Disclosure

The authors report no conflicts of interest.

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Negative dimension stability across clinical stages and sociodemographic characteristics in schizophrenia

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Negative symptoms are a challenge to schizophrenia treatment and an obstacle to functional recovery. Although a deeper knowledge of the disorder's neurobiology is needed to change this, reliable assessment of these symptoms remains a shortcoming in the field.[1] The most accepted structures of the negative symptoms include two to five dimensions.[2] However, there is limited data on whether such structures are stable in different groups of patients with schizophrenia. Therefore, we aimed to verify the relationship between clinical variables and the fit of a two-factor model of the Positive and Negative Syndrome Scale's (PANSS) negative dimension, considering different clinical stages, sex, age, and current antipsychotic use. As secondary objectives, we analyzed the effect of a multilevel structure on the psychometric quality of the two-factor dimensional structure in a Brazilian sample.

We recruited 692 individuals from four different Brazilian centers diagnosed with schizophrenia according to DSM-IV,[3] of either sex, aged between 15 and 65 years, and without severe intellectual disability. The Universidade Federal de São Paulo ethics committee approved the study protocol (project 1.052.059).

We performed confirmatory factor analysis to test a correlated two-factor model in which items N1, N3, N6 and G7 expressed the ''expressive deficits'' factor and N2, N4 and G16 expressed the ''social amotivation'' factor. The items used to express the negative dimension were based on Higuchi et al.,[4] while the model was based on Fervaha et al.,[5] Khan et al.,[6] and Kagan et al.[7] We used multilevel modeling to determine the impact of pooled data in psychometric analyses. Finally, we tested the model's invariance using the multiple causes and multiple indicators model[8] according to sex, age, current antipsychotic type (first- vs. second-generation), and clinical stage (treatment-resistant vs. non-resistant).

The majority of the sample was men (64.3%), and the mean age was 34.9 years (SD, 10.31). Other demographic and clinical characteristics of the sample are provided in Table S1, available as online-only supplementary material. In traditional confirmatory factor analysis, the two-factor model of the negative dimension showed a poor fit (Table S2). However, it achieved good fit when a multilevel structure was included. Likewise, subsequent analysis with the multiple causes and multiple indicators method adjusted by multilevel structure revealed a good fit (Figure 1). No covariates directly affected item responses, and all showed model invariance: clinical staging, age, sex, and current antipsychotic type (first- vs. second-generation). Sex and age significantly influenced the means of both factors – male sex and younger age showed the highest means among the factors. Treatment-resistant patients had higher means only in the ''expressive deficits'' factor.

The results did not support a distinct underlying structure for negative symptoms in patients with treatment-resistant schizophrenia. The exclusivity of positive symptoms in treatment-resistant criteria may also explain the invariance of negative symptoms among treatment-resistant and non-resistant patients.

Our results suggest that a negative two-factor dimension of the Positive and Negative Syndrome Scale is stable across different groups of patients regardless of sex, age, or current antipsychotic type. The results also

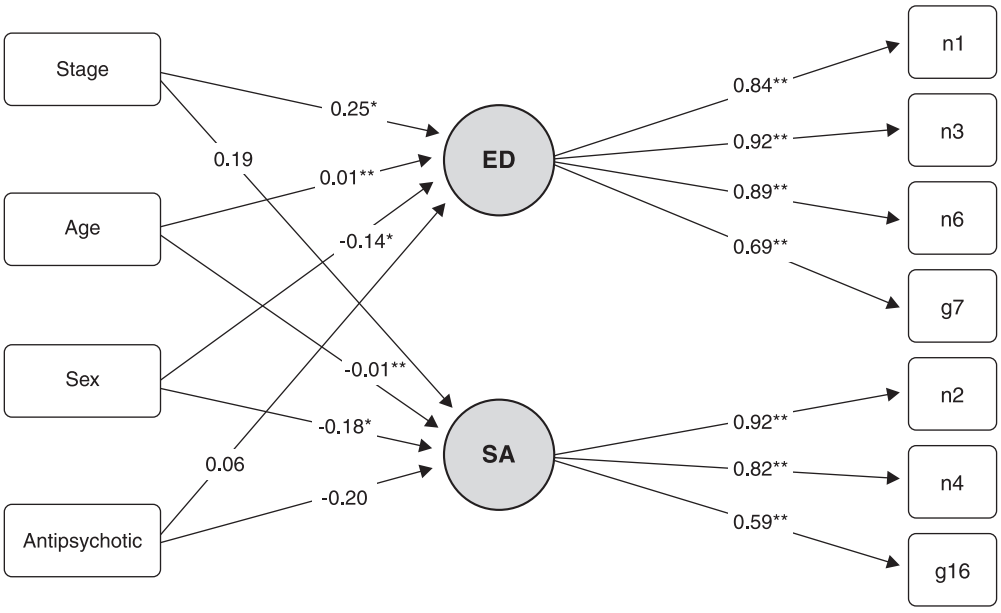

Figure 1 Multiple Causes and Multiple Indicators modeling to test the impact of demographics and clinical covariates on negative symptom factors in the Positive and Negative Syndrome Scale (n=606). Standardized estimates are showed. Values of categorical variables are interpreted as Cohen's D effect sizes. ED = expressive deficits; SA = social amotivation; n1: Blunted affect; n2: Emotional withdrawal; n3: Poor rapport; n4: Passive/apathetic social withdrawal; n6: Lack of spontaneity and flow of conversation; g7: Motor retardation; g16: Active social avoidance. * $p < 0.05$, ** $p < 0.001$.

support the need for a multilevel approach when performing confirmatory factor analysis of the Positive and Negative Syndrome Scale using multicenter samples.[9] Finally, we encourage the use of instruments specifically designed to assess negative symptoms in future investigations on negative dimension invariance, such as the Brief Negative Symptom Scale and the Clinical Assessment Interview for Negative Symptoms.

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Cervical cancer screening and psychosis: a longitudinal retrospective study comparing women with schizophrenia spectrum disorders and the general population

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Cervical cancer (CC) is more frequent and occurs at earlier ages among patients with psychosis compared to the general population.[1] CC screening as a preventive strategy is highly effective in reducing its incidence and mortality, but adherence to such screening among women with psychosis is significantly lower than in the general population.[2] Non-adherence to screening protocols may be related to an increased risk of presenting with CC.[3] We aimed to explore the presence of differences in CC screening rates between women with psychosis and a control group.

We studied 286 women with psychosis and 86 women without mental disorders, all over 25 years old, from the First Episode Psychosis clinical Program cohort (PAFIP; Cantabria, Spain).[4] The study was approved by the Clinical Research Ethics Committee of Cantabria. Cervical screening and pathology data were retrieved retrospectively from medical records in December 2021. Protocol adherence (yes vs. no) was defined according to previous literature[2] and to international protocols, whereby women should undergo their first cytology at age 25 and every 3 years thereafter. We used analysis of variance (ANOVA) to compare continuous variables and the chi-square test for categorical variables. All statistical tests were two-tailed, and significance was determined at the 0.05 level.

A significantly greater proportion of women in the control group had undergone at least one cytology test in their lifetime compared to women in the psychosis group (81.6% vs. 67.1%; $\chi^2 = 5.986$, $p = 0.009$). Women with psychosis also entered the CC screening protocol significantly later than healthy controls (33.4 vs. 28.7 years; $F = 12.433$, $p = 0.001$). Fewer women with psychosis (34.3%) met criteria for CC protocol adherence compared to those in the control group (55.3%; $\chi^2 = 11.162$, $p = 0.001$). Moreover, the time elapsed since last cytology was significantly longer among psychosis patients than in the control group (4.7 vs. 3.3 years; $F = 4.808$, $p = 0.029$). We found no significant differences between groups (14 women with psychosis vs. 6 controls) in the proportion of altered cytology tests, nor in the proportion of biopsies with pathological results (3.5% of women with psychosis vs. 1.3% of controls; Yates' $\chi^2 = 0.537$; $p = 0.463$): one woman with cervical intraepithelial neoplasia (CIN)-III in the control group versus 10 cases of cervical pathology among women with psychosis (one of cervical cancer, seven of CIN-III, and two of CIN-II). Comparisons between women in the psychosis group with (n=98, 34.3%) or without (n=188, 65.7%) CC protocol adherence showed relevant differences (Table 1).

Over one-third of women diagnosed with psychosis in our cohort had never undergone a CC screening test; those who had ever attended screening did so at an older age than the general population, and 8 years after the optimal age defined in international protocols.[5] Furthermore, women with psychosis presented a significantly lower rate of good screening protocol adherence, which is consistent with previous research.[2] Women in the psychosis group were three times more likely to present with cervical pathology and 10 times more likely to exhibit high-grade cervical pathology than control women. These differences in abnormal findings, although not statistically significant due to the small number of cases, may be the result of patients not attending CC screening.

These results should be taken into account when treating women with psychosis, who should be encouraged to enter a CC screening program if they are sexually active.