



Nature's way: Treats the Cause rather than the Symptom

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Abstract

Negative symptoms of schizophrenia including social withdrawal, diminished affective response, lack of interest, poor social drive, and decreased sense of purpose or goal directed activity predict poor functional outcomes for patients with schizophrenia. They may develop and be maintained as a result of structural and functional brain abnormalities, particularly associated with dopamine reward pathways and by environmental and psychosocial factors such as self-defeating cognitions and the relief from overstimulation that accompanies withdrawal from social and role functioning. While antipsychotic medications to treat the symptoms of schizophrenia have been around for decades, they have done little to address the significant functional impairments in the disorder that are associated with negative symptoms. Pharmacologic treatments may be somewhat successful in treating secondary causes of negative symptoms, such as antipsychotic side effects and depression. However, in the United States there are no currently approved treatments for severe and persistent negative symptoms (PNS) that are not responsive to treatments for secondary causes. Pharmacotherapy and psychosocial treatments are currently being developed and tested with severe and PNS as their primary targets. Academia, clinicians, the pharmaceutical industry, research funders, payers and regulators will need to work together to pursue novel treatments to address this major public health issue. Negative symptoms of schizophrenia including social withdrawal, diminished affective response, lack of interest, poor social drive, and decreased sense of purpose or goal directed activity predict poor functional outcomes for patients with schizophrenia.

Symptoms of Schizophrenia

□ Negative symptoms

- Negative symptoms are associated with disruptions to normal emotions and behaviors. These symptoms are harder to recognize as part of the disorder and can be mistaken for depression or other conditions. These symptoms include the following:
 - "Flat affect" (a person's face does not move or he or she talks in a dull or monotonous voice)
 - Lack of pleasure in everyday life
 - Lack of ability to begin and sustain planned activities
 - Speaking little, even when forced to interact.

Keywords: Persistent Negative Symptoms (PNS); Schizophrenia

Introduction

Schizophrenia is one of the top 10 disabling mental conditions and impacts 1% of the adult population worldwide. Patients suffering from schizophrenia struggle with cognitive and functional impairment. Due to the often chronic course of illness, patients with schizophrenia have poor educational attainment, reduced quality of life, impairment in independent living and major socio-occupational dysfunction. Impairment arising from schizophrenia is so severe that only 10% - 20% of patients work full time or part time. The majority of patients suffering from schizophrenia require some form of public funding for support. The loss of productivity associated with schizophrenia is a major driver of cost which is estimated to be over 60 billion dollars annually; or more than \$1000 for every man, woman, and child in the United States. There is an additional burden on the family members and relatives who care for such patients.

Description of negative symptoms

Negative symptoms are defined as absence or reduction of behaviors that are normally present in the general population. Negative symptoms of schizophrenia include social withdrawal, diminished affective response, lack of interest, poor social drive, and decreased sense of purpose or goal directed activity. DSM-V emphasizes two negative symptom domains: expressive deficits and avolition. Expressive deficits include blunted facial expression, few changes in voice tone, and a paucity of expressive gestures which are normally present in conversation. Avolition refers to a lack of initiative for daily activity and interaction with others. Individuals with avolition may have difficulty even generating an idea to do something and have low levels of productive activity during the day. They may spend a lot of time sitting or lying around, have few interests and relate little to others.

Negative symptoms of schizophrenia persist longer than positive symptoms and are more difficult to treat. In addition, negative symptoms of schizophrenia serve as better predictors of concurrent and future socio-occupational functioning than do positive symptoms. A large number of studies have found attenuated negative symptoms in patients with at risk mental states.

Types of Negative Symptoms

Approximately 20% - 40% of patients with schizophrenia have persistent or deficit negative symptoms. Primary (deficit) negative symptoms are defined as symptoms that are idiopathic to schizo-

phrenia, arising from a distinct yet ultimately mysterious underlying pathologic process. These symptoms are present during and between episodes of symptom exacerbation and are not always dependent on whether the patient is taking medication.

Secondary (non-deficit) symptoms are defined as those that are caused by factors other than the illness of schizophrenia. Secondary causes of negative symptoms can include medication side effects, notably extrapyramidal side effects (EPS) of antipsychotic medication, neuroleptic akinesia, or drug withdrawal from Central Nervous System stimulants. Secondary negative symptoms can also be due to depression, social deprivation or personality disorders. Secondary negative symptoms may be non-persistent or appear for a shorter duration when compared to primary negative symptoms.

Pharmacological Treatment of Negative Symptoms

Treatment of negative symptoms depends upon their causes. If negative symptoms such as social withdrawal are secondary to a patient's positive symptoms, then increasing the dosage of antipsychotic medication or switching to a different antipsychotic medication may be helpful. Alternatively, if negative symptoms are associated with depressed affect, then treatment for depression should be considered. A recent Cochrane review of the literature indicated that antidepressants may have a positive impact on negative symptoms; however additional prospective studies are needed on a larger-scale to reach this definitive conclusion. Moreover, it is not clear from the existing literature whether antidepressants improve negative symptoms in the long term, as most randomized blinded trials have been brief. If the occurrence of negative symptoms is secondary to EPS of antipsychotic medications, these can be potentially decreased by reducing the dosage of antipsychotic medication to a level that does not produce EPS or by prescribing atypical antipsychotics with lower potential for EPS side effects. Of course, problems with increasing positive symptoms may result from lowering the dose of antipsychotic medications.

Conclusion

Negative symptoms are devastating for patients and families. They contribute to the high levels of disability observed in schizophrenia. Negative symptoms are difficult to treat with currently available pharmacotherapies. While some improvements have been noted with psychosocial treatments, few have been studied with design features needed to establish their efficacy in the

treatment of PNS. Brief reliable and valid assessments of negative symptoms are available but need to be made widely available to clinicians. Causal beliefs are associated with treatment choices. Such preliminary results highlight the value of continued studies, not only to establish the causal nature of these associations, but also to demonstrate the utility of modifying such beliefs for both parents' and child's benefits. Identifying parents' beliefs about their child's illness may be an important step in formulating interventions facilitating appropriate care. Treatments of secondary causes of negative symptoms are important to attempt. Despite these challenges, continued work on treatment development involving a concentrated effort from academia, clinicians, the pharmaceutical industry, payers, research funders, and regulators is needed to address these devastating symptoms.

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