PSYCHIATRY ALERTS NOS

Volume XI / February 2019 / Number 2 www.alertpubs.com

The 2018 Issue Volume is now available online. See last page for details.

Suicide Risk After Hospital Discharge

Risk of suicide is known to be elevated in the period immediately following discharge from inpatient psychiatric treatment. A cohort study revealed several clinical characteristics that may be particularly associated with risk.

Background: Compared with general-population rates, risk of suicide is increased >100 times in the first 3 months following psychiatric hospital discharge. Although a history of self-harm is a robust predictor of suicide, no large studies have evaluated the effects of recent self-harm on suicide risk after discharge.

Methods: The study population included all patients discharged from a psychiatric hospital in Sweden between 1973 and 2009. Data on discharge diagnosis, deliberate self-harm in the 30 days prior to hospitalization (both suicidal and nonsuicidal), and completed suicide in the 30 days post discharge were collected from linked registries. Rates of postdischarge suicide were compared across diagnostic groups and between patients with and without prior self-harm.

Results: The study cohort comprised nearly 700,000 patients who were discharged from a psychiatric hospital during the study period. The most common discharge diagnoses included alcohol use disorder (34%), depression (16%), and schizophrenia (10%), and >4% of patients had a documented self-harm episode in the 30 days prior to admission. A total of 3695 suicides occurred in the month following discharge (rate, 181 per 10,000 person-years).

Among the patients who died by suicide, the most common diagnosis was depression (32%; hazard ratio [HR],* 2.97). This association was stronger in men (HR, 4.5) than in women (HR, 2.4). Nearly 17% of those who died by suicide had a recent history of self-harm prior to admission (HR, 4.75). The association between prior self-harm and suicide was present across diagnoses, with the greatest risk found among patients with schizophrenia (HR, 8.9) and other nonorganic psychoses (HR, 6.8).

Discussion: Overall, high rates of post-discharge suicide were found in the study cohort, regardless of diagnosis and recent self-harming behavior. However, the present results

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.

© 2019 by M.J. Powers & Co. Publishers. Written permission from M.J. Powers & Co. is required to reproduce material from this publication.

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.

suggest the risk may be particularly elevated among patients with depression (unipolar or bipolar) regardless of the presence or absence of previous self-harm. Subgroup analyses indicate that the group at greatest risk for suicide after discharge are those with schizophrenia who have previously engaged in self-harm.

Haglund A, Lysell H, Larsson H, Lichtenstein P, et al: Suicide immediately after discharge from psychiatric inpatient care: a cohort study of nearly 2.9 million discharges. *Journal of Clinical Psychiatry* 2019;80 (March/April) doi 10.4088/JCP.18m12172. From the Karolinska Institutet, Stockholm, Sweden; and other institutions. **Funded by the Karolinska Institutet; and other sources. Two of 5 study authors disclosed potentially relevant financial relationships; the remaining authors declared no competing interests.**

***See Reference Guide.**

Brain Stimulation for Substance Use Disorders

Limited evidence supports the use of noninvasive brain stimulation for the treatment of substance use disorders, according to a review. The techniques offer a simple, direct way to enhance disrupted brain circuits that are important in addiction. However, research findings have been mixed, and implementation in treatment settings is not yet recommended.

Brain stimulation may work in substance use disorders by enhancing top-down control within mesolimbic brain circuits. The 2 most commonly used noninvasive brain stimulation techniques are transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS). tDCS uses a weak electric current applied directly to the scalp, and can either enhance or inhibit neuronal activity, depending on electrode placement. In TMS, a coil placed next to the head generates electrical current throughout the brain, which may be excitatory or inhibitory depending on the pulse rate.

Randomized, sham-controlled trials have evaluated the efficacy of both techniques in a range of addictive behaviors, including tobacco dependence, alcohol use disorder, and cannabis use, as well as their effects on diverse outcome measures such as craving and relapse. Studies show variable support for both stimulation modalities as potential adjuvant treatments for addictive behaviors, with no significant differences in effect between tDCS and TMS. Specifically, tDCS has been associated with reduced substance craving and reduced objective measures of cue reactivity compared with sham treatment. However, effect sizes* varied across trials, and some studies found no effect. Fewer studies have evaluated actual substance use with tDCS, and results have been more equivocal. In contrast to tDCS, TMS had no overall effect on craving. However, targeting the right dorsolateral prefrontal cortex (DLPFC) had promising effects. Limited evidence suggests TMS may affect abstinence rates, relapse rates, and consumption outcomes. Some studies suggest that TMS techniques that upregulate DLPFC activity may bring about increased control over substance use.

Studies of the effects of noninvasive brain stimulation on cognitive outcomes important in substance use have also had mixed results. Impaired executive function, impulsivity, decision making, and attentional biases are implicated in substance use disorders and possibly amenable to neuromodulation techniques. Reviews of studies of these functions have shown mixed effects.

Much of the published evidence is characterized by small sample sizes, lack of a control group, lack of follow-up, and emphasis on self-reported craving rather than measures of actual substance use. Studies are limited in their generalizability because they exclude patients with treatment contraindications and psychiatric comorbidity, who may represent the majority of patients with substance use disorders. The available trials have been characterized by differences in patient samples regarding treatment-seeking status, duration of abstinence, and

severity of substance use, characteristics whose potential effects on outcomes are unknown. Despite these limitations, preliminary evidence suggests a potential role for brain stimulation in the treatment of substance use disorders; further research appears to be warranted.

Stein E, Gibson B, Votaw V, Wilson A, et al: Non-invasive brain stimulation in substance use disorders: implications for dissemination to clinical settings. *Current Opinion in Psychology* 2019;30:6–10. doi 10.1016/j.copsyc.2018.12.009. From the University of New Mexico, Albuquerque. **Funded by the National Institute on Alcohol Abuse and Alcoholism. The authors declared no competing interests.**

***See Reference Guide.**

Possible MRI Marker for Psychosis

According to the results of an NIMH-funded study, neuromelanin-sensitive MRI (NM-MRI) may have the ability to identify patients with or at-risk for psychosis and may also act as an indicator of the severity of symptoms in patients with psychosis.

Neuromelanin is a pigment created within dopamine neurons of the midbrain. Previous research in patients with neurodegenerative disease has shown the NM-MRI signal is lower in the substantia nigra of patients with Parkinson's disease. Through a series of validation studies, researchers at Columbia University have now shown that NM-MRI can serve as a marker of dopamine function in individuals without neurodegenerative disorders.

To examine the detection ability, NM-MRI measurements of neuromelanin were compared with chemical measurements of neuromelanin in postmortem brain tissue. A higher NM-MRI signal was associated with higher chemical concentrations of neuromelanin, confirming the ability of NM-MRI to measure regional concentrations. In the next series of testing, variations in neuromelanin concentrations were confirmed in smaller anatomical subregions of the substantia nigra in patients with and without Parkinson's disease. Subsequent evaluations confirmed a connection between NM-MRI and dopamine function by showing that individuals with a higher NM-MRI signal had greater dopamine release capacity in the striatum. Finally, higher NM-MRI signals in the nigrostriatal pathway were found in patients with or at-risk for schizophrenia.

Psychosis is associated with increased dopamine release and synthesis capacity in the striatum. The present findings suggest that NM-MRI captures this dysfunction, supporting its role as a potential biomarker for psychosis. Ongoing research will attempt to detect abnormalities in the neuromelanin signal that could predict which individuals are more likely to develop a psychotic disorder. In addition, the researchers plan to investigate whether NM-MRI could be used to determine which patients might benefit from dopaminergic treatments. In contrast to other measures of dopamine function, NM-MRI does not involve radiation or invasive procedures, making it more suitable for a wider range of patients and for repeated scanning, which could be useful to monitor the progression of illness or response to treatment.

Neuromelanin-sensitive MRI identified as a potential biomarker for psychosis [press release]. Rockville, Maryland; NIMH: February 20, 2019. Available at www.nih.gov/news-events/news-releases/neuromelanin-sensitive-mri-identified-potential-biomarker-psychosis.

Neurofeedback for Negative Symptoms

Dysfunction of frontocortico-temporal networks may underlie the negative symptoms of schizophrenia. This "hypofrontality" does not typically respond to pharmacology, but limited evidence suggests cognitive behavioral therapy, skills training, and repetitive transcranial magnetic stimulation may be helpful. Neurofeedback, which has not previously been evaluated for treatment of negative symptoms, registers the cortical activity of the brain using EEG.

Patients receive real-time feedback on their brain activity and are trained to regulate it, making it a potentially effective therapy for negative symptoms.

A 45-year-old woman and a 30-year-old man both with long-standing schizophrenia who continued to experience marked negative symptoms despite positive-symptom control with antipsychotic drug therapy were randomly selected from a single psychiatric clinic population. Both patients underwent 20 sessions of neurofeedback (35 min each) over 4 weeks. The primary outcomes were change from pre to post treatment in reaction time, global functioning, and negative symptom severity. In both patients, reaction times were significantly reduced after neurofeedback, indicating improved alertness and attention. Negative symptom scores on the Positive and Negative Syndrome Scale were reduced in both patients following treatment (scores not detailed). Both patients also demonstrated 10-point improvements in Global Assessment of Functioning scores post treatment (baseline scores, 51–55). In addition, both patients demonstrated marked increases in spontaneous verbal behavior, considerable improvement in sociability, and motivation for self-initiated activities.

Positive results in 2 single cases cannot be generalized to all patients with negative symptoms; these results need to be replicated in systematic studies. However, this preliminary evidence suggests that replication studies may be warranted as there are few effective and acceptable treatments available for negative symptoms.

Pazooki K, Leibetseder M, Renner W, Gougleris G, et al: Neurofeedback treatment of negative symptoms in schizophrenia: two case reports. *Applied Psychophysiology and Biofeedback* 2019;44:31–39. doi 10.1007/s10484-018-9417-1. From Group Psylux, Neuroacademy and Traumainstitut, Luxembourg; and other institutions. T**he authors declared no competing interests.**

Videoconferencing Therapy for Anxiety

Psychological therapy via videoconferencing is a promising approach to increase access to anxiety-disorder treatment, according to a systematic review. Telemedicine can address shortages of mental health providers, lower costs, provide convenience, and overcome some barriers to care that are specific to anxiety disorders.

Background: Despite a high prevalence of anxiety disorders, a large percentage of patients do not receive treatment, in part because of difficulties accessing care. These may include a shortage of trained mental health providers, difficulty making appointments, distance to care, time concerns, and fear of stigma. Telemedicine could address many of these barriers.

Methods: A comprehensive literature review was undertaken to identify studies of live, one-on-one psychological therapy provided via videoconferencing. Included studies evaluated outcomes related to anxiety disorders or symptoms using validated measures, although anxiety was not necessarily the primary focus of treatment. The review excluded patients with a medical illness, such as chronic pain, treatments offered in conjunction with self-help online therapy, and those involving other media, such as email.

Results: A total of 21 studies met inclusion criteria and were included in the systematic review—10 from the U.S., 5 from Canada, and 6 from Australia. Of these, 10 programs offered care in a mental health clinic, 7 in patients' homes, 2 in schools, and 2 in outpatient primary care settings. Studies included randomized controlled trials (n=6), quasi-experimental studies (n=4), and uncontrolled trials (n=11, including 3 single-case reports). The interventions evaluated were cognitive behavioral therapy (n=12), behavioral activation therapy (n=3), and less frequently (in one study each) problem-solving therapy, acceptance-based behavioral therapy, a proprietary intervention, and mixed modalities. Nearly all studies provided weekly treatment, with 2–25 sessions lasting 45–90 minutes each.

The majority of studies (n=14) reported statistically significant improvement in anxiety outcomes, 2 did not find statistically significant improvements, and the rest did not report statistical significance. Of the 14 studies that reported on clinical significance, 7 reported improvement in the aggregate, 4 reported improvement on a case-by-case basis, and 3 reported no clinically significant changes. In the studies that calculated effect sizes,* the range was 0.22–0.77 (median, 0.41) in controlled studies and 0.25–5.96 (median, 1.91) in uncontrolled studies. Of the 6 controlled studies, 4 showed similar improvements in videoconferencing patients and those treated with face-to-face therapy.

Discussion: Interpreted cautiously, and combined with evidence from other mental health diagnoses, this review suggests videoconferencing psychological therapy for anxiety disorders may be effective across a range of age groups, clinical settings, and environmental situations. However, because of important limitations in the included studies (i.e., the anxiety disorder was not always the primary outcome, most focused on young adults, and less than half were conducted in rural areas), additional research is needed.

Berryhill M, Halli-Tierney A, Culmer N, Williams N, et al: Videoconferencing psychological therapy and anxiety: a systematic review. *Family Practice* 2019;36:53–63. doi 10.1093/fampra.cmy072. From the University of Alabama, Tuscaloosa. **This review was conducted without funding. The authors declared no competing interests.**

***See Reference Guide.**

Response Patterns with rTMS

Secondary analysis of data from a clinical trial identified 4 distinct patterns of response to repetitive transcranial magnetic stimulation (rTMS) in patients with resistant depression, with those achieving rapid response having the best outcomes. Baseline symptom severity, patient age, and concurrent benzodiazepine use appeared to be associated with likelihood of response.

Methods: The multicenter THREE-D study compared conventional high-frequency rTMS with intermittent theta burst stimulation in adult outpatients, aged 18–65 years, with resistant major depression. For study inclusion, patients were required to have a baseline Hamilton Rating Scale for Depression (HAM-D) score of ≥18 and to have undergone at least 1 adequate or 2 inadequate, unsuccessful antidepressant trials. Left dorsolateral prefrontal cortex rTMS was delivered 5 days/week for 4–6 weeks (total number of sessions, 20–30) while patients continued previous pharmacotherapy unchanged. Depression severity was evaluated weekly by blinded raters. Response was defined as a ≥50% decrease in HAM-D score, and remission as a final score of <8. For the present analysis, the rTMS protocol groups were combined, and response patterns were evaluated in 388 participants (mean age, 42 years; 41% men) who received ≥1 rTMS treatment.

Results: At the 4-week assessment, 4 distinct patterns of depression symptom improvement were identified: nonresponse (11%); rapid response (19%) with near maximal improvement by week 3; and linear response in patients with higher and lower baseline severity (30% and 40%, respectively), with both groups showing slower but steady improvement that continued through the last rTMS session. By study end, remission was achieved by 79% of the rapid-response group and by 28% and 9% of the lower and higher baseline symptom linear response groups, respectively. Between-group differences were evident after the first week of treatment and continued throughout the study period.

Baseline depression severity (both clinician- and patient-rated), age, and current benzodiazepine use were significantly associated with response trajectory. Patients who achieved rapid response were more likely to be older (odds ratio* [OR], 1.04), to have lower self-rated baseline depression (OR, 0.79), and to not be receiving benzodiazepine treatment (OR, 0.4). Nonresponse was

associated with higher baseline symptom severity (OR, 1.2 and 1.3 for patient- and clinician-ratings, respectively) and current benzodiazepine use (OR, 2.25), although that association did not reach statistical significance.

Discussion: Rapid response to rTMS, characterized by dramatic improvement by week 2, is associated with a high rate of remission by treatment end. Although the majority of patients who improved at a slower rate did not achieve remission by study end, their improvement did not appear to have reached a plateau by the last study assessment. The association between benzodiazepine use and poorer response may be of particular importance, and discontinuing these drugs before starting rTMS may improve outcomes.

Kaster T, Downar J, Vila-Rodriguez F, Thorpe K, et al: Trajectories of response to dorsolateral prefrontal rTMS in major depression: a THREE-D Study. *American Journal of Psychiatry* 2019; doi 10.1176/appi.ajp.2018.18091096. From the Temetry Centre for Therapeutic Brain Intervention, Toronto, Canada; and other institutions. **Funded by the Canadian Institutes for Health Research; and other sources. Eight of 12 study authors disclosed potentially relevant financial relationships; the remaining authors declared no competing interests.**

***See Reference Guide.**

Reference Guide

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.

Hazard Ratio: A measure of the risk of an event relative to exposure, or the probability of an event occurring in an exposed group versus a non-exposed group. A hazard ratio of 0.5 indicates that 1 group has half the risk of the other group.

Odds Ratio: A comparison of the probability of an event in 2 groups. An odds ratio of 1 implies that the event is equally likely in both groups. An odds ratio greater than 1 indicates that the event is more likely to occur in that group than in the comparison group.

Did You Know . . .

Now you can easily search the collection of 2018 *Psychiatry Alerts NOS* issues and/or use the Index to find a topic. Save a copy on your device for handy reference or use the link below as needed.

Psychiatry Alerts NOS 2018 Volume X.

Executive Editor: **Trish Elliott** Associate Editor: **Tara Hausmann**
Contributing Editors: **Kate Casano, MSHyg, Bennett Silver, MD**
Assistant Editor: **Donna Foehner** Consulting Editor: **John C. Rose, MD**
Founding Editor: **Michael J. Powers**

Statement of Editorial Policy: All of the information and opinions presented in each *Psychiatry Alerts NOS* article are strictly those contained in the cited article unless otherwise noted. Reader comments are welcome by mail, by telephone, or by email.