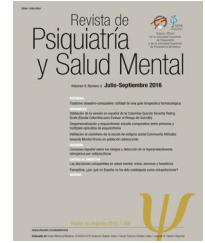




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## EDITORIAL

### Negative Symptoms: A Brief Story and Advances in Spain

### Síntomas negativos: breve historia y avances en España

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What we refer to as negative symptoms Kraepelin conceptualized as a weakening of the well-springs of avolition and placed as one of the two aspects of psychopathology defining dementia praecox.<sup>1</sup> The terminology, negative symptoms, was suggested in 1974<sup>2</sup> as a pathological diminishing of human actions/experiences and positive symptoms referred to pathological excessive human action/experience. The context at that time was schizophrenia and now may be used in a transdiagnosis context. This terminology is also consistent with the view of psychopathology along a continuum rather than a present/absent dichotomy.

Assessment and conceptualization of negative symptoms advanced over three decades leading to a turning point in understanding the concept and assessment methodology. This is reported in Schizophrenia Bulletin from a 2005 meeting<sup>3</sup> and a later update.<sup>4</sup> Two new assessment/rating tools have been put in place and address a key problem associated with earlier methods.<sup>5</sup> A key problem in the earlier methods, including the widely used PANSS, is the failure to determine whether an observation such as social withdrawal represented a negative symptom mechanism. A person with low interest and gratification from social interaction as a trait would not be distinguished from a person who withdraws

from social interactions based on a paranoid interpretation of social action.

A major difficulty relates to distinguishing primary from secondary negative symptoms. Kirkpatrick et al defined the problem and provided assessment methods to distinguish negative symptoms as part of the illness from negative symptoms from secondary sources.<sup>6</sup> Examples of the latter include low motivation caused by antipsychotic medication, reduction in the experience of pleasure caused by depression, and lack of social engagement caused by fear. This failure to distinguish primary from secondary negative symptom pathology confounds virtually all studies of negative symptoms. This is illustrated by two major reviews of treatment studies where the vast majority fail to assess or even mention the primary/secondary confound.<sup>7,8</sup>

Identifying primary negative symptoms is essential to advancing knowledge regarding this aspect of schizophrenia. There is substantial evidence supporting the validity of this distinction.<sup>9,10</sup> A focus on primary negative symptoms is essential for therapeutic discovery as current treatment efficacy has not been established and therapy for secondary negative symptoms will be based on different causal mechanisms including side-effects of positive symptom medications. It is also important to recognize that primary negative symptoms may precede psychosis as developmental psychopathology.

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An important task involves translating and establishing methodology to provide state-of-the-art assessment of negative symptoms in Spanish speaking person. Studies presented in this issue address methods and provide illustration of acquiring clinical knowledge in the context of Spanish language investigation. Martinez-Cao and colleagues<sup>11</sup> validate the Spanish addition of the Apathy Evaluation Scale-self rated version and Garcia-Alvarez and colleagues validate in Spanish people the Self-evaluation of Negative Symptoms, SNS<sup>12</sup>. Rekhi and colleagues find the Brief Negative Symptom Scale effective in determining negative symptom remission<sup>13</sup>. There is much of value in this issue regarding the understanding of negative symptom pathology in schizophrenia.

Rapidly shifting views regarding the diagnosis of schizophrenia will open important new opportunities to advance understanding and care for persons with negative symptoms. Recognizing schizophrenia as a syndrome rather than a disease entity shifts focus to heterogeneity and the several specific psychopathologies associated with each case. Positive psychosis symptomatology is found in multiple disorders and transdiagnostic approaches are being developed. This will result in the search for negative symptom pathology in disorders other than schizophrenia. An interesting question will be whether anhedonia in major depression has the same mechanism as anhedonia in non-depressed persons with a schizophrenia diagnosis. If the field moves to a nosology with "primary psychosis" incorporating schizophrenia and other diagnoses where psychosis is prominent, there will be increased opportunity to determine the boundaries of negative symptom pathology. As a field we may return to the designations of state versus trait psychopathology. It seems likely that primary negative symptoms are trait pathology preceding full psychosis while secondary negative symptoms will be associated with the duration of the cause (e.g., medication side effects that reduce energy and diminish interpersonal engagement). Viewing primary negative symptoms in a developmental framework will increase attention to this aspect of psychopathology in conditions not involving psychosis.

One last comment. What is the relationship of psychopathology mechanisms or therapeutic responsiveness between identified components of the negative symptom construct? What is the relationship between apathy, anhedonia, asociality, avolition, alogia, and affective flattening?

Much has been learned, but advance in therapeutics is minimal. Kraepelin's avolitional pathology was an excellent start. Much more is now needed.

## References

1. Kraepelin E. *Dementia Praecox and Paraphrenia*. Chicago: Chicago Medical Book Co.; 1919, ?
2. Strauss JS, Carpenter WT Jr, Bartko JJ. The diagnosis and understanding of schizophrenia Part III. Speculations on the processes that underlie schizophrenic symptoms and signs. *Schizophr Bull*. 1974;Winter:61–9.
3. Kirkpatrick B, Fenton WS, Carpenter WT Jr, Marder SR. The NIMH-MATRICES Consensus Statement on Negative Symptoms. *Schizophrenia Bulletin*. 2006;32:214–9.
4. Marder SR. Lessons from MATRICS. *Schizophrenia Bulletin*. 2011;37:233–4.
5. Carpenter WT, Blanchard JJ, Kirkpatrick B. New standards for negative symptom assessment. *Schizophr Bull*. 2016;42:1–3.
6. Kirkpatrick B, Buchanan RW, McKenney PD, Alphas LD, Carpenter WT. The Schedule for the Deficit Syndrome: An instrument for research in schizophrenia. *Psychiatry Research*. 1989;30:119–23.
7. Fusar-Poli P, Papanastasiou E, Stahl D, Rocchetti M, Carpenter W, Shergill S, McGuire P. Treatments of Negative Symptoms in Schizophrenia: Meta-Analysis of 168 Randomized Placebo-Controlled Trials. *Schizophr Bull*. 2015;41:892–9.
8. Darba J, Minoves A, Rojo E, Jimenez F, Rejas J. Efficacy of second-generation-antipsychotics in the treatment of negative symptoms of schizophrenia: a meta-analysis of randomized clinical trials. *Rev Psiquiatr Salud Ment*. 2011;4:126–43.
9. Kirkpatrick B, Buchanan RW, Ross DE, Carpenter WT. A separate disease within the syndrome of schizophrenia. *Archives of General Psychiatry*. 2001;58:165–71.
10. Kirkpatrick B, Mucci A, Galderisi S. Primary Enduring Negative Symptoms: An Update on Research. *Schizophr Bull*. 2017;43:730–6.
11. Rekhi G, Ang MS, Chan YH, et al. Defining negative symptoms remission in schizophrenia using the Brief Negative Symptom Scale. *Rev Psiquiatr Salud Ment (Barc.)*. 2022;15:3–13.
12. Garcia-Álvarez L, et al. Validation of a European Spanish adaptation of the Apathy Evaluation Scale-self-rated version (AES-S) in patients with schizophrenia. *Rev Psiquiatr Salud Ment (Barc.)*. 2022;15:14–21.
13. Martinez-Cao C, et al. Validation of a European Spanish adaptation of the Apathy Evaluation Scale-self-rated version (AES-S) in patients with schizophrenia. *Rev Psiquiatr Salud Ment (Barc.)*. 2022;15:22–8.