PSYCHIATRY ALERTS NOS

Bringing Clinical Research to Practice

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Group Psychoeducation for Borderline Personality Disorder

A short-term group psychoeducation intervention reduced the severity of borderline personality disorder (BPD) in an underserved, community-based setting.

Methods: Study subjects were adults referred to an outpatient psychiatry service by community-based psychiatrists after receiving a diagnosis of BPD. Of 96 patients whose diagnoses were confirmed at the clinic, the first 48 received the study intervention and the next 48 were placed on a waitlist and received treatment as usual (i.e., monthly medical management with no disorder-specific treatments or other group therapy). The study intervention consisted of 6 weekly 90-minute group sessions with content based on the Good Psychiatric Management (GPM) generalist model for treating borderline personality disorder. Groups consisted of 8 patients each and were stratified by patient age in order to provide appropriate content and to facilitate sharing. The sessions used didactic material from the GPM handbook covering 6 content areas: diagnosis and symptoms, origins of the disorder, comorbid disorders, clinical course, a review of evidence-based treatments, and medications. The primary study outcome measure was change from baseline to the end of treatment (or a comparable period in wait listed patients) on the Zanarini Rating Scale for DSM-IV Borderline Personality Disorder (ZAN-BPD). Raters were uninvolved in treatment, but not blind to treatment assignment.

Results: Study participants had an average age of about 35 years, a mean disease history of about 5 years, and 55% were women. About 80% of patients were receiving pharmacotherapy for BPD. As indicated by ZAN-BPD scores, baseline symptoms were moderate to severe.

After 6 weeks, both groups demonstrated considerable improvement in ZAN-BPD total score, as well as the affect, cognitive, and interpersonal subscales ($p<0.001$ for all endpoints). Scores on the impulsivity subscale were not improved. The group psychoeducation intervention had large effects on the primary outcome compared with baseline (effect size,* 1.16; $p<0.001$) and compared with the control condition (effect size, 0.80; $p<0.001$). Improvements were generally maintained at follow-up evaluations 8 weeks after the end of treatment.

Of the 96 patients, 22 (46%) achieved full response (i.e., ≥50% symptom reduction) after psychoeducation, compared with 3% of the control group. A total of 13 patients (27%) in the

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psychoeducation group reached the mild symptom category from moderate or severe categories, while 8 patients (17%) in the psychoeducation group and 32 controls (67%) remained the same or worsened.

Discussion: Although positive, these results require replication in studies with stronger methodology. However, group psychoeducation does appear to be an attractive alternative for patients in settings with low access to individual psychotherapy, who are typically managed with medications.

Ridolfi M, Rossi R, Occhialini G, et al: A randomized controlled study of a psychoeducation group intervention for patients with borderline personality disorder. *Journal of Clinical Psychiatry* 2020; doi 10.4088/JCP.19m12753. From Fano Outpatient Services, Italy; and other institutions. **This study was conducted without funding. The authors declared no competing interests.**

***See Reference Guide.**

Autoimmune Psychosis

According to an expert consensus, increasing evidence links low-grade neuroinflammation and immune dysfunction to the pathophysiology of psychosis in a subset of patients with acute symptoms. The newly recognized disorder autoimmune psychosis is characterized by an isolated psychotic presentation with minimal or no neurologic features and positive tests for neuronal antibodies. Patients with autoimmune psychosis tend to have a personal or family history of autoimmunity. Serum and CSF biomarkers of inflammation are consistent with increased permeability of the blood-brain barrier and possible penetration of immune cells or other inflammatory mediators into the brain.

Diagnosing autoimmune psychosis can be difficult, and some experts believe clinical red flags exist that should raise suspicion of CNS autoimmunity in patients with new-onset psychosis. These red flags include an infectious prodrome, rapid progression, headache, movement disorder, seizures, and several other phenomena. In addition, there are 7 clinical criteria for "possible" autoimmune psychosis. (See table.) Probable autoimmune psychosis requires at least 1 of the 7 criteria, plus positive CSF, MRI, or EEG findings or positive serum anti-neuronal antibodies. Autoimmune psychosis is "definite" if the patient also has IgG class anti-neuronal antibodies in CSF.

Criteria for "Possible" Autoimmune Psychosis

The patient must present with psychotic symptoms of abrupt onset (rapid progression of <3 months) with at least one of the following:

- Currently or recently diagnosed with a tumor
- Movement disorder (catatonia or dyskinesia)
- Adverse response to antipsychotics resembling neuroleptic malignant syndrome (e.g., rigidity, hyperthermia, or raised creatine kinase)
- Severe or disproportionate cognitive dysfunction
- Decreased level of consciousness
- The occurrence of seizures not explained by a previously known seizure disorder
- A clinically significant autonomic dysfunction (i.e., abnormal or unexpectedly fluctuating blood pressure, temperature, or heart rate)

Treatment of autoimmune psychosis typically involves antipsychotics, but these can precipitate autonomic instability, recognized as suspected neuroleptic malignant syndrome. Antipsychotics should be dosed cautiously, and agents with a low potential for extrapyramidal symptoms should be selected. Immunotherapies have been effective anecdotally but have not been investigated in clinical trials.

Pollak T, Lennox B, Muller S, et al: Autoimmune psychosis: an international consensus approach to the diagnosis and management of psychosis of suspected autoimmune origin. *Lancet Psychiatry* 2020;7 (January):93–108. doi 10.1016/S2215.0366(19)30290-1. From King's College London, U.K.; and other institutions. **Source of funding not stated. Seven of 27 authors disclosed potentially relevant financial relationships; the remaining authors declared no competing interests.**

Adjunctive Deep TMS for Negative Symptoms

In patients with schizophrenia, deep transcranial magnetic stimulation (dTMS) resulted in a striking improvement in negative symptoms that was only partially attributable to its antidepressant effects. Results of this small uncontrolled study, if replicated, suggest that high-frequency stimulation of the prefrontal cortex can lead to improvements in brain-function deficits that contribute to negative symptoms.

Background: Reduced activity of the prefrontal cortex is associated with negative symptoms in schizophrenia, leading to the exploration of brain stimulation as a possible treatment. H-coil or deep TMS has been developed to stimulate deep cortical areas with low magnetic fields.

Methods: The study was a retrospective analysis of 16 patient treated with dTMS at a single center. All had schizophrenia with positive symptoms successfully controlled with antipsychotic medication, but significant remaining negative symptoms. Patients had a mean age of 28 years and a duration of illness of about 8 years. All patients were treated with dTMS using the H2 coil over the lateral prefrontal cortex 5 days per week for an average of 25 sessions. Clinical outcomes were measured at baseline, after the 10th session, and at the last treatment visit. Changes in negative symptoms were measured with the Scale for the Assessment of Negative Symptoms (SANS) and the Positive and Negative Syndrome Scale (PANSS). Depression was measured with the Calgary Depression Scale (CDS), using the usual cutoff of ≥7 points for depression.

Results: Repetitive dTMS produced large improvements on all measures of negative symptoms. (See table.) Response rates (i.e., ≥20% decrease in symptom score) ranged from 56% to 100% depending on the measure. At baseline, 11 patients met criteria or depression and 5 did not. Of the 11 patients with baseline depression, all but 3 no longer reached the cutoff for depression at the end of treatment. Negative symptom effects did not differ between patients with and without depression at baseline.

Results of dTMS in patients with residual negative symptoms

Evaluation	Baseline Mean	% Decrease in Symptoms	Response Rate
SANS	58	48%	100%
PANSS-negative subscale	30	38%	94%
PANSS-general psychopathology	48	37%	88%
PANSS positive subscale	15	25%	56%
CDS	9.3	70%	88%[±]

[±]For depression, a ≥50% improvement was the cutoff for response.

Discussion: Prefrontal cortex hypoperfusion may be involved in both depression and negative symptoms. If, as suggested by these results, the improvements in negative symptoms are not entirely due to antidepressant effects of dTMS, an alternate mechanism may by activation of prefrontal circuitry involved in cognition, memory, attention, planning, and social skills.

Linsambarth S, Jeria A, Avirame K, et al: Deep transcranial magnetic stimulation for the treatment of negative symptoms in schizophrenia: beyond an antidepressant effect. *Journal of ECT* 2019;35 (December):e46-354. doi 10.1097/YCT.0000000000000592. From Universidad Andres Bell, Santiago, Chile; and other institutions. **Funded by FONDECYT (the Chilean National Fund for Scientific and Technological Development); and other sources. The authors declared no competing interests.**

Ocular Complications of TMS

A 58-year-old woman experiencing a third episode of major depression was referred for repetitive transcranial magnetic stimulation (rTMS) following nonresponse to 4 antidepressant trials, 1 augmentation trial, and multiple psychotherapy programs. Scores on a pretreatment evaluation with the Depression Anxiety Stress Scale indicated severe depression, extremely severe anxiety, and moderate for stress. Her baseline Hamilton Depression Rating Scale (HAM-D-17) score was 12.

The patient underwent high-frequency stimulation of the left dorsolateral prefrontal cortex each weekday. After 4 weeks of treatment, her depression was substantially worsened (HAM-D score, 22) and she was experiencing irritability, fatigue, and migraine. Following the subsequent 3–4 stimulation sessions, she reported left-sided ocular adverse effects including seeing spots, white-outs, and floaters. After the 26th stimulation session she reported photopsia, and rTMS was discontinued. At that time, she reported having experienced left eye and cheek pain during previous treatments. Evaluation by her general practitioner and an ophthalmologist found no evidence of retinal detachment, posterior vitreous detachment (PVD), or microvascular retinal changes. Visual acuity was unchanged. However, the patient continued to experience photopsia and floaters for months before a PVD was identified.

TMS is generally well tolerated and safe, and serious adverse events rarely occur. Very few adverse ophthalmic events have been previously reported. In the present case, while a temporal association was evident and photopsia could have resulted from vitreal syneresis related to stimulation of extra-ocular muscles, causality could not be confirmed. TMS use is increasing, and a concurrent increase in reports of ophthalmic symptoms would support a causal association. Regardless, the potential risk of ophthalmic adverse events should be discussed and patients should be monitored for these symptoms during treatment.

Wallace D, Hazell L, Loo C: Transcranial magnetic stimulation and photopsiae. *Brain Stimulation* 2019; doi 10.1016/j.brs.2019.12.021. From St John of God Health Services; and the University of New South Wales, Australia. **The authors declared no competing interests.**

DBS for Refractory OCD

Deep brain stimulation of the ventral anterior limb of the internal capsule (vALIC) had rapid and robust effects in a cohort of patients with resistant OCD.[1] Treatment resulted in a high rate of response and was generally safe and well tolerated.

Background: Deep brain stimulation appears to be effective and well tolerated in patients with refractory obsessive-compulsive disorder, but evidence is limited, with probably only a few hundred patients having received the procedure worldwide. Most existing studies have had <5 subjects and many have been industry-funded. The present study, comprising the largest cohort to date, was conducted without industry funding.

Methods: Patients (n=70) were treated at the University of Amsterdam between 2005 and 2017. The first 16 were treated as research subjects,[2] and the subsequent 54 received DBS in a regular clinical setting. Patients had a DSM diagnosis of OCD, with a Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score of ≥28, a ≥5-year history of OCD, and substantial functional impairment. All were required to have undergone ≥2 SSRI trials at maximum dosage for at least 12 weeks, treatment with clomipramine (*Anafranil*), ≥1 augmentation trial with an atypical antipsychotic, and ≥1 trial of cognitive-behavioral therapy. Diagnoses of severe comorbidity, such as bipolar disorder, autism, or personality disorder, were not absolute contraindications to DBS.

Patients underwent bilateral implantation of DBS electrodes to the vALIC. The pulse generator, implanted in the chest, was nonrechargeable and required replacement about every 14 months. DBS was activated 2 weeks after implantation, and stimulation parameters were subsequently optimized based on evaluation every 2 weeks. Individual CBT was also provided, starting during or after optimization for the majority of patients. A total of 13 patients did not receive CBT: 8 who had a good early response to DBS, 4 who had a poor initial response, and 1 who had physical complaints. The primary efficacy measure was change from pre-treatment to 12 months in Y-BOCS score. Response was defined as a ≥35% decrease in score and partial response as a 25–34% decrease.

Results: At DBS implantation, patients had a mean age of 42 years, had been ill for an average of 25 years, and the mean Y-BOCS score was 34. At the 12-month evaluation, the mean Y-BOCS score was 20, a 40% reduction (effect size,* 1.5; $p<0.001$). Most of the decrease occurred in the first 2–3 months of treatment, with stable scores for the remainder of the year. Of the 70 patients, 36 (52%) met response criteria and an additional 12 (17%) were partial responders. Patients also experienced rapid and substantial average decreases in anxiety (55% decrease in Hamilton Rating Scale for Anxiety score; effect size, 1.4) and depression symptoms (54% decrease in Hamilton Rating Scale for Depression score; effect size, 1.3). Mood improvements were evident even in some Y-BOCS nonresponders.

DBS was generally well-tolerated, and no patient requested discontinuation of stimulation. There were 8 surgery-related adverse events requiring a second surgery. Transient hypomanic symptoms, usually related to changes in stimulation, occurred in 40% of patients. There were 3 suicide attempts, 2 explained by underlying comorbidity and 1 in a patient disappointed with the results of DBS. Other adverse events included headache (36%), pain around the burr holes (17%), feeling the implantable pulse generator in the chest (16%), pulling of the extension leads (30%), and paresthesia (20%).

Discussion: These results confirm the efficacy of DBS in patients with resistant OCD. However, patients should be monitored for suicidality during optimization, which should be conducted at an unhurried pace. The authors also recommend including a consolidation phase during which patients also receive psychoeducation and psychotherapy.

[1]Denys D, Graat I, Mocking R, et al: Efficacy of deep brain stimulation of the ventral anterior limb of the internal capsule for refractory obsessive-compulsive disorder: a clinical cohort of 70 patients. *American Journal of Psychiatry in Advance* 2020; doi 10.1176/appi.ajp.2019.19060656. From the University of Amsterdam, Amsterdam, the Netherlands, and other institutions. **This study was conducted without funding. The authors declared no competing interests.**

[2]Denys D, et al: Deep brain stimulation of the nucleus accumbens for treatment-refractory obsessive-compulsive disorder. *Archives of General Psychiatry* 2010;67 (October):1061–1068. See Psychiatry Alerts NOS 2010;2 (October):65–66.

***See Reference Guide.**

Remote Cognitive Remediation for Schizophrenia

In a small pilot study, CIRCuiTS, a computerized cognitive remediation program, was effective and feasible when a proportion of the sessions were delivered remotely, in patients' homes.

Background: CIRCuiTS is a program designed to help patients with schizophrenia improve metacognitive skills and apply these skills to daily life. Previous research has demonstrated its effectiveness in a setting where therapists could judge whether to administer some sessions remotely.

Methods: Eligible participants had a confirmed diagnosis of schizophrenia, stable clinical status, and neurocognitive impairment verified with a standardized test battery, the MATRICS Consensus Cognitive Battery (MCCB). The CIRCuiTS intervention comprises up to 40 sessions (1 hour each) delivered 3 times a week. Sessions include a series of tasks that target different

cognitive domains, and program content is individualizable and supervised by a therapist. In the present study, patients and therapists met in person in the hospital for the first 3 weeks. Subsequently, patients participated in 1 of the weekly sessions from home. Patients maintained their background antipsychotic therapy while participating in the CIRCuiTS program.

Results: A total of 10 patients were offered CIRCuiTS treatment; 2 declined because of transportation problems. The remaining 8 patients (mean age, 36 years; mean duration of illness, 14 years) completed the entire protocol. At baseline, participants had moderate to large impairment in neurocognitive domains measured by the MCCB, and most (75%) had participated in previous social skills training, other cognitive remediation interventions, or psychoeducation.

Patients indicated a high level of satisfaction with the program. Significant improvement was observed in multiple categories of the MCCB, with effect sizes in the medium to large range. (See table.) MCCB domains of attention/vigilance, reasoning and problem solving, and social cognition did not improve significantly. All but 1 patient showed substantial improvement in ≥2 cognitive domains, and 4 patients had a change in severity level, from moderate/severe to absent/mild, in ≥1 domain. Patients also showed improvements in functional capacity, self-esteem, and the disorganization dimension of the Positive and Negative Syndrome Scale (PANSS), although other PANSS dimensions were unaffected. Real life functioning, measured using the Specific Level of Functioning (SLOF) scale, was improved in 4 of 6 dimensions—self-care, interpersonal relationships, social acceptability, and working abilities.

Significant changes from baseline on neurocognitive domains

Domain	Effect Size*
MCCB	
Neurocognitive composite	2.32
Processing speed	2.08
Working memory	1.46
Verbal learning	0.89
Visual learning	0.86
Wisconsin card sorting test	
Total errors	0.98
Perseverative errors	0.91

Discussion: Compared with previous research on the program, autonomous use of CIRCuiTS for a proportion of the sessions does not appear to worsen its effectiveness and has the potential to increase access while reducing program costs and dropouts. However, these results require replication in studies with larger samples and more rigorous methodology.

Palumbo D, Mucci A, Giordano J, et al: The efficacy, feasibility and acceptability of a remotely accessible use of CIRCuiTS, a computerized cognitive remediation therapy program for schizophrenia: a pilot study. *Neuropsychiatric Disease and Treatment* 2019; 15:3103–3113. From the University of Campania Luigi Vanvitelli, Naples, Italy; and King's College London, U.K. **Source of funding not stated. The authors declared no relevant financial relationships.** See related story in *Psychiatry Alerts NOS* 2019;11 (November):63–64.

***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.