# PSYCHIATRY ALERTS NOS





Volume X / July 2018 / Number 7 www.alertpubs.com


**Change Coming . . . See back page for details.**

## Mobile Motivational App for Schizophrenia

Motivational deficits are crucial in determining outcomes in schizophrenia, are best addressed early in the course of the disease, and do not generally respond to traditional treatment approaches. According to the results of a randomized trial, the personalized real-time intervention for motivational enhancement (PRIME) smartphone app, designed to improve motivation, was effective, feasible, and acceptable in adolescents and young adults with schizophrenia.

***Methods:*** Participants were recruited using online classifieds, message boards, and flyers in clinics. The trial enrolled patients from 13 states, Canada, and Australia. Patients were aged 16–36 years, met DSM-IV-TR criteria for any schizophrenia spectrum disorder, and were within 5 years of first diagnosis. They were guided through informed consent over the telephone; tasks and questionnaires were administered using an online platform; and interview-based assessments were done using internet telephony. The PRIME intervention consisted of a supportive online community; a list of long-term goals and suggested activities, graded in difficulty, to complete for each goal; and on-demand access to motivation coaches. The comparison group received 12 weeks of wait-list treatment as usual, followed by the option to receive PRIME. The primary study outcome, motivation, was assessed after 12 weeks using the Trust Task, in which the patient had a series of interactions with simulated social partners. Feasibility was assessed with usage statistics.

***Results:*** A total of 43 patients were randomly assigned to the PRIME or control groups. Of these, 19 of 22 patients in the PRIME group completed treatment, and 19 of the 21 wait-listed participants remained in follow-up and chose to use PRIME after 12 weeks. Most patients (86%) were taking an antipsychotic medication at study entry, but these were required to have been unchanged for ≥1 month before entry and throughout the study.

Compared with the waitlist group, patients who received PRIME had larger increases in several components of the Trust Task: anticipated pleasure during the task (p=0.02; effect size,* 0.64), effort expended to increase the likelihood of future interactions with positive outcomes (p=0.03;


**PSYCHIATRY ALERTS NOT OTHERWISE SPECIFIED** (ISSN 1559-5625) 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. Periodicals postage paid at Butler, NJ, and at additional mailing offices. Postmaster: Send address changes to Psychiatry Alerts NOS, 45 Carey Ave. Ste 111, Butler, NJ 07405.


© 2018 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. Back issues and single copies are available for $10.00 each, prepaid. 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.

effect size, 0.58), and a near-significant improvement in learning from positive outcomes (p=0.07). Participants in the PRIME intervention also had significant improvement in several secondary outcomes, relative to controls: depressive symptoms, defeatist beliefs, and self-efficacy, with effect sizes ranging from 0.59 to 0.64. Improvements generally persisted after 3 months of follow-up.

Patients rated their overall satisfaction with PRIME at a mean of 8.2 on a 10-point scale. Participants logged in an average of 4 days per week and frequently interacted with each other and with the coach. Many patients noted that this was their first contact with other young people with a schizophrenia spectrum disorder. On-demand coaching was the best-liked feature of the program, and participants initiated contacts with coaches 10 times more often than contact with peers.

***Discussion:*** In addition to supporting the feasibility and effectiveness of the PRIME intervention as an adjunctive treatment, the study also demonstrated that it is possible to launch and conduct a clinical trial entirely remotely, with no in-person contact with study subjects.

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

Schlosser D, Campellone T, Truong B, Etter K, et al: Efficacy of PRIME, a mobile app intervention designed to improve motivation in young people with schizophrenia. *Schizophrenia Bulletin* 2018; doi 10.1093/schbul/sby078. From the University of California, San Francisco; and other institutions including IDEO, Palo Alto, CA. **Funded by the NIH. The authors declared no competing interests.**

***See Reference Guide.**

## Mantram Repetition for PTSD

In a randomized controlled trial, mantram repetition therapy was an effective treatment for posttraumatic stress disorder in military veterans. The therapy may appeal to veterans who prefer a treatment that is non-trauma focused and includes some elements of spirituality.

***Methods:*** The experimental program was based on silently repeating a mantram, a spiritually related word or phrase selected by each patient from a recommended list. This practice is believed to help patients focus attention, relax, and be aware of the present moment. Two other skills were also taught: "slowing down" thoughts and "one-pointed attention." Patients were taught to use these techniques to interrupt stressful feelings and to manage behavioral symptoms. The comparison treatment, present-centered therapy, is a supportive treatment with demonstrated efficacy in PTSD that has been used as an active comparator in other trials. Both treatments were delivered one-on-one in 8 weekly 1-hour sessions using standardized manuals. Study participants were treatment-seeking veterans with ≥1 traumatic experience and meeting DSM-IV-TR criteria for PTSD. Background medications were continued, and patients were asked to avoid other psychotherapy or complementary therapy. A total of 173 patients were randomly assigned to treatment. About 85% were men, and 65% were receiving medication for PTSD. The primary study outcomes were change from baseline on the Clinician-Administered PTSD Scale (CAPS) and self-reported symptoms on the PTSD Checklist–Military (PCL-M).

***Results:*** Patients in the mantram group demonstrated significantly greater improvement in CAPS score at the end of treatment (p=0.006; effect size,* 0.49) and at 2-month follow-up (p=0.04; effect size, 0.46). Improvements in self-reported symptoms were also significantly greater with mantram repetition at the end of treatment (p=0.04; effect size, 0.43), but not at follow-up. At 2 months, 59% of the mantram group who remained in follow-up no longer met criteria for PTSD, compared with 40% of the present-centered therapy group (p<0.04). The proportion of patients who had clinically significant improvement (i.e., a ≥10-point reduction in CAPS score) did not differ significantly between groups: 75% for mantram

repetition and 61% of the present-centered therapy group. Patients who used mantram repetition had significantly greater improvement in insomnia ($p<0.05$), but other secondary outcomes, including depression, anger, spiritual well-being, mindfulness, and quality of life, improved to a similar extent in both groups.

***Discussion:*** While it is premature, based on the present results, to suggest that mantram repetition therapy is similarly effective to cognitive processing therapy or prolonged exposure (the 2 evidence-based psychotherapies currently used by the VA for PTSD treatment), the authors note that the effect size in this study for CAPS score reduction is generally similar to or greater than the effect sizes observed for these treatments.

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

Bormann J, Thorp S, Smith E, Glickman M, et al: Individual treatment of posttraumatic stress disorder using mantram repetition: a randomized clinical trial. *American Journal of Psychiatry* 2018; doi 10.1176/appi.ajp.2018.17060611. From the **VA San Diego Healthcare System, CA; and other institutions. Funded by the VA. The authors declared no competing interests.**

***See Reference Guide.**

## Psychoeducation in Bipolar Disorder

According to a systematic review, there is considerable randomized clinical trial support for the positive effects of group and family psychoeducation in managing bipolar disorder. There are fewer trials of individual and internet-based psychoeducation, and those trials show mixed or no effects.

***Background:*** Psychoeducation is not limited to providing information but refers to therapist-led, personalized behavioral training that involves the patient and family members in the same session or separate sessions, or within groups. This systematic review was conducted to compare the evidence for these 3 formats and internet-based psychoeducation.

***Methods:*** A comprehensive literature search was undertaken to identify all English-language, randomized controlled trials of each type of psychoeducation. Studies were required to use standardized assessments to evaluate clinical outcomes (e.g., symptom severity), treatment outcomes (e.g., adherence), or functioning (e.g., quality of life). In nearly all cases, treatment-as-usual was the study comparator.

***Results:*** The review identified 8 trials of individual psychoeducation in >600 patients, 18 trials of group psychoeducation in >2300 patients, 10 trials of family psychoeducation in >750 families, and 4 trials of internet psychoeducation in >770 patients. The average follow-up duration was 15 months. Individual psychoeducation was associated with shorter depressive episodes in 1 study, but effects on symptom severity, relapse, and quality of life were inconsistent across the remaining studies. In the internet psychoeducation studies, patients and controls did not differ in recurrences, illness perception, or quality of life.

The majority of studies of group and family psychoeducation reported positive findings, which extended to a wide range of outcomes. Studies of group psychoeducation showed reductions in symptom severity, affective episodes recurrence, the number and duration of hospitalizations, and bipolar disorder-associated stigma. Treatment adherence was positively impacted by group psychoeducation, as was overall functioning. Family psychoeducation was also associated with improvements in symptom severity, reductions in relapse and rehospitalization rates, and longer relapse-free intervals, as well as lowered levels of illness burden in the patients. In addition, family members reported increases in caregiver knowledge, skills, support, and wellbeing; a more positive family attitude; and reduced levels of family burden.

***Discussion:*** Many of the positive effects of the group and family formats are likely to be interrelated. For example, with group psychoeducation, better treatment adherence probably results in more optimal therapeutic medication levels and improved clinical outcomes. Decreased stigma through group psychoeducation may also contribute to improved clinical outcomes. Discussions in group psychoeducation can enhance self-acceptance and self-efficacy. Skills gained in family psychoeducation can help the family deal with and possibly delay relapses.

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

Soo S, Zhang Z, Khong S, Low J, et al: Randomized controlled trials of psychoeducation modalities in the management of bipolar disorder: a systematic review. *Journal of Clinical Psychiatry* 2018; doi 10.4088/JCP.17r11750. From the Institute of Mental Health, Singapore; and other institutions. **This review was conducted without direct funding. The authors declared no competing interests.**

***See Reference Guide.**

## Mitochondrial Agents for Bipolar Disorder

Therapies that target the mitochondria are of growing interest for the treatment of bipolar disorder. Evidence to support the emerging mitochondrial hypothesis of bipolar disorder includes an increased prevalence of mood disorders in patients with mitochondrial diseases and morphological abnormalities of mitochondria and abnormal energy metabolism in patients with bipolar disorder. Some already approved drugs for bipolar disorder—notably lithium, valproic acid, and atypical antipsychotics—improve mitochondrial function. According to a literature review, many other agents affect the function of the mitochondria, including supplements like N-acetylcysteine, coenzyme Q10 (CoQ10), alpha-lipoic acid, S-adenosyl methionine (SAMe), melatonin, and a long list of vitamins. Most of these agents have plausible mechanisms of action involving the mitochondria, are well tolerated, and in some cases, have shown promise in preclinical and preliminary clinical studies. However, there is a need to develop novel candidate mitochondrial modulators and to conduct rigorous clinical trials.

Pereira C, Chavarria V, Vian J, Ashton M, et al: Mitochondrial agents for bipolar disorder. *International Journal of Neuropsychopharmacology* 2018; doi 10.1093/ijnp/pyy018. From the Centro Hospitalar Lisboa Norte, Lisbon, Portugal; and other institutions. **Source of funding not stated. Three of 7 study authors disclosed potentially relevant financial relationships; the remaining authors declared no competing interests.**

***Common Drug Trade Names*: ramelteon—*Rozerem*; valproate—*Depakene, Depakote***

## Cognitive/Exposure Therapy for Hoarding Disorder

In a randomized trial, an exposure-based therapy was superior to intensive case management in treating hoarding disorder in older adults.

***Background:*** Neurocognitive impairment may reduce the efficacy of standard cognitive behavioral therapy (CBT) for hoarding disorder in older adults. Cognitive Rehabilitation and Exposure/Sorting Therapy (CREST) is a manualized treatment developed and previously pilot-tested by the study authors. The treatment addresses neurocognitive weaknesses that may contribute to hoarding disorder while targeting the core symptoms of the disorder. It does not include cognitive restructuring or other elements of CBT. CREST consists of 26 weekly 40–60-minute individual sessions involving teaching such skills as cognitive flexibility and problem solving, exposure sessions in the clinic and the patient's home, and relapse prevention and maintenance. Patients receive daily homework assignments.

***Methods:*** Study subjects, recruited from the community, were 58 adults aged ≥60 years (mean age, 67 years; 71% women) who met DSM-5 criteria for primary diagnosis of hoarding disorder. Participants were randomly assigned to receive either CREST or case management, which had similar intensity to CREST and was delivered by nurses who provided support, referral for needed medical and social services, and safety recommendations. Symptom

severity was assessed by blinded raters at baseline, 3 months (mid-treatment), 6 months (post-treatment), and 9 and 12 months. Primary outcome measures were the self-report Saving Inventory-Revised and the clinician-rated UCLA Hoarding Severity Scale (UHSS).

***Results:*** More than 80% of CREST participants and 70% of the case-management group completed the 6-month post-treatment assessment. Patients in both treatment groups showed significant decreases in symptom severity from baseline to 6 months on all primary and secondary outcome measures. Symptom scores on the SI-R decreased by 38% in the CREST group, compared with 25% in the case-management group (p=0.03; effect size,* 0.63). Among the 3 SI-R subscales, CREST was associated with significantly greater improvement than case management in clutter (p=0.022), but not acquisition or difficulty discarding. Patients also showed improvement in the UHSS, favoring CREST numerically but not reaching statistical significance. Analysis of secondary outcomes showed that CREST was associated with larger mean percent improvement on the Activities of Daily Living–Hoarding scale (32% vs 13%; p=0.035); in anxiety on the Hospital Anxiety and Depression Scale (38% vs 14%; p=0.04); and on the Clinical Global Impression (CGI)–Severity Scale (27% vs 12%; p=0.04). More CREST participants met treatment response criteria on the CGI-Improvement scale (i.e., ratings of much or very much improved; 78% vs 28%; p=0.001). Additionally, more patients who received CREST achieved subclinical symptom status with odds ratios* ranging from 2.4 to 7.3 and numbers needed to treat* ranging from 2.6 to 4.5 depending on the symptom measure. Improvements in both treatment groups were stable through the 12-month follow-up interview.

***Discussion:*** The efficacy of CREST may be due to its inclusion of compensatory cognitive training and emphasis on exposure therapy, rather than cognitive therapy. Case management may have improved multiple areas of patients' lives, allowing them to focus on addressing their hoarding problems. In the study, the frequency of sessions of case management, which is currently the most widely used intervention for hoarding disorder, was scheduled to match CREST and was much higher than is usually the case.

Ayers C, Dozier M, Twamley E, Saxena S, et al: Cognitive rehabilitation and exposure/sorting therapy (CREST) for hoarding disorder in older adults. *Journal of Clinical Psychiatry* 2018;79 (March/April):85-93. doi 10.4088/JCP.16m11072. From the VA San Diego Healthcare System, CA; and other institutions. **Funded by the VA. The authors declared no competing interests.**

***See Reference Guide.**

## rTMS for Comorbid Anxiety, Insomnia

In a pilot study, repetitive transcranial magnetic stimulation of the right parietal cortex had promising results in patients with comorbid generalized anxiety disorder (GAD) and insomnia.

***Methods:*** Study participants, recruited from outpatient neurology clinics, met criteria for both GAD (DSM-IV-TR) and insomnia (DSM-IV) related to another mental disorder, with insomnia duration of ≥3 months. Patients were randomized to double-blind treatment with either low-frequency (1 Hz) rTMS administered over the right parietal cortex on 10 consecutive days or sham rTMS. The primary study outcome measure was the Hamilton Rating Scale for Anxiety (HAM-A). Responder status was defined as a ≥50% improvement in the HAM-A score and remission as a score of <8. Secondary outcome measures were the Pittsburgh Sleep Quality Index and the Hamilton Rating Scale for Depression. Symptoms were assessed at baseline, immediately after the final treatment, and 2 weeks and 4 weeks after the end of treatment.

***Results:*** A total of 36 patients were enrolled, and all completed the 10 days of treatment. Active rTMS was associated with a larger mean improvement in anxiety symptoms than sham rTMS at all evaluation points. The mean baseline HAM-A score was 20 in both treatment groups. Patients who received active treatment showed a significant 44% reduction in HAM-A score at

the post-treatment evaluation, while the sham group showed little change (8% reduction in score). At 1 month follow-up, 4 patients met remission criteria and an additional 6 met response criteria, compared with a single patient meeting response criteria in the sham group. Patients who received active treatment also had significant improvements in insomnia and depressive symptoms, while the sham group demonstrated no significant changes.

***Discussion:*** The few previous studies of rTMS in GAD have targeted the right dorsolateral prefrontal cortex, with promising results. The choice of the right parietal cortex as a treatment target in the present study is based on the role of the parietal cortex in attention networks, which may bias attention toward threat-related stimuli. Functional MRI studies suggest these networks are abnormal in patients with GAD. rTMS may modulate the interaction between top-down attention and emotion processing, influencing both anxiety and insomnia.

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

Huang Z, Li Y, Bianchi M, Zhan S, et al: Repetitive transcranial magnetic stimulation of the right parietal cortex for comorbid generalized anxiety disorder and insomnia: a randomized, double-blind, sham-controlled pilot study. *Brain Stimulation* 2018; doi 10.1016/j.brs.2018.05.016. From Capital Medical University, Beijing, China; and other institutions. **Funded by the Natural Science Foundation of China; and other sources. The 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.

**Number Needed to Treat:** Indicates how many patients need to be treated for 1 to benefit. The ideal NNT is 1, where everyone improves with treatment. The higher the NNT value, the less effective the treatment.

**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.

**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.

**IMPORTANT REMINDER**

**Starting with the next issue, the delivery of *Psychiatry Alerts NOS* will be 100% electronic**. Please note that our **CME exams will be printed and mailed to you as usual**.

If you have not yet done so, please register your email address with us by logging in to your account at www.alertpubs.com with your customer number (see envelope) and using the "Change Address" feature at the top of the page. If you don't have an online account, you can quickly and easily create one on the website. **And don't worry, we will never share your email address without your permission.**

If you need help accessing your monthly issues, email Donna at custservice@alertpubs.com or call her at 973-898-1200 between the hours of 9 AM and 3 PM EST weekdays.

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**