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Editorial

A new era for the negative symptoms of schizophrenia

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Summary

Negative symptoms remain one of the major unmet needs for people with schizophrenia, and the past decade has witnessed a surge in interest in negative symptoms. In this themed issue, we present new concepts of negative symptoms and recent findings on their epidemiology and pathophysiology and on therapeutic options for their management.

Keywords

Motivation; emotion; anhedonia; alogia.

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A progressive deterioration in people's will and emotional life was central to Kraepelin's concept of his newly described illness, *dementia praecox*. When Bleuler coined the term schizophrenia, the 'four As' that defined the fundamental symptoms of schizophrenia (alogia, affect blunting, autism and ambivalence) strongly resemble what we now call negative symptoms. The advent of the antipsychotic era brought about a focus on a disorder centred on positive symptoms, shunting motivation and emotional life to the outskirts of the disorder's definition. Although treatment frequently ameliorates psychosis, most people do not achieve a return to a satisfactory level of functioning owing to untreated negative and cognitive symptoms. Interest in these symptoms resurfaced in the 1970s under the 'negative symptoms' term, in part as a response to this clinical need. Fifty years later, these symptoms are still a major unmet therapeutic need in people diagnosed with schizophrenia.

The quest for defining and understanding negative symptoms resulted in the creation of new symptom scales, including the Scale for the Assessment of Negative Symptoms (SANS) and the Positive and Negative Syndrome Scale (PANSS). These were important contributions but unsatisfactory for several reasons, including the assessment of cognitive deficits and disorganisation, as well as poor coverage of motivation-related negative symptoms in the PANSS. Both scales rely on behavioural proxies for internal experiences that are at the core of motivation or experiential impairments in individuals with schizophrenia spectrum disorders. The recent second-generation scales,[1] such as the Brief Negative Symptom Scale (BNSS) and the Clinical Assessment Interview for Negative Symptoms (CAINS), were developed to cover the five consensus domains of negative symptoms: anhedonia, asociality, avolition, blunted affect and alogia. Furthermore, they assess not only the observed behaviour but also internal experience in the experiential domains.[1]

This themed issue of the *BJPsych* is intended to clarify and integrate, for researchers and clinicians, current knowledge of negative symptoms in four main areas: psychopathology, clinical course, pathophysiology and treatment.

There is growing evidence that negative symptoms is an umbrella term with at least two distinct dimensions: deficits in motivation/pleasure, i.e. an experiential dimension, and deficits in expression (alogia and blunted affect) that may have different underlying biological mechanisms. This issue contains some evidence for that idea, and for the need to study each of the five domains (anhedonia, asociality, avolition, blunted affect and alogia) independently.

Three papers explore the different factors of the negative symptoms construct, also discussed in Kirkpatrick et al's editorial.[1] Canal-Rivero et al[2] found that emotional expression, not motivation, correlated with thinning in specific frontal lobe areas in a cohort with first-episode psychosis over a 10-year follow-up. Wolpe et al[3] explored the longitudinal impact of the side-effects of antipsychotics as a source for secondary negative symptoms, finding that clozapine-induced sedation negatively affects the motivation and pleasure dimension (i.e. anhedonia, asociality and avolition) of the BNSS but not the expressive one (alogia and blunted affect). O'Brien et al[4] explored the effect of anhedonia in three groups – a group at high risk of psychosis, a group with depression and a group without known psychiatric illness. They found that an abnormal perception of current stress in those reporting early abuse was a risk factor for anhedonia, independently of the disorder, suggesting that adverse childhood events are a risk factor for negative symptoms. Taken together, these three findings indicate the need to use specific scales to evaluate negative symptoms and consider the five separate domains of negative symptoms, as outlined by Kirkpatrick et al.[1]

A reduction in motivational and emotional life is no longer considered the end state of schizophrenia. In this issue, the meta-analysis of Salazar and colleagues found a high prevalence of negative symptoms in children and adolescents during the early stages of a psychotic disorder, with 79.6% of those at risk of psychosis and 60.8% of those with early-onset psychosis exhibiting negative symptoms. It is unclear whether those negative symptoms represent the outcome of faulty developmental trajectories, are secondary to other psychopathological aspects, or result from some form of bias. In any case, these results indicate the need for early recognition of negative symptoms in psychotic disorders.

There has been relatively little progress in the pharmacological treatment of negative symptoms. Non-pharmacological treatments are widely recommended, and Cella and colleagues[5] reviewed their efficacy. Unfortunately, their review highlights the relative methodological weakness of the studies conducted to date and the modest positive effect they show for ameliorating negative symptoms.

How should the field progress?

Careful characterisation of negative symptoms will become increasingly important as more evidence emerges about differences among

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the five domains of negative symptoms with regard to risk factors and correlates. The second-generation scales should be more widely implemented in clinical and research settings. Indeed, poorly designed studies relying on inadequate scales might have yielded negative results in recent large trials. For the progress of pathophysiological studies and treatment development, the poor characterisation of negative symptom domains and the failure to distinguish primary and secondary negative symptoms have been major obstacles, as outlined in the editorial by Galderisi & Kaiser in this issue. Some alternatives to assessment scales for better characterisation and modelling of negative symptoms are in progress, but the research is in the early stages.[1]

The cognitive computational neuroscience approach holds the promise of dissecting the different components of negative symptoms from a transdiagnostic perspective using the framework of the Research Domain Criteria (RDoC) promoted by the US National Institute of Mental Health (NIMH). It has shown its value in the study of apathy in neurodegenerative conditions. There are promising results for motivation-related negative symptoms in schizophrenia, albeit much larger studies are needed for such complex phenomena in a heterogeneous disorder such as schizophrenia.

In any case, the refinement in assessment and neuroscience modelling will probably lead to a new era of clinical epidemiology, pathophysiological studies and treatment trials. We hope that the works in this themed issue will provide clues to find the much-needed new treatments in the future.

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

Author contributions

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