



## Original article

## Amendment of traditional assessment measures for the negative symptoms of schizophrenia

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## ABSTRACT

Schizophrenia research based on traditional assessment measures for negative symptoms appears to be, to some extent, unreliable. The limitations of the Positive and Negative Syndrome Scale (PANSS) and the Scale for the Assessment of Negative Symptoms (SANS) have been extensively acknowledged and should be taken into account. The aim of this study is to show how the PANSS and the SANS conflate negative symptoms and cognition and to offer alternatives for the limitations found.

**Methods:** A sample of 117 participants with schizophrenia from two independent studies was retrospectively investigated. Linear regression models were computed to explore the effect of negative symptoms and illness duration as predictors of cognitive performance.

**Results:** For the PANSS, the item “abstract thinking” accounted for the association between negative symptoms and cognition. For the SANS, the “attention” subscale predicted the performance in verbal memory, but illness duration emerged as a stronger predictor than negative symptoms for outcomes of processing speed, verbal and working memory.

**Conclusion:** Utilizing alternative models to the traditional PANSS and SANS formats, and accounting for illness duration, provide more precise evidence on the relationship between negative symptoms and cognition. Since these measures are still extensively utilized, we recommend adopting more rigorous approaches to avoid misleading results.

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## 1. Introduction

“My experience is what I agree to attend to. Only those items which I notice shape my mind.” – William James

During the last decade, there has been increasing interest in negative symptoms (NS) of schizophrenia together with a re-evaluation of the scales measuring them. Novel instruments have been developed although they have yet to be generally adopted, whilst studies based on traditional scales appear to be to some extent unreliable.

The characteristics of the Positive and Negative Syndrome Scale (PANSS) [1] and the Scale for the Assessment of Negative Symptoms (SANS) [2] have been a matter of discussion over the

last 20 years. For example, further PANSS-subscscales including four, five, or six factors have been proposed with several studies underlining that five-factor models show an adequate reliability when tested in different subgroups of individuals with schizophrenia, confirming the suitability of this approach [3,4]. On the other hand, cross-sectional studies of the SANS identify three, four and five different symptom factors; and longitudinal research has replicated three factors [5]. In particular, the NS subscale within the traditional PANSS consists of seven items tapping blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity, and stereotyped thinking. And the original SANS consists of 19 items representing five domains: affective flattening, avolition-apathy, anhedonia-asociality, and attention.

A number of studies have adapted these scales to provide the two dimensions of NS, Diminished Expression and Amotivation/Avolition. For the PANSS, Liemburg et al. [6] studied the two-factor structure for NS in early psychosis participants. These factors were named “core NS”, related to the expressive deficits, and “social emotive withdrawal”, described as social amotivation. Similarly,

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Fervaha et al. [7] extended these findings to patients with chronic schizophrenia, calling the two factors “diminished expression” and “amotivation”; and comparable two-factor results were recently published by Lim and colleagues [8]. For the SANS, similar factor models accounting for diminished expression and anhedonia-asociality have emerged. For example Sayers et al. [9] confirmed a general three factor approach for the SANS including “diminished expression”, “inattention-alogia” and “social amotivation”, while Kelley et al. studied primary and secondary negative symptoms of schizophrenia employing the two factor approach of “affective flattening” and “diminished amotivation” [10].

Factor analysis studies have indicated that cognitive items in the PANSS and SANS do not cohere well with the other NS ratings [11], and cognitive deficit appears to be conceptually distinct from NS [e.g. [12]. Possible confounding instances include items of “difficulty of abstract thinking” and “stereotyped thinking” in the PANSS, and the “attention” subscale in the SANS (See Blanchard and Cohen for a review [13]). As an illustration, Bell et al. [14] demonstrated that performance on neuropsychological tests was associated with the cognitive component of the PANSS (“abstract thinking” and “stereotyped thinking”) but not with other NS items within the PANSS. For the SANS, Vadhan et al. [15] found a correlation between the “attention” subscale and neuropsychological tasks which discriminated “attention” from the other SANS subscales. Similarly, Liemburg et al. [6] and Lim et al. [8] reported an association between the “diminished expression” PANSS factor and cognition.

Both cognitive impairment and NS are formally considered as core features of schizophrenia contributing to poor functional and community outcomes (e.g. [16,17]). The present study was motivated by the ongoing utilization of traditional approaches to the PANSS and the SANS albeit the limitations stated above. Our aim is to show possible misleading associations between negative symptoms and cognition when using the original PANSS and SANS factors, and to offer alternatives to overcome them while still utilizing the PANSS and the SANS.

Specifically, our aim is to illustrate how the traditional PANSS and SANS may perform differently on the associations between NS and cognition depending on the factor approaches utilized. Findings from a previous study by our group suggested that NS could hamper the expression of cognition on behavioural tasks and functional outcomes [18]. These findings were of interest since common theoretical backgrounds generally assume that cognition would have an effect on NS (e.g., [19]) but not vice versa.

Finally, illness duration will be taken into account as a confounder variable since the study included chronic and institutionalized participants and this might perform a detrimental effect on both cognition and NS. Our hypothesis is that longer illness duration may have an impact on the association between NS and cognitive performance, particularly in hospitalized participants. A decline in cognition has been also reported after ten years of illness duration [20] and in geriatric patients with schizophrenia [21]. Likewise, chronicity and hypostimulating environments can cause secondary negative symptoms such as decreased spontaneity, reduced curiosity, reduced drive to interact and blunted affect [22,23].

## 2. Method

### 2.1. Participants

Two samples of participants with schizophrenia were retrospectively studied. Both groups belonged to the same mental health services from Barcelona metropolitan area and were recruited in independent investigations. *Group 1* involved outpatients recruited with the purpose of studying the efficacy of

Cognitive Remediation group treatment [24]. *Group 2* included inpatients recruited to study cognitive impairment in schizophrenia [25]. Both studies were approved by the Parc Sanitari Sant Joan de Déu Ethics Committee.

*Group 1* - Sixty-two participants with a diagnosis of schizophrenia or schizoaffective disorder following DSM-IV criteria were recruited from Parc Sanitari Sant Joan de Déu community services [26]. To verify the stability of the diagnosis we checked the medical histories to corroborate that the required DSM-IV criteria were appropriately described. Two cases were unconfirmed and the Structured Clinical Interview for DSM-IV (SCID; [27]) was utilized to verify their diagnoses. The participants included were between 18 and 65 years of age, with disease duration of over two years. Patients were excluded if they were suffering acute illness exacerbation that required hospitalization, had intellectual disability or neurological disorder, had switched antipsychotic drugs the month before the assessment, and/or had a diagnosis of alcohol or drug dependence within 6 months prior to inclusion. Initially, 70 participants referred by their community teams or rehabilitation services were assessed for eligibility. Of these, two were excluded for not meeting inclusion criteria (change of diagnosis to bipolar disorder and presence of learning disability), four refused consent, and two were not interested.

*Group 2* - Fifty-five participants with schizophrenia were recruited from Parc Sanitari Sant Joan de Déu inpatient services. The diagnosis was made by consensus on the basis of DSM-IV criteria by two experienced psychiatrists who used patient histories and chart reviews. Inclusion criteria were age between 18 and 65, fluency in Spanish, and the capacity to provide informed consent. Exclusion criteria were current or recent alcohol or drug abuse (DSM-IV criteria), organic mental disease, intellectual disability, history of brain injury, dementia, and current severe physical disease. Participants were hospitalized and had been receiving stabilized doses of antipsychotic medication over two weeks at the time of testing. Clinical records were reviewed thoroughly by the psychiatrist recruiting the participants (J Cuevas-Esteban) and only those inpatients meeting all inclusion criteria were asked to participate. The rates of consent were about 75% of those eligible to take part.

For both groups the antipsychotic medication included first-generation antipsychotics (clozapine, fluphenazine, haloperidol, levomepromazine, zuclopenthixol) as well as second-generation (amisulpride, aripiprazole, clozapine, olanzapine, quetiapine, risperidone). Predominantly within *Group 2*, participants were taking a combination of two or more antipsychotic drugs and/or were administered benzodiazepines (clonazepam, diazepam, flunitrazepam, lorazepam, lorazepam, lorazepam) and/or antidepressant (duloxetine, fluoxetine, paroxetine, trazodone) medication.

### 2.2. Measures

*Group 1* - The cognitive assessment included the following domains: *Executive Function* using the Behavioural Assessment of the Dysexecutive Syndrome (BADS) [28], which consists of six tests involving cognitive flexibility, inhibition of impulsive responses, planning and organization, working memory, and time-estimation capacity. Attention, processing speed, and cognitive flexibility were measured with The Trail Making Test forms A and B (TMT A; TMT B) [29]. Verbal memory, both immediate and delayed, was assessed with the Logical Memory I and II subscales respectively, from the Wechsler Memory Scale (WMS-III) [30].

Negative symptoms were measured with the Spanish validation of the PANSS [31]. The negative PANSS factors employed in this study were the original 3-factor approach by Kay et al. [1] including 7 items: blunted affect, emotional withdrawal, poor rapport, passive-apatetic social withdrawal, lack of spontaneity, difficulty

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