Associations between clinical phenotypes and polygenic risk of anorexia nervosa and suicidality

13. Vulnerable groups

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Abstract text

Anorexia nervosa (AN) is a severe psychiatric disorder with high premature mortality rates, frequently due to suicide. Understanding the genetic underpinnings of AN and its association with suicidality is crucial for improving clinical outcomes. This study investigated the phenotypic overlap between AN and suicidality, associations between polygenic risk scores (PRS) for these traits, and the impact of genetic factors on clinical profiles of eating disorders (EDs) in individuals with AN.

A case-control cohort of 5,468 participants (3,189 AN cases, 2,279 controls) from the Swedish site of the Anorexia Nervosa Genetics Initiative (ANGI-SE) was analyzed. Participants, born between 1977 and 2000, were followed through December 31, 2018. AN was identified via the ED100K-v1 questionnaire and/or Swedish national registers; controls had no lifetime AN diagnosis. PRS for AN, suicide attempts (SA), and suicidal thoughts and behaviors (SITB) were assessed alongside eight suicide-related outcomes and 18 ED clinical indicators, including illness severity, treatment, and persistence.

Our results revealed higher SA prevalence in AN cases (13%) versus controls (2.5%). Among AN cases, those with SA showed distinct ED characteristics, including earlier onset, lower illness-related BMI, and more severe clinical scores. AN PRS was significantly associated with SA risk (OR [95%CI]: 1.13 [1.03, 1.24]) only in the full cohort. PRSs for SA and SITB were consistently associated with suicidality-related traits in full- (e.g., SA PRS for SA 1.37 [1.21, 1.55]) and stratified samples. Moreover, suicidality PRS was significantly associated with earlier ED onset, higher scores on eating pathology questionnaires, and lower scores on general functioning.

These findings underscore the shared genetic basis of AN and suicidality and highlight the potential of PRS in sharpening clinical evaluations of suicidality among individuals with AN. Further development of genetic risk assessments could inform targeted prevention and intervention, ultimately improving outcomes for those most at risk.