Applying a co-twin control design to clarifying the relationship between education and dementia

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Background

Low educational attainment is recognized as a modifiable risk factor for Alzheimer's disease and related dementias. Yet, mechanisms for the association remain unresolved.

Study Setup

We apply a between-within twin design to 8 twin studies in the IGEMS (Interplay of Genes and Environment in Multiple Studies) consortium, from Sweden, Denmark, Australia, and the US. We compare likelihood of dementia within monozygotic (MZ) and dizygotic (DZ) twin pairs who differ in educational attainment. We separately examined age- and sex-matched non-related pairs. If MZ pairs discordant for education also differ in likelihood for dementia, its suggests a causal role for education in protecting against dementia. If MZ twins discordant for education show no difference in likelihood of dementia, this suggests that the education-dementia association reflects genetic confounding. If both MZ and DZ pairs show a weaker association between education and dementia than non-related pairs, it suggests that the education-dementia association is driven by environmental influences shared by siblings.

Results

Higher educational attainment is associated with lower risk of dementia in non-related matched pairs and in between-family effects in twin models. Within-family differences were observed in DZ but not MZ twins, implying a genetic confound effect. Attenuation of differences for DZ twins compared to non-related pairs further suggested familial confounding attributable to non-genetic sources.

Discussion

In these analyses, the effect of educational attainment on dementia risk is largely explained by genetic influences in common to educational attainment and dementia risk but also by environmental influences shared between members of a family.

Learning Outcomes

1. recognize possible mechanisms and confounders in explaining the association between attained education and Alzheimer's disease and related dementias
2. appreciate how a twin design permits distinguishing within family versus between family sources of individual differences