

## **Common genetic and shared environmental confounds in the association between life events and dementia**

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Negative life events correlate with dementia risk. Life events index stress but also encompass other modifiable risk factors related to social engagement, socioeconomic conditions, and physical health considered to raise dementia risk. It is unclear whether common genetic and shared environmental confounds account for the correlation between negative life events and dementia risk. We investigated whether there was evidence for an effect of life events on dementia after adjusting for these confounds in the Swedish Adoption/Twin Study of Aging (SATSA).

We analyzed 885 same-sex twin families (C 50 years) from the first three waves of SATSA using six life event domains constructed from exploratory and confirmatory factor analysis of variables measuring ever-occurrence of life events (multidomain loss, negative filial events, self-illness, family strife, negative spousal events, positive life events). Dementia onset occurred after wave 3 (15.06% diagnosed). The total phenotypic effect of life events on dementia and biometric regression models of MZ/DZ twins for life events and dementia were then examined.  $r_A$ ,  $r_C$ ,  $r_E$  were estimated from the best-fitting models.

The phenotypic effect of life events on dementia could only be detected for two life events, multidomain loss and negative spousal events. Social selection factors likely play a role in the association between these life events and dementia (multidomain loss— $r_{CE}$ ; negative spousal events— $r_{GE}$ ). No significant within-family effect of these life events on dementia were found, which suggests limited evidence of a quasi-causal effect of life events on dementia.