Negative Symptoms in Schizophrenia: An Update on Identification and Treatment

November 24, 2014 | Schizophrenia [1], Psychopharmacology [2]

What signs are generally regarded as negative symptoms? What etiological factors contribute to a negative symptom presentation? How to treat these symptoms? Insights here.

Schizophrenia remains among the top 10 disabling conditions worldwide for young adults. Including care expenditures and disability, the costs of serious mental illnesses are more than $317 billion annually in the United States, or more than $1000 per year for every man, woman, and child.¹,² In the US, the cost of treatment and loss in productivity associated with schizophrenia are estimated to be above $60 billion annually.²,³ More than three-quarters of this amount is associated with loss in productivity.

Patients with schizophrenia struggle with many functional impairments, including performance of independent living skills, social functioning, and occupational/educational performance and attainment. Most patients require some public assistance for support, and only 10% to 20% of patients are able to sustain full- or part-time competitive employment.⁴,⁵ Improving functional outcomes for these individuals is a significant mental health priority. It may be that the negative symptoms of schizophrenia, including problems with motivation, social interactions, affective experience and responsiveness, prosody and clarity of speech, and slowed movement, contribute more to poor functional outcomes and quality of life for individuals with schizophrenia than do positive symptoms. Caregivers report high levels of burden secondary to negative symptoms. In a nutshell: 5 Domains of Negative Symptoms of Schizophrenia

Negative symptoms tend to persist longer than positive symptoms and are more difficult to treat. Improvements in negative symptoms were associated with a variety of improved functional outcomes, including independent living skills, social functioning, and role functioning.⁶ Moreover, such improvements predicted future improvements in global functional outcomes for patients with schizophrenia. Thus, targeting negative symptoms in the treatment of schizophrenia may have significant functional benefits.

Current antipsychotic agents are most effective for treating the positive symptoms of schizophrenia. During brief medication visits, physicians typically focus on considerations related to delusions, hallucinations, disorganized and aggressive behavior, and hostility. These common symptoms may increase during relapse, resulting in hospitalization, emergency department visits, and crisis center services, or in incarceration in the criminal justice system.

Physicians may not be aware of the impact of negative symptoms on the patient’s and caregiver’s lives, may not know how to assess these symptoms, and may be unfamiliar with treatment strategies that favorably impact negative symptoms. In this article, we describe the signs generally regarded as negative symptoms, some of the etiological factors that contribute to a negative symptom presentation, and ways of treating these symptoms.

Recognizing negative symptoms
Negative symptoms represent a reduction of emotional responsiveness, motivation, socialization, speech, and movement. Analytic studies of multiple instruments indicate that these domains load onto 2 primary factors: avolition-apathy and diminished expressiveness. Primary negative symptoms are thought to be etiologically related to the core pathophysiology of schizophrenia, whereas secondary negative symptoms are derivative of other symptoms of schizophrenia, other disease processes, medications, or the environment. For example, antipsychotic medications variably produce both akinesia and blunted affect. Depression can cause anhedonia, lack of motivation, and social withdrawal. Lack of stimulation in impoverished institutional environments can lead to complacency and problems with motivation and initiation of productive activities.

A negative symptom presentation can also be the result of psychotic processes. Social withdrawal can be caused by paranoia or by immersion in the psychotic process to the exclusion of real-life
relationships. Primary and enduring negative symptoms are frequently referred to as the “deficit syndrome.” Individuals with the deficit syndrome have been found to have greater cognitive deficits and poorer outcomes than patients who do not have this syndrome. This brief narrative describes a typical day in the life of a patient with schizophrenia. It is apparent that the patient demonstrates several classic negative symptoms, including blunted emotional responsiveness, blunted affect, and decreased motivation.

**CASE VIGNETTE**

Jesse is a 32-year-old Hispanic man with a 12-year history of schizophrenia. He responds slowly to questions and elaborates very little. He presents with blunted affect and makes few expressive gestures during the interview. Below he describes a typical day.

**Jesse:** I get up about 2 or so.

**Interviewer:** In the afternoon?

**Jesse:** Yes. Then I smoke a cigarette. Then I eat.

**Interviewer:** What do you usually have?

**Jesse:** Cereal or something leftover like a hamburger from [fast food restaurant].

**Interviewer:** OK, what do you do next?

**Jesse:** After I eat? I smoke another cigarette.

**Interviewer:** What about after that?

**Jesse:** Then . . . I don’t know, I watch TV.

**Interviewer:** Anything else?

**Jesse:** Sometimes I walk to the store if I am out of cigarettes.

Further questioning by the interviewer gets each piece of the information.

**Jesse:** I haven’t done that in a while. I take a nap around 6. Then I eat dinner.

**Interviewer:** And what do you do between dinner and bedtime?

**Jesse:** Smoke and watch TV.

**Interviewer:** What do you watch?

**Jesse:** Bonanza, Get Smart . . . that stuff.

**Interviewer:** Can you tell me about a show you saw in the past week?

**Jesse:** Not really. Don’t remember [further coaxing produces no additional information].

**Interviewer:** OK, do you ever watch the news?

**Jesse:** Sometimes it goes to news.

**Interviewer:** Can you tell me about something going on in the world right now?

**Jesse:** The war.

**Interviewer:** Anything specific about the war?

**Jesse:** It’s bad.

**Interviewer:** Anything else?

**Jesse:** No.

**Interviewer:** Do you call anyone or go see any family or friends?

**Jesse:** My dad comes over once a week to check on me.

**Interviewer:** Do you see anyone else, or call someone?

**Jesse:** I don’t have anyone to call.

**Interviewer:** Do you have any hobbies, things you like to do.

**Jesse:** Smoke [and after further questioning] I like to play basketball.

**Interviewer:** When was the last time you played?

**Jesse:** I don’t have a ball.

Jesse seldom speaks spontaneously and needs to be prompted repeatedly by the interviewer to describe his day. When he speaks, he does not elaborate, which requires more detailed questioning. He is not physically active and spends most of his day watching television and smoking. He has no friends and is visited by his father once a week. In response to questions about his interests, he indicates that he likes basketball, but he neither plays nor watches basketball games. His affect is blunted throughout the conversation, and he is not emotionally responsive. Indeed, he cannot convincingly describe any recent emotional experiences from any portion of the emotional spectrum. When asked, Jesse states that he wants to get a job, but he has done nothing to find a job in more than a decade. In general, Jesse claims to be content with his life and has no issues that he wishes to bring to his doctor’s attention. Interviews with family members reveal that these traits have characterized Jesse for many years.
Jesse is seen every 3 months for brief medication visits. His treating physician seldom inquires about the quality of Jesse’s life, the manner in which he spends his time, or his overall functioning. Because there are no obvious positive symptoms and no problems with acting out or hostility, changes in medication that are initiated are limited to those relating to considerations of tolerability. Even these changes are made cautiously so as not to result in an exacerbation of his positive symptoms. Jesse’s case is illustrative of thousands of cases in psychiatric practice. Some of the reluctance to get into such issues is related to the limited time public sector physicians have to spend with each patient. Consequently, these clinicians tend to focus on the patient’s most pressing needs, such as suicidal or aggressive behaviors or severe symptom exacerbations. The patient’s overall functioning and symptoms characterized by the negative syndrome are generally not considered an important focus of treatment by either the physician or the patient. Note that Jesse does not have a “chief complaint.” He is content with his life and his family seems to accept these symptoms. This lack of awareness of negative symptoms, often confused with anhedonia, is common in individuals with schizophrenia living in the community. For the most part, neither clinicians nor society has targeted these symptoms as an unmet health care need.

Assessing negative symptoms

Individuals with schizophrenia are often unaware of the extent of their negative symptoms. They frequently do not spontaneously report negative symptoms as problems and are less concerned about them than their relatives may be. It is important to make accurate assessments of negative symptoms. Although there are no well-established clinical assessment tools to measure treatment progress or failure, there are several instruments that measure negative symptoms (primarily used in research). The Table presents the domains of negative symptoms identified from the Negative Symptom Assessment (NSA) and describes the behaviors that might be observed in each domain. In addition to observation, it is important to ask questions regarding the person’s daily activities and engagement with others. The NSA-16 may be too labor-intensive for routine use in a public outpatient setting. To quickly identify and record negative symptoms in these settings, two 4-item versions of negative symptom rating scales are available. Direct-care workers can be trained to reliably administer and score these brief negative symptom scales. A clinically useful question derived from the NSA asks, “Starting from the time you get up, could you tell me how you have spent a typical day in the past week?” From this one question, many different levels of clinical information can be gathered. Does the person generate a multifaceted answer without prompting or, as described in the interview above, does the psychiatrist have to pull out every detail? Is the individual enthusiastic about specific activities? Is the individual actively engaged with hobbies, friends, and productive activity during the day? How does this individual compare with a young person without schizophrenia?

Options for treatment of negative symptoms

If negative symptoms are secondary to extrapyramidal syndrome (EPS) or antipsychotic treatment, they can be decreased by prescribing an antipsychotic with a lower likelihood of producing EPS or by reducing the dosage of the current antipsychotic to a level that does not produce the adverse effects. In the latter case, care must be taken to observe for an increase in other clinical symptoms. Similarly, if negative symptoms are related to depressed affect, treatments for depression may be considered. While there is increasing evidence that antidepressants may have a positive impact on negative symptoms, more evidence from larger-scale prospective studies is needed before definitive conclusions can be reached regarding the value of this option. A recent double-blind, placebo-controlled study of the efficacy of reboxetine and citalopram as adjunctive treatment with antipsychotics did not support their use in the treatment of negative symptoms. Alternatively, if negative symptoms, such as social withdrawal, are caused by the patient’s response to positive symptoms, increasing the dosage of antipsychotic medication or switching to a different antipsychotic may be warranted. If options for treating secondary causes of negative symptoms have failed, the options for pharmacological treatment are limited at present. Current antipsychotic treatments appear to have a modest impact at best on negative symptoms. Novel compounds to specifically address negative symptoms are being studied in large-scale clinical trials. Some promising compounds that affect the glutamate system initially demonstrated improvements in negative symptoms. Bitopertin (a glycine transporter type 1 inhibitor) added to current antipsychotic treatment improved negative symptoms after 8 weeks compared with antipsychotic treatment plus placebo. Moreover, a strong trend for improved functional outcome as measured by the Personal and Social Performance Scale was seen in the bitopertin group. Unfortunately, phase 3 trials of bitopertin did not support its efficacy for the treatment of negative symptoms.
symptoms. Several companies have recently stopped development of glycine transporter type 1 inhibitors. Boosting cholinergic signaling may be an alternative for improving both cognitive and negative symptoms, and α7 nicotinic acetylcholine receptor co-agonists are being investigated in phase 2 and 3 trials. Folic acid and vitamin B12 improved negative symptoms, but treatment response was related to genetic variation in folate absorption. Other studies of various compounds are ongoing and represent hope for the pharmacotherapy for negative symptoms.

Combining antipsychotic and adjunctive treatments with psychosocial interventions may also improve negative symptom outcomes more than pharmacotherapy alone. Environmental supports to prompt and cue adaptive behaviors led to improvement on the motivation factor of the NSA. Improvements on this factor showed individuals with better everyday-living outcomes. They were more involved in activities, more engaged in the world around them, took better care of themselves (eg, grooming, hygiene), and were more likely to pursue goals. It may be that some of this improvement has to do with decreasing the environmental impoverishment that contributes to secondary negative symptoms rather than improving primary negative signs of schizophrenia. Environmental supports may also prompt individuals to take part in activities they would otherwise not initiate, bypassing some of the apathy associated with negative symptoms. Social skills training has been found to improve social adjustment for individuals with schizophrenia. Teaching the skills needed to interact with others gives patients the tools needed to initiate conversations and maintain relationships.

Results from a study by Grant and colleagues showed that cognitive-behavioral therapy (CBT) improved negative symptoms. Patients learned to address self-defeating thoughts, which often underlie problems in motivation. A novel treatment, motivation and enhancement therapy (MOVE) is currently being tested for severe and persistent negative symptoms. MOVE combines environmental supports, CBT, skills training, and several other components in an attempt to address all domains of negative symptoms. Preliminary results suggest that MOVE improves overall negative symptoms, but only after 9 months of treatment. While more work on psychosocial treatments that specifically target negative symptoms is necessary, referral to psychosocial treatment is an important option to consider in dealing with enduring negative symptoms.

Finally, it is important to educate families about the nature of schizophrenia and negative symptoms. When the family is more aware that poor motivation, flat affect, and decreased involvement and activity reflect symptoms of schizophrenia rather than problems with the character of the individual, it reduces the likelihood that the family will be overly critical of these behaviors.

**Conclusion**

Negative symptoms represent an important treatment target in schizophrenia. It is essential to assess for negative symptoms, treat the secondary causes of these symptoms, keep informed of innovations in pharmacotherapy, and refer patients and families to psychosocial therapy in an attempt to improve outcomes and quality of life for these individuals. New pharmacological treatments to address negative symptoms are awaiting the results of phase 3 trials.

**Table:** Domains of negative symptoms and observed behaviors from the Ne...

**Disclosures:**

Dr Velligan is Professor and Director of the Division of Schizophrenia and Related Disorders in the department of psychiatry at the University of Texas Health Science Center at San Antonio. Dr Alphs is Therapeutic Area Leader in Psychiatry, Medical and Scientific Affairs, for Janssen, LP, Ortho-McNeil Janssen Scientific Affairs, LLC, Titusville, NJ. Dr Velligan reports that she has the following
relationships: Lundbeck-Otsuka: consultant, travel expenses, honoraria, speakers’ bureau, and advisory board; Bristol-Myers Squibb: consultant, honoraria; Janssen: consultant, honoraria advisory board; Genentech-Roche, consultant, honoraria, travel expenses, advisory board, research grant. Dr Alphs reports that he is employed by Ortho-McNeil Janssen.

References:


17. Goff DC, Lamberti JS, Leon AC, et al. A placebo-controlled add-on trial of the Ampakine, CX516, for cognitive deficits in schizophrenia. Neuropsychopharmacology. 2007 May 9; [Epub ahead of print].


Source URL: http://www.psychiatrictimes.com/printpdf/negative-symptoms-schizophrenia-update-identification-and-treatment/page/0/1

Links: