PSYCHIATRY ALERTS NOS

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Social Recovery Therapy for First-Episode Psychosis

In a randomized trial, social recovery therapy was a useful addition to other intensive recovery-oriented services in highly impaired patients with first-episode psychosis.

Background: Social recovery therapy is a manualized treatment developed by the authors of this study to help first-episode patients who have continuing severe problems in social functioning. The therapy is delivered in 3 stages consisting of therapeutic engagement, assessment, and goal-setting; identifying pathways to meaningful new activities; and engagement in these activities. Other aspects of the treatment include referral to vocational, educational, and recreational resources in the community; behavioral experiments; assertive outreach with the patient at home or in the community; and work with family members, employers, and educators to address potential problems.

Methods: Study participants were aged 16–35 years, had a diagnosis of non-affective psychosis, and had been receiving early intervention services for 12–30 months. To be eligible for the study, participants were required to have low levels of structured activity, defined as ≤30 hours per week spent in activities as measured with the Time Use Survey. Subjects were randomly assigned to receive social recovery therapy in addition to their other specialized services or to receive the ongoing specialized services alone. Outcomes were assessed at 9 months (the end of treatment) and at 15 months by observers who were unaware of patients' treatment assignment. The primary efficacy outcome was change from baseline to the end of treatment in structured activity on the Time Use Survey, which measures economic activity (the sum of work, education, voluntary work, house work, and child care) and structured activity (economic activity plus leisure and sports). Secondary outcomes included measures of clinical symptoms.

Results: A total of 155 patients were randomized. Participants were predominantly men, single, and of white British ethnicity. At study entry, the mean total time spent in structured activity was 12 hours per week, compared with >60 hours for an age-matched healthy sample. Participants received a mean of 16.5 sessions of social recovery therapy, and 61 patients (81%) in the therapy group received what was considered an adequate dose of treatment.

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The program resulted in a clinically important gain in time spent in structured activity by the end of treatment: an average of 8.1 hours compared with early intervention services alone (p=0.005). This increase is double the minimum clinically important difference of 4 hours that was estimated by a consensus group before the study. Constructive economic activity increased by a mean of 6.2 hours at 9 months, relative to the control group (p=0.02). Secondary outcomes, including scores on the Positive and Negative Syndrome Scale and Schedule for the Assessment of Negative Symptoms, also showed improvement with social recovery therapy, but the between-group differences were not statistically significant, possibly because attrition rates were high and missing evaluations were common in the placebo group.

Discussion: Adding social recovery therapy appears to improve functional outcomes in people with first-episode psychosis. It may be particularly useful for those not motivated to engage in existing psychosocial interventions targeting functioning, or for those who have comorbid difficulties that prevent them from doing so.

Fowler D, Hodgekins J, French P, Marshall M, et al: Social recovery therapy in combination with early intervention services for enhancement of social recovery in patients with first-episode psychosis (SUPEREDEN3): a single-blind, randomised controlled trial. *Lancet Psychiatry* 2018;5 (January):41–50. From the University of Sussex, Brighton, U.K.; and other institutions. **Funded by the National Institute for Health Research. The authors declared no competing interests.**

Adaptive Deep Brain Stimulation for Tourette Syndrome

According to the results of several small clinical experiments in patients with severe Tourette syndrome along with a literature review, adaptive deep brain stimulation (aDBS) appears to be a promising treatment for patients with refractory disease.

Conventional DBS is gaining favor as a treatment in refractory Tourette syndrome. However, the continuous operation of conventional DBS devices contributes to adverse effects and leads to rapid battery depletion and frequent battery-replacement surgeries. The only alternative to continuous DBS studied thus far is intermittent DBS, with the device switched on for a few hours each day. In contrast, aDBS uses a closed-loop system that measures and analyzes a control variable reflecting the patient's clinical status. Stimulation settings are modified based on the readings in order to control the patient's symptoms. This results in a new control variable, which is then measured and analyzed again, thus closing the loop. Local field potentials (LFPs) are sums of pre- and post-synaptic activity directly recorded from the implanted DBS electrodes. These can function as a marker for tics and can be used to modify DBS parameters in response. When the LFPs return to their background state, the DBS device can revert to its usual settings.

aDBS has been extensively investigated in Parkinson's disease. The present report describes LFP recordings at rest and during both voluntary and involuntary movement in 7 patients with severe Tourette syndrome. The recordings showed activity patterns suggestive of increased firing of thalamic cells in the low-frequency range. Chronic LFP patterns were also observed in 8 patients who returned to the clinical for battery replacement after 1–7 years of DBS treatment. Circumstances limited the observations to at-rest, with the DBS device turned on or off but with no voluntary movement or tic activity. aDBS was shown to modulate LFP patterns only by increasing low-frequency activity. When the device was switched off, low-frequency activity returned to baseline levels. These findings suggest that changes in low-frequency and alpha-band activity can be used to trigger changes in DBS parameters that would reduce or suppress this activity, hypothetically preventing tic onset.

Marceglia S, Rosa M, Servello D, Porta M, et al: Adaptive deep brain stimulation (aDBS) for Tourette syndrome. *Brain Science* 2018; doi 10.3390/brainsci8010004. From the Ospedale Maggiore Policlinico, Milan, Italy; and other institutions. **Funded by the European Research Area Networks Neuron Project; and other sources. Four of 7 study authors disclosed potentially relevant financial relationships; the remaining authors declared no competing interests.** See related story in *Psychiatry Alerts NOS* 2017;9 (November):62–63.

Direct Current Brain Stimulation for Bipolar Depression

In a randomized, sham-controlled trial, adjunctive transcranial direct current stimulation (tDCS) was associated with improvement in bipolar depression. The treatment did not appear to induce mania or hypomania.

Methods: Study participants were adults with bipolar I or II disorder, currently experiencing a depressive episode, with a Hamilton Rating Scale for Depression (HAM-D) score of >17. Participants were included only if their depression had previously not responded to ≥1 antidepressant treatment, in addition to ongoing mood-stabilizer therapy. Anxiety disorders were the only permitted psychiatric comorbidity. Participants were randomly assigned to receive real or sham tDCS. The anode and cathode electrodes were placed over the left and right dorsolateral prefrontal cortex, respectively. Each of the active sessions consisted of 30 minutes of 12 2-mA stimulations. Patients received 10 treatments on consecutive weekdays, followed by 1 session at week 4 and another at week 6. The primary study outcome was change from baseline in HAM-D score at week 6. Secondary outcome measures included the Montgomery-Asberg Depression Rating Scale (MADRS) and the Young Mania Rating Scale.

Results: A total of 59 patients were enrolled, and 52 completed all tDCS sessions. About two-thirds of patients had bipolar I disorder. About half had severe depression, and 86% had a concomitant anxiety disorder. One third met formal criteria for treatment-resistant depression. Patients had taken a mean of 1.3 antidepressants in the current episode, and three fourths were taking antidepressant medication at the start of the trial.

In the intent-to treat analysis, patients who received active tDCS had significantly larger reductions in depressive symptoms than those who received sham treatment (p=0.01; see table). Sustained response (HAM-D decrease of >50%, lasting until the end of the study) occurred in 19 actively treated patients, compared with 8 controls (68% vs 30%; hazard ratio,* 2.86; p=0.01). Sustained remission (HAM-D ≤7) was achieved by 10 patients in the active tDCS group and by 5 in the control group (37% vs 19%; p=ns). Skin redness occurred after treatment in higher proportions of active versus sham tDCS groups. Despite this, blinding was preserved, and <60% of patients correctly identified their treatment. The frequency of other adverse effects did not differ between groups. There were no episodes of emergent mixed features, mania, or hypomania.

Depressive Symptom Measures Over 6 Weeks with Active vs Sham tDCS

	Treatment group	Baseline	Week 2	Week 4	Week 6
HAM-D	**Active**	23.1	11.4	10.7	10.3
	Sham	23.5	15.8	14.7	16.2
MADRS	**Active**	28.7	15.1	14.2	13.6
	Sham	27.9	19.5	18.3	19

Discussion: This appears to be the first sham-controlled trial of tDCS in a purely bipolar patient population. As a result, although positive, the findings should be viewed as preliminary.

Study Rating*—17 (100%): This study met all criteria for a randomized controlled trial.

Sampaio-Junior B, Tortella G, Borrione L, Moffa A, et al: Efficacy and safety of transcranial direct current stimulation as an add-on treatment for bipolar depression: a randomized clinical trial. *JAMA Psychiatry* 2017; doi 10.1001/jamapsychiatry.2017.2040. From the University of Sao Paulo, Brazil; and other institutions. **Funded by the Brain and Behavior Research Foundation; and other sources. Two of 16 study authors disclosed financial relationships with commercial sources; the remaining authors declared no competing interests.**

***See Reference Guide.**

E-Prescribing and Medication Errors

The effects of e-prescribing on medication errors in outpatient psychiatry have not been evaluated, but preliminary evidence from inpatient psychiatry and other areas of medicine suggest some types of errors are reduced drastically. Nonetheless, e-prescribing has created the potential for some new types of error, according to a review.

In outpatient psychiatry, medication errors have the potential to not only harm patients directly, but could also jeopardize the clinician–patient alliance. The integration of e-prescribing into clinical practice was anticipated to drastically reduce errors from illegible handwriting, lost prescription slips, and incomplete/inaccurate instructions. Government incentive programs within Medicare have dramatically increased rates of e-prescribing and reduced the rates of these types of error. However, potential for error still exists because e-prescribing does not fully prevent the omission of the dose or strength, prescribing the wrong medication, failing to discontinue a prescription, or prescribing the same medication multiple times. Accuracy may suffer from too many distracting on-screen alerts and from the loss of interaction between prescriber and pharmacist. Internet-based refill systems may contain duplicate or outdated prescriptions. Pharmacists may still have difficulty communicating to clarify prescriptions.

E-prescribing systems could simplify medication reconciliation by matching what the patient is taking to what is in the record. Because patients often use multiple clinicians and multiple pharmacies, interoperability between the related prescribing systems should be improved. However, increased interoperability may reveal too much sensitive information to nonpsychiatric providers and may be perceived as an invasion of the patient's privacy. Systems should allow for real-time chat between pharmacists and prescribers. Most e-prescribing systems do not allow for prescription of controlled substances such as stimulants and benzodiazepines, which are commonly used in psychiatry. However, linking an e-prescribing system to a state's monitoring program for controlled substances poses difficulties. Finally, implementing e-prescribing in small-group and solo practices, where a large portion of psychiatric care takes place, would be costly. Including financial incentives or assistance in state or federal mandates could improve accessibility to e-prescribing platforms.

Hirschtritt M, Chan S, Ly W: Realizing e-prescribing's potential to reduce outpatient psychiatric medication errors. *Psychiatric Services* 2018;69 (February):129–132. From the University of California, San Francisco. **Funded by the NIMH; and other sources. One study author disclosed financial relationships with commercial sources; the remaining authors declared no competing interests.**

EMDR in Substance Use Disorder

In a preliminary study, eye movement desensitization and reprocessing improved post-traumatic, dissociative, and general psychiatric symptoms in patients with substance use disorder.

Background: Several lines of evidence suggest a role for childhood trauma, stress-related brain systems, and PTSD in substance use disorder. Originally developed for treating psychological sequelae of traumatic events, EMDR is now used to treat trauma-associated symptoms in other psychiatric disorders. Addiction-focused EMDR has had promising results in substance use disorders, but no studies as yet have evaluated the efficacy of combined trauma-focused and addiction-focused EMDR.

Methods: Study participants were 40 adults with a DSM-5 diagnosis of substance use disorder who had been referred for addiction treatment. Patients could choose whether or not to receive EMDR as an add-on to treatment as usual (TAU). When the 20 available EMDR slots were filled, all remaining patients were assigned to TAU. EMDR was delivered in 24 weekly sessions by

specialized clinical psychotherapists and incorporated elements of both the classic trauma-focused protocol and addiction-focused EMDR. TAU included clinical specialist interviews, medication, group and individual psychology, psychoeducation, and treatment of comorbid psychiatric conditions.

Results: All enrolled patients completed treatment. The 2 groups were demographically similar at baseline, with a mean age of 32 years and an average of about 20 years of substance use. Patients who chose EMDR reported a significantly higher average number of adverse childhood experiences as well as higher baseline levels of post-traumatic stress and anxiety symptoms and more comorbid psychiatric symptoms.

Over time, both groups showed statistically significant improvement in dissociative and psychiatric symptoms, measured using standardized scales. Improvements were larger in the EMDR group, so that at the end of treatment, there were few significant between-group differences in symptom measures despite significantly higher baseline levels in the EMDR group. Depressive symptoms were not significantly improved in either treatment group. Anxiety, which often accompanies abstinence from substance use, worsened in the TAU group for both state and trait measures. In contrast, the EMDR group experienced significant reductions from baseline in trait anxiety and a trend-level improvement that did not reach significance in state anxiety. At endpoint, there were no significant differences between the groups in levels of anxiety, again despite significantly higher baseline levels in the EMDR group. There were no differences between the groups in the proportion of negative urine drug assays after treatment.

Discussion: All study participants showed clinical improvement in anxiety and dissociative and psychiatric symptoms, regardless of the type of treatment. However, the effects were stronger in patients who received EMDR. Although preliminary and requiring replication, these results suggest that EMDR may be useful in the treatment of substance abuse disorders particularly in patients with more adverse childhood experiences and higher levels of symptoms.

Carletto S, Oliva F, Barnato M, Antonelli T, et al: EMDR as add-on treatment for psychiatric and traumatic symptoms in patients with substance use disorder. *Frontiers in Psychology* 2018; doi 10.3389/fpsyg.2017.02333. From the University of Turin, Orbassano, Italy; and other institutions. **Source of funding not stated. Four of 10 study authors disclosed potentially relevant financial relationships; the remaining authors declared no competing interests.**

Botulinum Toxin for Depression

Results of early clinical trials and meta-analyses have suggested that a single treatment with onabotulinumtoxinA (BTX; *Botox*) to glabellar frown lines can improve depressive symptoms in women. According to the present large consecutive case series, BTX is also effective in men and in individuals with severe, resistant depression.

Methods: Records were reviewed for 42 patients who received treatment at 2 private specialty practices in India. All patients had severe depression without psychotic features, either single-episode or recurrent. In all cases, the present episode of depression was refractory to 4–6-week courses of ≥2 different antidepressants at labeled dosages. All of the patients had glabellar frown lines, which were severe in most according to standardized criteria. All patients received a single treatment consisting of injections of BTX at 5 specific sites on the forehead according to the approved cosmetic indication, as an adjunct to antidepressant medication that had been stable for ≥6 weeks. Depression severity was measured before and 3 weeks after BTX injection using the 17-item Hamilton Rating Scale for Depression (HAM-D), the Montgomery-Asberg Depression Rating Scale (MADRS), and the Beck Depression Inventory (BDI). Patients were observed clinically for ≥6 additional weeks, although psychometric depression scales were not administered during that time.

Results: The patients (23 men, 19 women) did not differ from each other in average age (about 45 years), duration of the current depressive episode (about 8 months), or baseline depression severity. On average, patients experienced a nearly 30% decrease in symptoms over the 3 weeks post injection. Mean HAM-D scores decreased from 33 at baseline to 24 after 3 weeks, mean MADRS scores decreased from 48 to 35, and mean BDI scores decreased from 46 to 34 ($p<0.0001$ for all). All but 1 patient experienced what was considered a clinically meaningful improvement in depression symptoms, and 57% experienced partial response, defined as a ≥25% reduction in HAM-D score. However, at 3 weeks, depressive symptoms remained in the moderate to severe range despite the improvement occurring with BTX injection. Treatment effects did not differ between women and men. Improvement in frown-line severity showed a weak positive correlation with improvement on the HAM-D (correlation coefficient,* 0.37; $p<0.05$). During additional follow-up, all patients reported continued improvement in their depressive symptoms, with no further change in their treatment.

Discussion: The study results suggest BTX injection may produce early improvement in depressive symptoms, which has consistently been shown to predict later response and remission. In resource-rich environments, patients with severe depression would likely receive multimodal treatment; however, this level of care may not be available to all patients. BTX injection, because it requires limited aftercare, may be a viable option for treatment-resistant depression in more limited domains.

Chugh S, Chhabria A, Jung S, Kruger T, et al: Botulinum toxin as a treatment for depression in a real-world setting. *Journal of Psychiatric Practice* 2018;24 (January):15–20. From private practice, New Delhi, India; and other institutions. **This study was conducted without outside funding. Two of 5 study authors disclosed financial relationships with commercial sources; the remaining authors declared no competing interests.** See related stories in *Psychiatry Alerts NOS* 2012;4 (March):14–15; 2014;6 (May):27; and 2015;7 (October)58–59.

***See Reference Guide.**

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Correlation Coefficient (r): A measure of the closeness of the relationship between 2 variables. The value of r can range from -1 to 1. An r value near 1 indicates a strong positive relationship. An r-value close to zero indicates no relationship, and a negative r-value indicates a negative relationship.

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.

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.