Objective

Cognitive decline, whether a feature of normative ageing or dementia, imposes enormous financial costs and societal burden globally. With no effective treatments, evidence for risk and protective factors for cognitive decline, with or without dementia, is urgently needed. We investigated a comprehensive set of such factors on a truly international scale, using longitudinal cohort data shared by members of the COSMIC (Cohort Studies of Memory in an International Consortium) collaboration.

Method

• Data were from 20 cohorts across 15 countries and 5 continents (Table 1), for 6,832 individuals aged 40–105 years (54% female) and non-demented at baseline. Each study had 2-6 assessment waves (median = 3) and a follow-up duration of 2–15 years.

• Primary outcome measures were standardized scores for the Mini-Mental State Examination (MMSE) and global cognition (averaged across tests of memory, language, attention/concentration speed, and executive functioning).

• The framework factors investigated were age, sex, education, alcohol consumption (quantity, 1 drink/wk, 2+ drinks/day), smoking, systolic and diastolic blood pressure, body mass index (BMI), cardiovascular disease (other than atrial fibrillation), depression (both current and history of), diabetes, weight, height, very good, good, poor), high cholesterol, hypertension, peripheral vascular disease, physical activity (moderate at least once a week, vigorous at least once a week), smoking (never, past, current), and stroke history.

• Single factor and combined factor linear mixed models were fitted by FID meta-analyses that pooled effects across cohorts.

• We also compared associations for white and Asian groups, based on all whites (n = 11,251, 71% male) while cohort 6 (n = 27,154) and all Asains from 5 cohorts (n = 10,286). Individuals from the Latin-American and Scandinavian cohorts were not included.

Results

Table 2. Factors showing significant associations with cognitive performance or decline*.

Table 2. Factors showing significant associations with cognitive performance or decline*.

Cognitive performance (Fig 1): Global cognitive scores for males were lower than females among whites but higher for females among Asians. For the MUSE and APÖE *4 carriers had higher scores than non-carriers among Asians but not among whites, and poor health was associated with lower scores among whites but not among Asians. Compared to whites, Asains showed more decline in MUSE performance compared with whites, showing associations with cognitive decline or rate of change in decline that differed between the groups.

Cognitive decline (Fig 2): Compared to whites, Asains showed more decline in MMSE scores associated with diabetes, as well as a growing rate of decline associated with each of diabetes, high cholesterol and increasing education.

Conclusions

We considered the most important factors those that combined factor models identified as independently associated with cognitive performance or decline.

- Ageing and being APÖE *4 positive have no direct resolution (currently), and it is not clear whether depression is a cause or prodrome of decline.

- Other factors are modifiable, suggesting or strengthening support for targeting them in interventions to delay or minimize cognitive decline, including that leading to dementia:
  - Increased levels of education
  - Smoking, past vs. never
  - Not smoking
  - Controlling other factors that lower the risk of diabetes and stroke.

- Different associations between some factors and cognition for white and Asians suggest that interventions may benefit from tailoring to particular ethnico-regional groups.

Contact

All researchers can apply to use COSMIC data. For details please contact: James Coffey (j.coffey@unsw.edu.au) or Permindar Sachdev (COSMIC lead), p.sachdev@unsw.edu.au. Website: https://cheba.unsw.edu.au/group/cosmic.