved in the app development. Only the Destressify app is supported by independent research. Most apps (74%) were free to download, but less than one-third were developed with input from a mental-health expert.

Evidence Support for Apps Targeting Depression or Anxiety Symptoms

App Name	Type of Evidence	Outcomes
Destressify	Randomized controlled trial	Stress, anxiety, depression
Agoraphobia Free	Randomized controlled trial	Anxiety (agoraphobia)
Catch It	Feasibility/Pilot Study	Positive/negative mood
Mindsurf	Feasibility/Pilot Study	Anxiety, depression
PTSD Coach	Randomized controlled trial	Anxiety, PTSD, depression
MoodMission	Randomized controlled trial	Anxiety, depression
SuperBetter	Randomized controlled trial	Depression
Thought Challenger	Randomized controlled trial	Depression
Smiling Mind	Randomized controlled trial	Stress, anxiety, depression
Headspace	Randomized controlled trial	Stress, anxiety, depression

Given the scarcity of adequate research, clinicians and patients have little guidance on which apps to recommend/use. However, efforts are underway by the FDA to regulate mental health apps, primarily based on risk of harm to the user. Information regarding FDA oversight can be found at www.fda.gov/medical-devices/digitalhealth. In addition, several reputable websites offer information on and reviews of mental health apps for both clinicians and consumers. Examples of these include: PsyberGuide (psyberguide.org); the National Health Service Mental Health Apps Library (www.nhs.uk/apps-library/category/mental-health); Head To Health (headtohealth.gov.au); and Health Navigator www.healthnavigator.org.nz/apps). Finally, multiple frameworks exist to evaluate mental health apps, including 1 from the American Psychiatric Association, which is available at www.psychiatry.org/ psychiatrists/practice/mental-health-apps/app-evaluation-model.

Use of mental health apps appears to be increasing. While these apps could potentially address some of the barriers to care (e.g., cost, accessibility), offer patients a convenient way to practice strategies learned in face-to-face therapy, and incorporate reminders that could increase treatment and medication compliance, there is little evidence supporting their use. Additional research evaluating a greater number of apps is needed, and future app development should incorporate input by mental health experts.

Marshall J, Dunstan D, Bartik W: The digital psychiatrist: in search of evidence-based apps for anxiety and depression. *Frontiers in Psychiatry* 2019; doi 10.3389/fpsyt.2019.00831. From the University of New England, Armindale, Australia. **Funded by a stipend from the Australian Government Research Training Program. The authors did not include disclosure of potentially relevant financial relationships.**

DSM-5 Attenuated Psychosis Syndrome

A systematic review of published research supports the validity of attenuated psychosis syndrome (APS) as a prognostic high-risk state for psychosis. Additional research is needed to clarify the epidemiology of APS and its risk factors, neurobiological correlates, and effective treatments.

Background: The diagnostic structure of DSM-5-APS is based on a subset of criteria for the clinical high risk state for psychosis (CHR-P) and largely overlaps with the Structured Interview for Psychosis-Risk Syndromes (SIPS-APSS). However, APS is measured clinically, and a diagnosis of DSM-5-APS requires symptoms to be sufficiently distressing and disabling to warrant clinical attention, which is not required in other criteria.

Methods: A comprehensive literature search identified all full-text articles describing attenuated psychosis symptoms or syndrome available through mid-June 2019. Studies were conducted in individuals meeting the DSM-5-APS or SIPS-APSS criteria or a SIPS version with an additional criterion measuring disability and distress, introduced for increased conformity to the DSM-5 criteria. A meta-analysis was conducted to test the risk of psychosis onset in individuals meeting these 3 sets of criteria.

Results: The search identified 56 articles for the systematic review: 46 using SIPS-APSS criteria, 5 using the DSM-5-APS diagnosis, 5 using both criteria, and none using SIPS with the additional criterion. Sample sizes of patients meeting diagnostic criteria ranged from 4 to 689, and patient ages ranged from 15 to 25 years. Overall, 0.3% of the non-help-seeking young general population met DSM-5-APS criteria and 1.3% met SIPS-APSS criteria. Prevalences were higher and highly variable in clinical populations. Retrospectively, 44% of patients with schizophrenia would have met DSM-5-APS criteria. Trauma was a predisposing risk factor, present in 48% of individuals. Comorbidities frequently present at the time of diagnosis included depression, bipolar disorder, anxiety disorders, substance use disorders, and

personality disorder traits, in particular schizotypal and borderline. Among help-seeking persons who met DSM-5-APS or SIPS-APSS criteria 26–39% had at least 1 past suicide attempt, and 78% had suicidal ideation. Neurobiological or neurocognitive correlates included impaired vigilance and processing speed, social cognition, and metacognition. Olfactory deficits were associated with the severity of negative symptoms. Baseline treatments were predominantly atypical antipsychotics, antidepressants or both; mood stabilizers, anxiolytics, and other medication were also used.

The meta-analysis was based on 23 studies that reported risk of psychosis at follow-up, with an overall sample size of nearly 2400 participants. The risk was 11% at 6 months, 15% at 12 months, 20% at 24 months, and 23% at 36 months. The median age at the time of onset of psychosis was 20 years in male subjects and 24 in females, and the average transition time was 234 days. Naturalistic studies found that patients were generally not helped by treatment, whether antidepressants, supportive therapy, or behavioral therapy.

Study Rating*—18 (100%): This study met all criteria for a systematic review/meta-analysis.

Salazar de Pablo G, Catalan A, Fusar-Poli P: Clinical validity of DSM-5 attenuated psychosis syndrome. Advances in diagnosis, prognosis, and treatment. *JAMA Psychiatry* 2019; doi 10.1001/jamapsychiatry.2019.3561. King's College London, U.K., and other institutions. **Funded by the Alicia Koplowitz Foundation and the European Commission. Two of 3 study authors disclosed potentially relevant financial relationships; the remaining author declared no competing interests.**

***See Reference Guide.**

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Effect Size: The effect size represents the amount of change in outcome that can be attributed to treatment, where 0.2 indicates a small effect, 0.5 a medium effect, and 0.8 a large effect. It is relatively independent of clinical significance, and large effect sizes do not ensure treatment efficacy.

Study Rating: A measure of how well a study conforms to quality standards. The study rating uses a checklist system based on the comprehensive Strength of Evidence Report from the Evidence-based Practice Center Program of the Agency for Healthcare Research and Quality (AHRQ). The rating checklists are posted at www.alertpubs.com.

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