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Associations between the subdomains of negative symptoms in the general population and genome-wide polygenic scores for major depressive disorder and schizophrenia

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ABSTRACT: Negative symptoms predict adverse outcomes within psychotic disorders, in individuals at high-risk for psychosis, and in young people in the community. Accumulating evidence suggests a 5-factor latent structure of these symptoms, but little is known about their underlying structure outside of clinical and high-risk samples. It is also unknown which aspects of negative symptoms show the strongest genetic links with clinically diagnosed depression and schizophrenia. We used confirmatory factor analysis to test the structure of parent-reported negative symptoms at 3 ages in adolescence and emerging adulthood (mean ages 16.32, SD 0.68; 17.06, SD 0.88; 22.30, SD 0.93) in the Twins Early Development Study ($N = 1468-5177$). We assessed associations between the negative symptom subdomains and genome-wide polygenic scores (GPS) for major depressive disorder (MDD) and schizophrenia. A 5-factor model of flat affect, avolition, anhedonia and asociality provided the best fit at each age and was invariant over time. Associations were observed between MDD GPS with avolition, flat affect, anhedonia and asociality, and between schizophrenia GPS with avolition and flat affect. We showed that a 5-factor structure of negative symptoms, previously identified in clinical samples, is present from ages 16 to 22 years in the community. Avolition was most consistently associated with known common genetic architecture underlying MDD and schizophrenia, and avolition was least associated. These findings highlight the value of dissecting negative symptoms into psychometrically derived subdomains and may offer insights into early manifestation of genetic risk for MDD and schizophrenia.

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