Heritability of subjective cognitive decline in older Australian twins

Vibeke Catts, Anbupalam Thalamuthu, Teresa Lee, John Crawford, Perminder Sachdev

Older Australian Twins Study (OATS), Centre for Healthy Brain Ageing (CHeBA), UNSW Sydney, Australia

Background:

- Subjective cognitive decline (SCD) has been promoted as a preclinical stage of dementia (Figure 1), being pre-mild cognitive impairment (MCI).
- Heritability for objective cognitive performance (current and trajectory), MCI, and the diagnosis of dementia/Alzheimer's disease has been extensively researched, with evidence for mainly moderate heritability.
- Heritability of SCD is less studied, but one study of Swedish twins found little or no heritability for SCD[1].
- The absence of heritability for SCD may be attributable to lack of sensitivity of instruments used to determine SCD, SCD being non-specific to MCI, or alternatively might suggest there is no biological underpinning of SCD. The latter challenges the assumption that SCD is an earlier, pre-MCI stage of dementia.

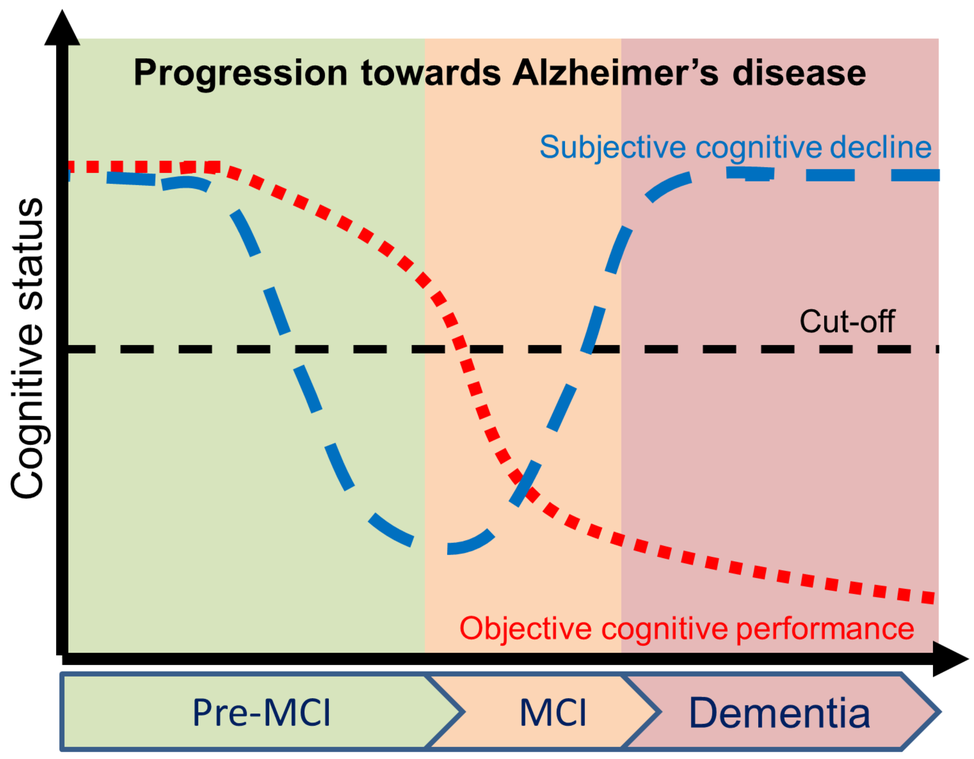

Figure 1: Theoretical temporal dynamic of subjective cognitive decline (SCD: dashed blue line) and objective cognitive performance (OCP: dotted red line) with progression towards Alzheimer's disease. MCI: Mild cognitive impairment, with both SCD and OCP below cut-off. Adapted from [2]

Methods:

- Participants in the longitudinal Older Australian Twins Study (OATS)[3] completed the self-report Memory Complaint Questionnaire (MACQ)[4].
- Participant-nominated informants completed the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE, short version)[5].
- Twin pair data were included from the first of three waves of assessment that provided complete data for either questionnaire**.**
- Genetic heritability MACQ and IQCODE ratings were estimated under the A(C)E model, using age, sex and education as covariates.

Inclusion criteria: Twin pairs > 65 years.

Exclusion criteria: Current or recent (<1 year) active cancer, self-report history of head trauma, diagnosis of Parkinson's disease or dementia, expert consensus diagnosis of MCI or dementia based on neuropsychological assessment.

Table 2: Demographic data	MAC-Q sample	IQCODE sample
Twin pairs	134	133
MZ/DZ pairs	77/57	76/57
Age (range) in years	71.7 (65-90)	71.3 (65-90)
Male/Female	95/173	88/178
Years of education (range)	11.6 (6-22)	11.4 (6-22)
IQ, NART ± S.D	108.6 ± 10.0	108.2 + 10.2

Results:

Sixteen participants were found to have subjective cognitive decline (memory impairment, difficulty learning new things) using the IQCODE completed by informants.

There was no suggestion of genetic heritability for SCD using IQCODE (h^2=0.13, 95% CI: 0-0.34).

On the MACQ, 71 participants self-reported their memory was "much better" or "about the same", 160 indicated their memory was somewhat poorer, and 37 that it was "much worse" compared to recent years. Rate of SCD across demographic variables are shown in Figure 2. Participants who self-reported cognitive decline did not differ in global cognitive ability at neuropsychology assessment.

Genetic heritability for MACQ estimated under the AE model was found to be h^2=0.59 (95% CI: 0.44-0.70). No significant effects were observed for the covariates age and sex, but education had a significant effect (p = 0.02).

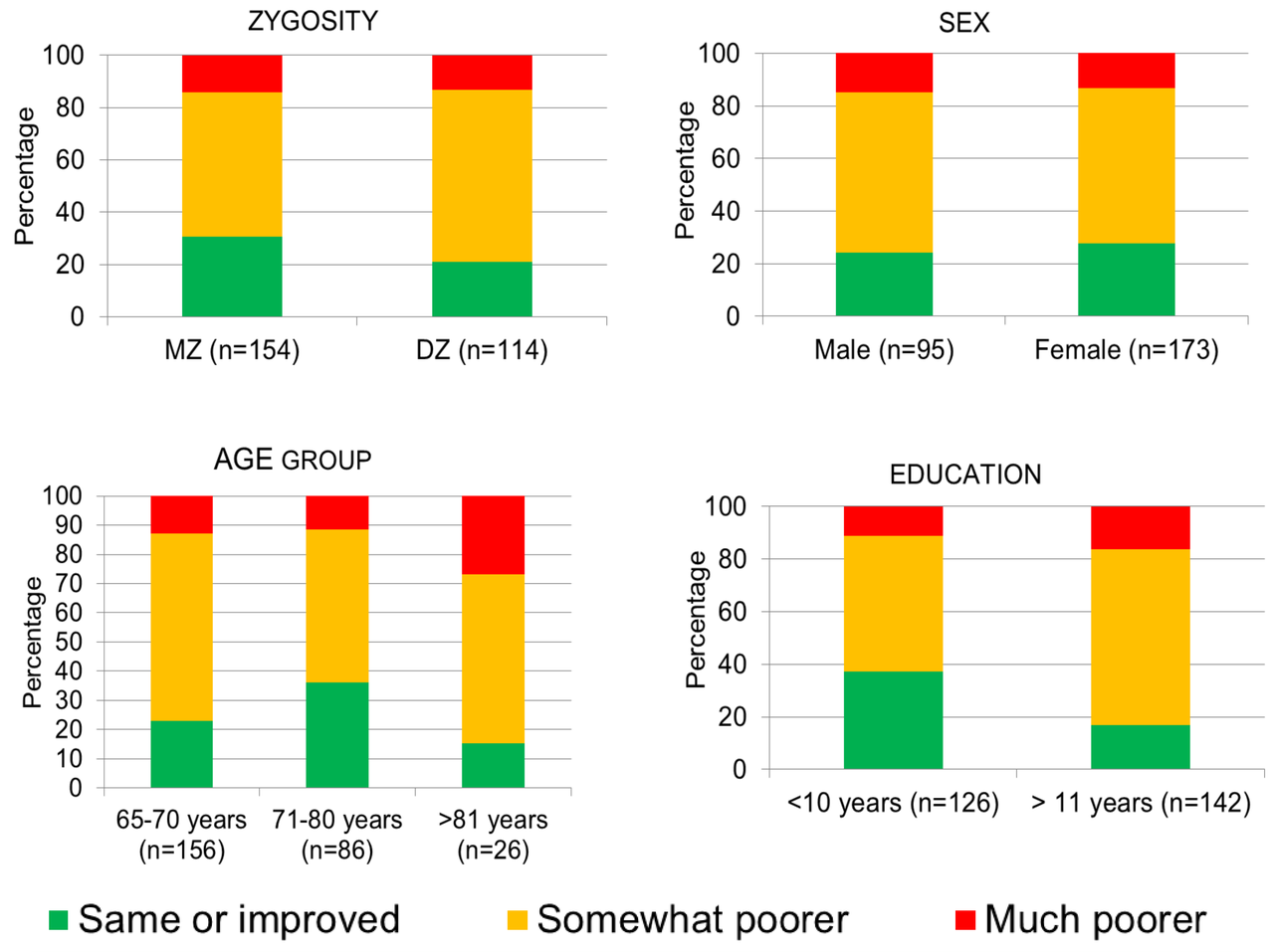

Figure 2: Self-report of SCD between MZ and DZ twins, males and females, by age group and years of education.

Discussion:

- The MACQ analysis suggests there is moderate genetic heritability for SCD.
- No heritability for SCD was found using the IQCODE, or the TELE in the Swedish twin study, suggesting the genetic influence on SCD is scale dependent.
- Future work will examine heritability of SCD determined by other scales administered as part of OATS.
- The contributions of influencing factors, such as personality traits and subjective well-being, will also be explored.

References:

1. Caracciolo B et al. 2012 J Alz Dis 29:393-403; 2. Avila-Villanueva M et al. 2017 Front Aging Neurosci 9:377;
3. Sachdev et al. 2009 Twin Res Hum Genet 12:573-82; 4. Caramelli & Beato 2008 Dement Neuropsychol 2:42-5;
5. Jorm 1994 Psychol Med 24:145-53