

COMBS: Feeling positive about negative symptoms of schizophrenia

Banu Ozkan Karadag, MD, and Rashi Aggarwal, MD, FACP, FAPA

Negative symptoms of schizophrenia—such as social withdrawal, avolition, avoidance, lack of spontaneity, anhedonia, poverty of speech, and blunted affect—often persist after successful treatment of positive symptoms, such as hallucinations and delusions.¹ Negative symptoms can be debilitating and are associated with poor social and occupational outcomes, as well as cognitive dysfunction. Currently, treatments for negative symptoms are not nearly as effective as treatments for positive symptoms. The mnemonic **COMBS** can be used to easily recall 3 treatment modalities often used to address negative symptoms.

Cognitive-behavioral therapy

Cognitive-behavioral therapy (CBT) and other psychosocial therapies derived from it, such as social skills training, recovery-oriented cognitive therapy, motivation and enhancement therapy, and cognitive-behavioral social skills training (CBSST), have shown to be effective for treating negative symptoms.² In a study of 149 patients with schizophrenia, CBSST reduced symptoms of avolition and apathy and improved functioning outcomes.²

Medications

Antipsychotics. Although second-generation antipsychotics (SGAs) were initially promising, accumulating clinical experience and research have shown that these agents have limited efficacy for treating negative symptoms.¹ Unlike first-generation antipsychotics, SGAs do not cause affective blunting, and are effective at treating depressive symptoms; however, depressive symptoms can sometimes be difficult to distinguish

from negative symptoms. Improvement of depressive symptoms observed with SGA treatment could be mistakenly interpreted as alleviation of negative symptoms; however, clinical trials that focused specifically on treating negative symptoms have found no specific efficacy of SGAs.¹

Antidepressants. Although clinical trials and meta-analyses have had mixed results,¹ antidepressants appear to be safe add-on treatments with small efficacy for negative symptoms.

Anticonvulsants have long been used as augmentation to antipsychotics for patients with treatment-resistant schizophrenia; however, there is no evidence that these medications can improve negative symptoms.¹

Stimulants. There is no strong evidence that stimulants could be an efficacious treatment for negative symptoms.¹

Other pharmacologic agents,¹ such as acetylcholine-related medications, oxytocin, and medications with a mechanism of action that is related to an inflammatory response and immunologic pathways (ie, minocycline), are being evaluated for treating negative symptoms. Research into the efficacy of glutamate-related agents also appears to be continuing.¹

Brain Stimulation therapies

Transcranial magnetic stimulation (TMS), transdirect current stimulation (tDCS), vagus nerve stimulation, and deep brain stimulation have been evaluated for treat-

Dr. Karadag is a PGY-3 Psychiatry Resident, Rutgers New Jersey Medical School, Newark, New Jersey. Dr. Aggarwal is Director, Residency Training Program, Associate Professor, Department of Psychiatry, Rutgers New Jersey Medical School, Newark, New Jersey.

Disclosures

The authors report no financial relationships with any companies whose products are mentioned in this article, or with manufacturers of competing products.



Discuss this article at
www.facebook.com/MDedgePsychiatry

CBT-related therapies and antidepressants appear to be helpful in treating negative symptoms

Table

Treatment approaches for negative symptoms of schizophrenia

Treatment	Efficacy
Cognitive-behavioral therapy	Statistically significant but clinically limited
Medications	
Antipsychotics	Limited; second-generation antipsychotics are not superior to first-generation antipsychotics
Antidepressants	Statistically significant but clinically limited. Safe as add-on treatment
Anticonvulsants	No significant evidence
Stimulants	No significant evidence
Glutamate Acetylcholine Minocycline Oxytocin	Further research is needed
Brain stimulation therapies	
tDCS TMS	Meta-analysis of RCTs comparing tDCS and rTMS with sham interventions show that both treatments have significant efficacy
VNS DBS	Further research is needed
DBS: deep brain stimulation; RCTs: randomized controlled trials; tDCS: transdirect current stimulation; TMS: transcranial magnetic stimulation; VNS: vagus nerve stimulation	
Source: References 1-3	

ing negative symptoms. A recent meta-analysis of randomized controlled trials comparing the effects of brain stimulation with sham interventions in patients with schizophrenia found that TMS and tDCS that targeted the left dorsolateral prefrontal cortex effectively reduced the severity of negative symptoms.³

The *Table*¹⁻³ summarizes available treatments for negative symptoms of schizophrenia and their efficacies. Although research investigating the improvement of negative symptoms is currently insufficient, CBT-related therapies and antidepressants

appear to be helpful. For more information, see “Treating negative symptoms of schizophrenia” (CURRENT PSYCHIATRY, December 2018, p. 19-22, 50) at www.MDedge.com/psychiatry.

References

1. Remington G, Foussias G, Fervaha G, et al. Treating negative symptoms in schizophrenia: an update. *Curr Treat Options Psychiatry*. 2016;3:133-150.
2. Granholm E, Holden J, Worley M. Improvement in negative symptoms and functioning in cognitive-behavioral social skills training for schizophrenia: mediation by defeatist performance attitudes and asocial beliefs. *Schizophr Bull*. 2018;44(3):653-661.
3. Kennedy NI, Lee WH. Efficacy of non-invasive brain stimulation on the symptom dimensions of schizophrenia: a meta-analysis of randomized controlled trials. *Eur Psychiatry*. 2018;49:69-77.