Cognition and mortality in older people: the Sydney Memory and Ageing Study

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Abstract

Background: both cognitive ability and cognitive decline have been shown to predict mortality in older people. As dementia, a major form of cognitive decline, has an established association with shorter survival, it is unclear the extent to which cognitive ability and cognitive decline predict mortality in the absence of dementia.

References


15. Hirschman KB, Kapo JM, Karlawish JH. Identifying the factors that facilitate or hinder advance planning by persons with dementia. Alzheimer Dis Assoc Disord 2008; 22: 293–8.

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Objective: to determine whether cognitive ability and decline in cognitive ability predict mortality in older individuals without dementia.

Design: the Sydney Memory and Ageing Study is an observational population-based cohort study. Participants completed detailed neuropsychological assessments and medical examinations to assess for risk factors such as depression, obesity, hypertension, diabetes, hypercholesterolaemia, smoking and physical activity. Participants were regularly assessed at 2-year intervals over 8 years.

Setting: a community sample in Sydney, Australia.

Subjects: one thousand and thirty-seven elderly people without dementia.

Results: overall, 236 (22.8%) participants died within 8 years. Both cognitive ability at baseline and decline in cognitive ability over 2 years predicted mortality. Decline in cognitive ability, but not baseline cognitive ability, was a significant predictor of mortality when depression and other medical risk factors were controlled for. These relationships also held when excluding incident cases of dementia.

Conclusions: the findings indicate that decline in cognition is a robust predictor of mortality in older people without dementia at a population level. This relationship is not accounted for by co-morbid depression or other established biomedical risk factors.

Keywords: cognition, cognitive impairment, dementia, mortality, older people

Introduction

Lower cognitive ability and greater decline in cognitive ability predict mortality in older people, even when controlling for other biomedical risk factors [1–6]. A number of mechanisms may be responsible for the relationship. Lower cognition may contribute to a less healthy lifestyle, including diet, physical activity and treatment compliance [7], and thus to poorer health outcomes. Alternatively, a common factor may cause both outcomes. Organ failure [8, 9] or the accumulation of cellular damage with ageing [10], for example, could lead to both lower cognition and greater mortality.

Dementia, a major form of cognitive decline, is associated with a reduced lifespan [11], so could be responsible for the relationship. Comparatively little research, however, has controlled for dementia. Whereas several studies have excluded participants with dementia at baseline [12], the only study that excluded participants who subsequently developed dementia [13] found that poorer cognition still predicted mortality. This study, however, lacked a formal assessment for dementia, relying instead on a brief telephone screening test to assess cognition; did not control for depression, which affects both cognition and mortality [14]; and did not examine whether decline in cognition over time predicted mortality. As such, it remains unclear the extent to which cognitive decline that does not meet the threshold of dementia predicts mortality.

To address these limitations, we examined predictors of mortality at 8 years in a population-based sample of older people without dementia. Participants completed detailed cognitive and medical assessments at 2-year intervals. We hypothesised that lower levels of cognition at baseline and greater decline in cognition would be associated with earlier mortality, even when excluding participants who subsequently developed dementia and controlling for depression and other risk factors.

Method

Participants

The Sydney Memory and Ageing Study (MAS) is a longitudinal study of community-dwelling older adults in Sydney, Australia [15]. Participants aged 70–90 years were recruited from the electoral roll (registration is compulsory in Australia). To ensure that participants did not have pre-existing dementia or psychopathology, participants were excluded if they had a history of dementia, suspected dementia based on baseline assessment and consensus diagnosis from an expert panel, or a Mini-Mental State Examination (MMSE) score <24 adjusted for age, education and non-English-speaking background. Participants were also excluded if they had insufficient English to complete psychometric assessment, experienced psychotic symptoms or received a diagnosis of schizophrenia, bipolar disorder, multiple sclerosis, motor neuron disease, developmental disability or progressive malignancy. The baseline sample consisted of 1,037 participants. This study was approved by the Ethics Committees of the University of New South Wales and the South Eastern Sydney and Illawarra Area Health Service. Written informed consent was obtained from all participants.

Instruments and methods

The baseline assessment involved three parts. First, participants were interviewed over the telephone to collect demographic data, such as age, sex and education. Second, participants completed a detailed face-to-face assessment that consisted of a medical history, a medical examination and a neuropsychological examination. The medical history included questions about vascular diseases and risk factors such as hypertension, hypercholesterolaemia, smoking and diabetes. The medical examination assessed participants’ height and weight, which were used to calculate body mass index (BMI); blood pressure and the time it took participants to complete a 6-m walk and stand from a seated position five
times. Participants also completed a fasting blood test to assess cholesterol and glucose levels.

The neuropsychological examination included the MMSE [16] and a battery of neuropsychological tests. Attention/processing speed was assessed using Digit-Symbol Coding [17] and Trail Making Test A [18]; memory using Logical Memory Story A [19], Rey Auditory Verbal Learning Test [18] and Benton Visual Retention Test [20]; language using the Boston Naming Test [21] and Semantic Fluency [18]; visuospatial ability using Block Design [17]; and executive function using the Controlled Oral Word Association Test [18] and Trail Making Test B [18]. Raw test scores were transformed to z-scores using baseline means and SDs of a subgroup who had spoken English before 10 years of age and were classified as cognitively normal at baseline (n = 504). Domain scores were calculated by averaging the z-scores of component tests, which were then transformed to make the means of the cognitively normal subgroup 0 and the SDs 1. The global cognition score was calculated by averaging across domain scores and transforming the scores as before. Finally, participants completed several questionnaires, including the 15-item Geriatric Depression Scale [22], and an inventory of current physical activity, which assessed the amount of time participants engaged in physical activity [23].

Participants were reassessed at 2-year intervals. Decline in cognition was calculated by subtracting the global cognition score at 2 years from the global cognition score at baseline. At each assessment, a panel of specialist clinicians assessed whether participants met criteria for dementia (DSM-IV) based on all available information [24]. Data about participants’ date and cause of death were obtained from the New South Wales Registry of Births, Deaths and Marriages 8 years after the study began.

### Statistical analyses

Analyses using Cox proportional hazard model were performed to determine whether baseline variables predicted mortality. Predictors were entered in three stages: age, sex, cognition (global Z-score) and decline in cognition (over 2 years) were entered first, followed by depression, and then other biomedical risk factors, namely: BMI, current smoking, diabetes (defined as a history of diabetes or a fasting blood glucose level of 7.0 mmol/l or greater), hypercholesterolaemia (defined as a history of high cholesterol or a measured LDL cholesterol of 4.1 mmol/l or greater), hypertension (defined as a history of hypertension, a systolic pressure >139 mmHg or a diastolic pressure >89 mmHg), 6-m walk (time in seconds), sit-to-stand (time in seconds) and amount of physical activity (minutes/week). Missing data for continuous variables were handled using expectation–maximisation imputation (see Supplementary data, Appendix, available in Age and Ageing online). A post hoc analysis compared the odds of dying for participants whose cognitive decline was in the highest 0.5 SD with other participants.

To rule out dementia as a contributing factor, a sensitivity analysis was conducted excluding participants diagnosed with dementia in biannual assessments over the 8-year period or whose death certificate listed dementia as a cause of death. To rule out terminal drop—cognitive decline that often occurs immediately before death [1–5]—as a contributing factor, participants who died within 3 months of cognitive assessment were also excluded in this analysis.

### Results

Participants’ demographic characteristics are summarised in Table 1. Of 1,037 participants at baseline, 236 (22.8%) died in the 8 years with a mean survival time of 4.33 years.

Table 1. Participants’ characteristics at baseline and mortality at 8 years

<table>
<thead>
<tr>
<th>Demographic variables</th>
<th>Overall</th>
<th>Deceased</th>
<th>Not deceased</th>
<th>Statistical comparison†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at baseline (y)</td>
<td>78.84 (4.82)</td>
<td>81.33 (4.71)</td>
<td>78.10 (4.60)</td>
<td>t(1,035) = 9.42, P &lt; 0.01</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>44.8</td>
<td>53.4</td>
<td>42.3</td>
<td>χ²(1) = 9.02, P &lt; 0.01</td>
</tr>
<tr>
<td>Education (years)</td>
<td>11.60 (3.47)</td>
<td>11.89 (3.84)</td>
<td>11.52 (3.36)</td>
<td>t(1,035) = 1.44, P = 0.15</td>
</tr>
<tr>
<td>Cognitive measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global cognition (z-score)</td>
<td>−0.72 (1.38)</td>
<td>−1.08 (1.54)</td>
<td>−0.62 (1.31)</td>
<td>t(1,030) = 4.52, P &lt; 0.01</td>
</tr>
<tr>
<td>Decline in global cognition</td>
<td>0.02 (0.66)</td>
<td>0.25 (0.91)</td>
<td>−0.03 (0.59)</td>
<td>t(859) = 4.81, P &lt; 0.01</td>
</tr>
<tr>
<td>MMSE</td>
<td>28.70 (1.35)</td>
<td>28.73 (1.26)</td>
<td>28.69 (1.37)</td>
<td>t(1,035) = 0.42, P = 0.67</td>
</tr>
<tr>
<td>Medical history and examination</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>27.08 (4.50)</td>
<td>26.71 (4.93)</td>
<td>27.18 (4.36)</td>
<td>t(1,008) = 1.34, P = 0.16</td>
</tr>
<tr>
<td>Current smoking (%)</td>
<td>3.9</td>
<td>5.5</td>
<td>3.4</td>
<td>χ²(1) = 2.18, P = 0.14</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>15.1</td>
<td>22.5</td>
<td>13.0</td>
<td>χ²(1) = 12.74, P &lt; 0.01</td>
</tr>
<tr>
<td>Hypcholesterolaemia (%)</td>
<td>63.8</td>
<td>62.3</td>
<td>64.3</td>
<td>χ²(1) = 0.32, P = 0.57</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>82.0</td>
<td>81.4</td>
<td>82.1</td>
<td>χ²(1) = 0.08, P = 0.78</td>
</tr>
<tr>
<td>6-m walk (s)</td>
<td>16.81 (5.64)</td>
<td>18.35 (6.47)</td>
<td>16.42 (5.34)</td>
<td>t(923) = 4.23, P &lt; 0.01</td>
</tr>
<tr>
<td>Physical activity (min/week)</td>
<td>406.97 (478.71)</td>
<td>315.24 (424.97)</td>
<td>434.13 (490.46)</td>
<td>t(1,005) = 3.33, P &lt; 0.01</td>
</tr>
</tbody>
</table>

Standard deviation is shown in brackets.

MMSE, Mini-Mental State Examination.

† Differences between deceased and not deceased participants.
predicts mortality once depression is controlled for. The decline in cognition over time, rather than baseline levels, 8 years prior to death [26]. It is also consistent with previously published evidence that deceased older people have a faster pre-mortem cognitive decline relative to survivors who had similar baseline cognition [27] and that shorter time to death is associated with faster cognitive decline in genetically similar individuals [28].

Given possible relationships between baseline levels and rates of change, both variables need to be considered in analyses. Change scores are also subject to measurement error, regression to the mean and practice effects, which can make it difficult to interpret small changes in an individual [29, 30]. Despite these limitations, however, decline in cognition appears to be a robust predictor of mortality at a population level.

### Key points
- Decline in cognition over 2 years predicts mortality in older people without dementia.
- Baseline cognition did not predict mortality when depression and other biomedical risk factors were controlled for.
- Cognitive assessments of older people can predict longevity at a population level.
Conflicts of interest

In the last 3 years, H.B. has worked on drug trials for patients with mild cognitive impairment and Alzheimer’s disease sponsored by major pharmaceutical companies including Eli Lilly and Company, Sanofi-Aventis, Servier and Tau Therapeutics. H.B. has been a consultant, advisory board member and/or sponsored speaker for Eli Lilly, Merck and Nutricia. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary data mentioned in the text are available to subscribers in Age and Ageing online.

References

Explanatory factors for the association between depression and long-term physical disability after stroke

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Abstract

Objectives: to identify explanatory factors for the association between depression at 3 months after stroke and physical disability at 3 years.

Methods: data from the South London Stroke Register (1998–2013) were used. Patients (n = 3,612) were assessed at stroke onset. Follow-up at 3 months included assessment for depression with the Hospital Anxiety and Depression scale (scores ≥ 7 = depression), physical disability (Barthel index) cognitive function, smoking habit, selective serotonin reuptake inhibitors (SSRIs) use, perception of recovery and social support. Physical disability was reassessed at 3 years. The associations between depression at 3 months and physical disability at 3 years were estimated with multinomial regression adjusting for age, gender, ethnicity, stroke severity and possible explanatory factors for the association (introduced in the models first individually and then sequentially): pre-stroke medical history and physical disability, cognitive function, smoking, SSRIs, perception of recovery and social support at 3 months.

Results: one thousand three hundred and seven survivors were assessed at 3 months, of which 418 (32.0%) had depression. Survivors with depression had a higher physical disability rate at 3 years. These associations remained significant after adjustment for individual explanatory factors but were not significant after adjustment for combined explanatory factors. Physical disability at 3 months was a relevant explanatory factor for this association. SSRIs were associated with severe, relative risk: 6.62 (2.92–15.02) P < 0.001, and moderate physical disability, relative risk: 3.45 (1.58–7.52) P = 0.002, at 3 years.

Conclusion: the association between depression and physical disability appears to be multifactorial. The use of SSRIs after stroke requires further research.

Keywords: stroke, depression, disability, antidepressive agents, cohort studies, older people