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Editorial

Negative symptoms in the clinic: we treat what we can describe

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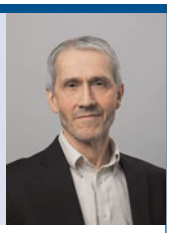

Summary

Recent research has led to important changes in the concepts and assessment of negative symptoms in schizophrenia. We review current negative symptom concepts and their clinical implications, as well as new methods of assessing these symptoms. These changes hold promise for improving our understanding and treatment of negative symptoms.

Keywords

Negative symptoms; schizophrenia; psychometrics; assessment; factor analysis.

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Recent findings have led to important changes in the concept of negative symptoms, including what should be considered a negative symptom, the relationships among these symptoms and how to measure them. These issues are often discussed in articles using advanced statistical methods, but the issues in such articles are key for clinicians and their patients, with implications for clinical evaluation and treatments.

The factor structure of negative symptoms

There is a growing consensus that there are five types or domains of negative symptoms: alogia (poverty of speech), blunted affect, avolition, asociality and anhedonia (decreased experience of pleasure).[1] New negative symptom rating scales, the Brief Negative Symptom Scale (BNSS) and the Clinical Assessment Interview for Negative Symptoms (CAINS), were developed in response to this consensus. However, the relationships among these five domains are under debate. This issue has been explored using factor analysis, a statistical method that defines groups or 'factors' of item scores that tend to correlate with each other. Initial studies using exploratory factor analysis found two factors, one comprising expressivity (alogia and blunted affect) and the second comprising the other three negative symptoms. However, confirmatory factor analysis (CFA), which permits the testing of alternative hypotheses about the factors within a scale, has most frequently found factors that reflect the five domains listed above. These five factors were found across the interview-based negative symptom rating scales, comprehensive self-report questionnaires, diverse cultures/languages (Eastern and Western), both genders, multiple phases of illness (clinical high risk, first episode, chronic) and different statistical techniques.[2] There is some covariation across these factors, but it is limited and people usually do not have significant impairment in all five factors.

This evidence, which crosses cultures, languages and scales, raises the possibility that these five factors reflect brain function, and possibly discrete functional circuits.[2] It also raises the possibility that there are five separate treatment targets.[2] That is, there may be biomedical or psychosocial treatments that are effective for one or more of the negative symptoms but not for others. In that case, a treatment study that does not improve the total score on a rating scale – the usual outcome measure for studies of negative symptoms – may be falsely negative, with an effect in one or two domains buried by the lack of response in others. On the other hand, there are network analysis studies – yet more psychometrics! – that suggest effective treatment of avolition may lead to improvement in the other negative symptoms.[3]

Transdiagnostic study

The factor analysis studies imply that it may be useful to study the five negative symptoms separately. Study of individual negative symptoms fits with an important research approach, the 'transdiagnostic' study of areas of psychopathology. To give one example, psychotic symptoms are transdiagnostic as they are found in a variety of illnesses, including schizophrenia, bipolar disorder and some forms of dementia. Pharmacological treatment of psychosis also has some efficacy across these disorders. Does psychosis also have biological underpinnings that are transdiagnostic? Negative symptoms also occur in disorders other than schizophrenia, for instance anhedonia is found in depression. Researchers are investigating whether negative symptoms share common correlates such as genetics, treatment response and functional circuits.

The current issue of the *BJPsych* has an example of a transdiagnostic study[4] of a single domain of negative symptoms, anhedonia. The authors found evidence for a transdiagnostic risk factor: people who reported childhood trauma had an increased risk of anhedonia in adulthood whether they were depressed or – a separate group – were at clinical high risk of psychosis.

The limitations of rating scales

Negative symptom rating scales have an inherent limitation that can lead to ambiguity in the interpretation of study results. Consider the example of asociality. A person may not socialise because he or she is depressed, paranoid, anxious, disorganised, etc., and so has a 'secondary' negative symptom. Alternatively, the person may simply

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have a lack of interest in social relationships that cannot be attributed to these other problems, and so has a 'primary' negative symptom. A change in asociality on a negative symptom rating scale score is therefore ambiguous: is the change due to increased interest in others or due to an improvement in one of these other problems, such as anxiety? The same ambiguity arises with all of the negative symptoms. The clinician who encounters evidence of improvement in negative symptoms, or reads about improvement in those symptoms in a treatment trial, should consider whether secondary symptoms also improved. Unfortunately, to date there is little evidence for an effective pharmacological treatment of primary negative symptoms.

Clinical rating scales have other problems as well. Their validity depends on a patient's memory of symptoms over the previous days to weeks, awareness of impairment, willingness to report symptoms and behaviours, and other factors. Moreover, all raters have their biases and difficulties in making ratings, which can decrease the reliability and validity of ratings. A method that overcomes some of the limitations inherent to symptom rating scales is digital phenotyping, which uses mobile technology such as smartphones and wearable devices to collect data during everyday life. Digital phenotyping data can be grouped into 'active' and 'passive' data collection methods.[5] Active data collection requires users to complete a task such as a survey or a video 'selfie', whereas passive approaches involve unobtrusive data collection that occurs automatically (e.g. via sensors in wearables). Several active and passive digital phenotyping measures have shown promise as measures of negative symptoms, including geolocation (GPS coordinate data that show location and location changes), accelerometry (measures of movements in three dimensions) and – using audio and video recordings – natural language processing and automated analysis of facial expressions and vocal characteristics.[5] There is preliminary evidence that the five negative symptoms can be distinguished by digital measures.

Conclusions

In the past 20 years, the concepts and assessments of negative symptoms have changed substantially: a new consensus on which features should be considered negative symptoms; ratings scales based on this consensus; recognition of the factor structure of negative symptoms, and the implications of these factors for research and possibly treatment; wider recognition of the distinction between primary and secondary negative symptoms; and the development of digital measures. As concepts and assessment tools in part determine the treatments patients receive, these changes in concepts and measurement hold promise for improving the assessment and treatment of negative symptoms.

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Data availability

Data availability is not applicable to this article as no new data were created or analysed in this study.

Author contributions

B.K. led the writing and conceptual framework of the manuscript. L.L. and G.P.S. contributed to drafting and revising the manuscript and provided conceptual guidance.

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Declaration of interest

G.P.S. and B.K. are original developers of the Brief Negative Symptom Scale (BNSS) and receive royalties and consultation fees from Medavante-ProPhase in connection with commercial use of the BNSS and other professional activities; these fees are donated to the Brain and Behavior Research Foundation. G.P.S. and B.K. are also part owners and co-founders of Quantic Innovations, which provides digital phenotyping data collection, analysis and interpretation and has contracts with Karuna and Sunovion. B.K. has received honoraria and travel support from ProPhase LLC for training pharmaceutical company raters on the BNSS, consulting fees and travel support from Genentech/Roche, Minerva Neurosciences, Lundbeck, Acadia, Karuna, Otsuka and Medavante-ProPhase, consulting fees from anonymised pharmaceutical companies and investors through Decision Resources, Inc., and Guideposts, and from Wockhardt Bio AG for consulting on a legal issue. G.P.S. has consulted for Minerva Neurosciences, Acadia, Otsuka, Sunovion, Boeringher-Ingelheim, Karuna and Lundbeck.

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