

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

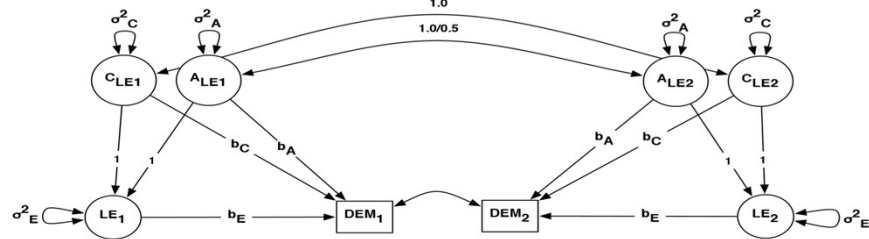


## Research Questions

- Is there an effect of life events on dementia after adjusting for genetic and shared environmental correlations?
- To what extent do common genetic and shared environmental confounds account for the association between life events and dementia?

## Figure and Tables

Fig. 1. Life event and dementia biometric regression model



## Background

- Negative life events correlate with dementia risk.
- Life event measures index stress but also encompass other factors:
  - Social engagement, socioeconomic conditions, and physical health.
- Life events consist of factors considered to raise dementia risk.
- It is unclear whether genetic and shared environmental effects account for the correlation between negative life events and dementia risk.

Table 2. Model-fitting results

Model Description	Model Comparison	Chi-square	df	$\Delta$ Chi-square	$\Delta$ df	$p$	RMSEA	TLI	SRMR
<b>LE 1 - General Loss</b>									
Model 1 - Baseline (ACE)	-	119.694	94	-	-	-	0.025	0.981	0.081
Model 2 - A=C	2 vs. 1	116.442	96	0.737	2	0.692	0.022	0.985	0.082
Model 3 - AE model	3 vs. 1	120.004	95	0.821	1	0.365	0.024	0.981	0.082
Model 4 - CE model	4 vs. 1	118.279	95	0.01	1	0.920	0.024	0.983	0.081
<b>LE 5 - Negative Spousal Events</b>									
Model 1 - Baseline (ACE)	-	152.779	138	-	-	-	0.016	0.990	0.112
Model 2 - AE model	2 vs. 1	148.329	140	0.167	2	0.919	0.012	0.994	0.112

## Methods

- **Participants**
  - 885 families of same-sex MZ/DZ twins  $\geq 50$  years (range: 50.1 – 92.9 years) from the Swedish Adoption/Twin Study of Aging (SATSA) measured between 1 – 3 occasions from 1984 to 1990<sup>1</sup>.
  - 15.06% of the sample received a dementia diagnosis  $\geq 1990$ .
- **Measures**
  - **Life events**
    - A 25-item negative and positive life event scale assessing whether life events ever occurred up to 1990<sup>2,3</sup>.
    - Factor analysis determined that items encompass 6 domains:
      - General loss; negative life events of children; illness of self; family strife; negative life events of spouse; and positive life events.
  - **Dementia diagnosis**
    - Clinical and registry sources of diagnosis<sup>4,5</sup>:
      - *Clinical* – Cognitive screening administered (cognitive battery, including MMSE and/or TELE screening).
      - A diagnostic consensus board assigned a consensus clinical diagnosis (DSM-III-R and DSM-IV criteria for dementia and NINCDS-ADRDA criteria for AD).
    - *Registry* – All who did not receive a cognitive screening or lost to follow-up were linked to the Swedish National Patient Register (NPR) and Cause of Death Register (CDR) containing International Classification of Disease (ICD) dementia codes.
  - Twins who were diagnosed with dementia < 1990 were excluded from this study.
  - *Controls* – Those who did not screen positive through any of these means were assumed to be non-demented and due for follow-up in three years.
- **Data Analysis**
  - Preliminary analyses (not shown):
    - Exploratory Factor Analysis of 25 life event items
  - Total phenotypic effect of life events on dementia (Table 1)
  - Biometric regression models of MZ/DZ twins for life events and dementia using Mplus 8.2 (Figure 1)
  - Model-fitting results for significant effects of life events (general loss and negative spousal events) on dementia (Table 2)
    - Model sequence:
      - Baseline (unrestricted)
      - A=C
      - AE
      - CE
  - Estimated  $r_A, r_C, r_E$  from best-fitting models (Table 3)

Table 3. Correlations

Model	$r_A$	$r_C$	$r_E$
LE 1 $\rightarrow$ Dem CE Model	-	0.20 (0.13)	0.004 (0.075)
LE 5 $\rightarrow$ Dem AE Model	0.20 (0.21)	-	-0.02 (0.11)

## Conclusions

- Independent ACE effects underlying life events unable to account for significant phenotypic effect of life events on dementia.
- Social selection factors most likely explain the association between life events and dementia.
- Limited evidence of a quasi-causal effect of life events on dementia.
- $r_{CE}$  may explain the association between general loss and dementia.
- $r_{GE}$  may explain the association between negative spousal events and dementia.
- Low power likely limiting factor for inferring etiological mechanisms.

## Results

- The phenotypic effect of life events on dementia could only be detected for two life events, general loss and negative spousal events.
- Social selection factors likely play a role in the association between these life events and dementia.
- No significant within-family (E) effect of life events on dementia:
  - LE 1:  $\beta_E = 0.006, p = 0.955$
  - LE 5:  $\beta_E = -0.027, p = 0.855$

Table 1. Phenotypic effect of life events on dementia

Phenotype	Estimate	SE	P-value
LE1	<b>0.143</b>	<b>0.049</b>	<b>0.003</b>
LE2	0.029	0.112	0.793
LE3	-0.049	0.075	0.511
LE4	-0.016	0.062	0.797
LE5	<b>0.098</b>	<b>0.049</b>	<b>0.045</b>
LE6	0.094	0.089	0.286

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## References

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