Investigating the genetics of sex difference in Medically Serious Suicide Attempt

5. Genetic, epigenetic and neurobiological factors

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Abstract text

Background: Suicide is a major public health issue, causing ~700,000 deaths annually, with many more attempting suicide. Suicidal behaviors, influenced by genetics and environmental factors, differ between males and females, but reasons remain unclear. This study examines whether genetics explain sex differences in medically serious suicide attempts (MSSA).

Methods: This population-based cohort study used Swedish national register data from 3.7M individuals (3.1% with MSSA). MSSA were identified in patient and death registers using ICD codes for intentional self-harm, any self-harm with lethal methods or requiring hospitalisation, or any self-harm resulting in death. We investigated sex-specific familial aggregation and coaggregation of MSSA using Generalised Estimating Equation, and estimated pedigree heritability and genetic correlations with 11 psychiatric disorders using Structural Equation Modelling.

Findings: MSSA occurred in 1/10 families, showing familial aggregation (OR=1.6–3.4), moderate heritability (41.9%), and small shared environmental influence (3.6%). Relatives of individuals with MSSA had increased risks for other psychiatric disorders (OR=1.2–2.9), and MSSA showed moderate-to-high genetic correlations with these disorders (r_g=0.4–0.9).

Familial risks were higher in female pairs (mother-daughter, female siblings) than male pairs (father-son, male siblings), especially for parent-offspring. Same-sex pairs had greater risks than cross-sex pairs.

Heritability was slightly higher in females (51.4%, CI=40.1-58.6%) than in males (45.1%, CI=32.3-52.5%). MSSA risks associated with having relatives with substance use, PTSD, and depression were higher for mother-offspring than father-offspring pairs. No sex differences were found in genetic correlations.

Conclusion: We observed sex differences in MSSA familial aggregation and coaggregation, but genetic component, as measured by heritability, did not differ significantly by sexes. These findings suggest that despite a substantial genetic component in MSSA, genetics do not fully explain the observed sex differences. These findings highlight the importance of exploring non-genetic factors, such as environmental and psychosocial influences, to better understand the observed sex differences in MSSA.