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P3-549: SEX DIFFERENCES IN DEMENTIA RISK: THE EFFECTS OF PRENATAL TESTOSTERONE EXPOSURE, APOE4, AND THEIR INTERACTION

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Background

Evidence has been reported for higher incidence rates of dementia in women than men, with hormones as one possible contributor. The current study examined whether differential prenatal exposure to testosterone is related to sex differences in dementia risk by comparing dementia rates in same- and opposite-sex dizygotic twin pairs. The twin testosterone transfer hypothesis suggests that, compared to the intrauterine presence of a female co-twin, the presence of a male co-twin exposes the other twin to higher levels of testosterone, which may lower dementia risk. Further, because it has been suggested that APOE4 disproportionally affects women's risk of dementia, we examined whether the interaction between APOE4 and twin type (same- vs. opposite-sex dizygotic twin pairs) is associated with differences in dementia rates and age of onset.

Methods

The sample comprised 15,098 same-sex female, 7,323 opposite-sex female, 12,627 same-sex male, and 6,682 opposite-sex male dizygotic twins from the Swedish Twin Registry. Survival analyses and Cox proportional hazards modeling were conducted separately for female and male pairs.

Results

Female twins from opposite-sex pairs showed significantly higher survival rates free from dementia than those from same-sex pairs beginning at age 88 (HR = 0.60 [0.363, 0.997]), while male twins from opposite-sex pairs displayed significantly lower survival rates than their same-sex counterparts starting at age 75 (HR = 1.18 [1.03, 1.36]). In the subsample of twins with measured APOE4 alleles, female twins from opposite-sex pairs were less likely to develop dementia than those from same-sex pairs while no difference was detected in male twins, starting at age 60. APOE4 genotype also displayed the expected significant effects on incidence dementia rates in both female and male twins, however, the interaction effects of twin type and APOE4

were not statistically significant (HR = 1.03 [0.78, 1.35] for female, HR = 0.84 [0.61, 1.14] for male).

Conclusions

Influences of prenatal testosterone exposure may protect against dementia risk in female twins. Additionally, effects of APOE4 on dementia risk extended to male and female twins equally.
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