LJMU Research Online

Lenehan, ME, Summers, MJ, Summers, JJ, Vickers, JC and Saunders, NL

 Relationship between education and age-related cognitive decline: A review of recent research

http://researchonline.ljmu.ac.uk/1523/

Article

For more information please contact researchonline@ljmu.ac.uk

http://researchonline.ljmu.ac.uk/

The relationship between education and age-related cognitive decline: A review of existing research

SCHOLARONE™
Manuscripts

The relationship between education and age-related cognitive decline: A review of

existing research

Megan Elizabeth LENEHAN [a], Mathew James SUMMERS [a,b †], Nichole Louise

SAUNDERS [b], Jeffery Joseph SUMMERS [a,d], & James C VICKERS [b,c]

[a]   School of Psychology, University of Tasmania, Australia
[b]   Wicking Dementia Research & Education Centre, University of Tasmania, Hobart, Tasmania, Australia.
[c]   School of Medicine, University of Tasmania, Hobart, Tasmania, Australia.
[d]   Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool, United Kingdom.

†   Corresponding author: Dr M.J. Summers, School of Psychology, Locked Bag 1342, Launceston, Tasmania, Australia, 7250; tel +61 3 6324 3266; facsimile +61 3 6324 3168; email: Mathew.Summers@utas.edu.au

Running Title: Education and age-related cognitive decline

Word Count:
- Abstract = 205 words
- Manuscript = 4058 words
- Figures = 1
- Tables = 1

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Abstract

Background: The association between level of educational attainment and cognitive performance is well-studied. People with higher education perform better across a broad range of cognitive tasks. However, there is uncertainty as to whether education moderates the trajectory of age-related cognitive decline.

Objective: This review paper addresses the potential link between education and age-related cognitive decline by evaluating relevant research published since the year 2000.

Methods: Studies reporting data on education and its association with the rate of cognitive decline across various cognitive domains were reviewed. A total of 10 studies were identified with a mean follow-up period of 7.6 years, each containing a population-based, non-demented sample.

Results: Results showed that, in the majority of studies, education did not moderate age-associated cognitive decline. The few studies that did find an association between education and decline in specific cognitive functions should be interpreted with caution due to methodological issues.

Conclusion: The literature reveals little consistent evidence that normal age-related cognitive decline is moderated by education attainment. This supports a passive theory of cognitive reserve: People with a higher level of education will continue to perform at a higher level of cognitive functioning than their lower educated peers, which may delay the onset of impairment in the future.

KEYWORDS: Education; Age-related cognitive decline; aging; dementia; neuropsychological

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

INTRODUCTION

Cognitive reserve theory posits that individuals possessing a greater ability to recruit and co-ordinate specific brain regions are able to cope with a higher level of brain pathology before clinical impairment is reached (Jones *et al.*, 2011; Stern, 2009). Quantifying an individual's level of cognitive reserve typically involves inferring cognitive reserve from indirect, or proxy, measures, such as lifetime experience, educational attainment or occupation (Jones*, et al.*, 2011; Stern, 2009). It has been argued that education increases cognitive reserve through fostering the development of new cognitive strategies (Manly *et al.*, 2004).

Multiple studies indicate that educational attainment modifies the association between a direct measure of brain pathology and neuropsychological test performance (Bennett *et al.*, 2003; Dufouil *et al.*, 2003; Rentz *et al.*, 2010). Such findings have led some researchers to consider education to be the key protective factor against dementia (Jones*, et al.*, 2011). In a review, Valenzuela and Sachdev (2006) demonstrated that individuals with a high level of education had a 47% decrease in risk for dementia compared to those with lower level educational attainment. A recent study has confirmed that education up to year 12 has a dose-related effect on reducing risk of dementia with advancing age, irrespective of the disease burden (Brayne *et al.*, 2010).

On the basis of such findings, subsequent studies have also examined whether educational attainment moderates the trajectory of normal age-related cognitive decline. In research published between 1985 and 1999 a number of studies report that education reduces the rate of age-related cognitive decline (Albert *et al.*, 1995; Bennett*, et al.*, 2003; Evans *et al.*, 1993; Jacqmin-Gadda *et al.*, 1997; Lyketsos *et al.*, 1999; Shichita *et al.*, 1986). Other studies noted

that the effect of education on ageing related decline was restricted to specific cognitive

domains (Arbuckle *et al.*, 1998; Christensen, Korten*, et al.*, 1997; Schaie, 1989). Such

findings support the concept of *active cognitive reserve*, which proposes that it is individual

differences in brain efficiency, flexibility or capacity which underpin task performance

(Stern, 2009). Thus, increasing levels of education confer on individuals the capacity to

process tasks more efficiently. As a consequence, possessing higher active cognitive reserve

allows greater capacity to cope more effectively with the subtle brain changes associated with

age-related cognitive decline (Stern, 2009).

Several studies published between 1985 and 1999 found no effect of education on rate of

cognitive decline (Carmelli *et al.*, 1997; Hultsch *et al.*, 1998). The absence of an effect of

education on the rate of cognitive decline supports a *passive* model of cognitive reserve,

whereby individuals with higher educational attainment will consistently perform at a higher

level of cognitive function as they age because of this greater level of baseline cognitive

reserve, but decline at a similar rate to their lower educated peers.

There are a number of possible explanations for these discrepant findings. In this regard, an

important consideration is the potential role of cohort differences. As the age-ranges vary

between studies, the age-related cognitive decline identified in some studies may be an

artefact of historically related cohort differences and therefore may over-estimate age-related

decline (Hedden and Gabrieli, 2004). It has been shown that adjusting for an individual's

cognitive function at baseline can contribute to a false or inaccurate association between

education and change in cognitive performance (Glymour *et al.*, 2005). Whether the rate of

change is calculated based on two or multiple time points is also an important consideration.

Earlier research predominantly based estimates of cognitive change on only two

measurement points. Such an approach is limited in its ability to estimate rate of change over time, as it is difficult to distinguish changes due to pathological or normal aging processes from changes due to learning and practice effects or random variation (Morris *et al.*, 1999).

The manner in which data is analysed can affect the reported outcomes. While earlier studies with two measurement points tended to adopt regression analysis (Christensen, Henderson*, et al.*, 1997) or repeated measures analysis of variance (Colsher and Wallace, 1991), recent studies with three or more time points utilise more sophisticated analytical techniques, including latent growth curve modelling (Alley *et al.*, 2007; Christensen *et al.*, 2001; Tucker-Drob *et al.*, 2009; Zahodne *et al.*, 2011), and linear mixed modelling (Der *et al.*, 2010; Van Dijk *et al.*, 2008). These more sophisticated techniques are better able to cope with both missing data and unevenly spaced assessment time points, which are common occurrences in longitudinal aging research.

A comprehensive review of research examining the association between education and age-related cognitive decline has not been completed since the review provided by Anstey and Christensen which was published in the year 2000. The review notes that while there is a body of research indicating a protective role for education, there is another body of research that disputes this claim (see Anstey and Christensen, 2000). More than a decade on, it is of interest to examine whether more advanced statistical techniques and longer ranges of data yield a more consistent finding regarding the potential protective benefit of education on normal age-related cognitive decline.

METHOD

As an existing review of the literature was published based on studies conducted up until the

year 2000, studies included in this review were published in English language journals after

this time. These studies included empirical data on education and its association with rate of

cognitive decline in older adults ($\geq$ 50 years of age). Studies were identified through searches

in the Web of Science and Psych Info databases. The search terms "education" and

"cognitive decline" and "age-related" were contained in the title, abstract or content of the

article.

Inclusion criteria were: (a) one of the dependent variables was education; (b) one of the

outcome variables was rate of cognitive decline; (c) the study was longitudinal; (d) the study

assessed participants on a minimum of two occasions; (e) the sample was initially healthy,

free from a significant health problem that could impinge on cognitive function *or* the study

statistically controlled the impact of health status; (f) participants were aged 50 years and

older; and, (e) cognitive function was assessed across multiple cognitive domains.

Studies were excluded if: (a) the main outcome was dementia; (b) the sample included

participants with dementia or cognitive impairments at baseline; (c) the participant sample

included chronic illness but did not statistically control for the effect of such conditions on

cognitive function; or, (d) cognitive function was assessed using solely a general mental

status measure. Studies which included measures of cognitive function at two time points but

did not analyse rate of decline or change overtime were not included in this review.

The results of each study were assessed qualitatively. The findings of each study were

discussed with reference to sample characteristics, the treatment of education as a continuous

or categorical variable, the analysis method and the sensitivity of testing instruments. A meta-

analysis of results was not attempted due to the range of different cognitive tests, education

measures and statistical techniques adopted within the various studies.

RESULTS AND DISCUSSION

The initial search yielded 168 articles from Web of Science and 190 articles from the Psych

Info databases. The majority of studies were excluded as they did not meet all inclusion

criteria. Ten studies were retained for this review that met all inclusion criteria.

Level of Education

The Effect of Education on Cognitive Performance

Consistent with previous literature (see Kramer *et al.*, 2004), all reviewed studies

demonstrated that education was related to better performance across most (Christensen*, et*

al., 2001; Proust-Lima *et al.*, 2008), if not all (Alley*, et al.*, 2007; Der*, et al.*, 2010; Seeman *et*

al., 2005; Tucker-Drob*, et al.*, 2009; Van Dijk*, et al.*, 2008; Zahodne*, et al.*, 2011), cognitive

domains (see Table 1).

[INSERT TABLE 1 HERE]

The Effect of Education on Rate of Cognitive Decline

Table 1 presents the results of studies that report data on the role of education on rate of

cognitive decline that met the inclusion criteria of this review. There are four patterns of

findings: (1) studies that report an effect of education (e.g. a higher level of educational

attainment is associated with a slower rate of cognitive decline) (Bosma *et al.*, 2003); (2)

studies that found an effect of education but only in particular subgroups (Seeman*, et al.*,

2005); (3) studies that report an education effect restricted to some cognitive functions but

not others (Alley*, et al.*, 2007; Cullum *et al.*, 2000; Proust-Lima*, et al.*, 2008); and (4) studies

that report no association between education and rate of cognitive decline (Christensen*, et al.*,

2001; Der*, et al.*, 2010; Tucker-Drob*, et al.,* 2009; Van Dijk*, et al.*, 2008; Zahodne*, et al.*,

2011).

Global Cognitive Function

When considering measures of global cognitive functioning, the selected studies demonstrate

inconsistent findings. Bosma*, et al.* (2003) and Alley*, et al.* (2007) found that higher levels of

education were associated with slower decline in global cognitive function. In

contrast,Proust-Lima*, et al.* (2008) report that individuals with higher education declined at a

faster rate. However, when repeating the same analysis using non-linear modelling

techniques, there was no significant difference in the rate of decline in global cognitive

performance between lower and more highly educated individuals (Proust-Lima*, et al.*,

2008), suggesting that analytical method could be an influential factor when exploring

cognitive change trajectories through ageing. Similarly, Christensen*, et al.* (2001), Seeman*, et al.* (2005) and Van Dijk*, et al.* (2008) found no significant differences in rates of decline in global cognition in older people as a function of education. However, when looking specifically at those individuals with the APOE e4 allele (Seeman*, et al.*, 2005), a non-significant trend ($p. < 0.1$) for a faster decline in global cognitive performance was found in individuals with greater educational attainment (>9 years).

Screening measures of global cognitive function are common to most studies included in this review, particularly the use of the Mini Mental State Examination (MMSE; Folstein *et al.*, 1975). However, it is important to consider the appropriateness of using a measure of general cognitive function in assessing age-related cognitive decline. The MMSE was designed to provide a brief measure of cognitive status in adults and as a screen for cognitive impairment (Monroe and Carter, 2012), but is not effective at distinguishing either subtle subclinical changes in cognition from normal performance (Galasko *et al.*, 1990) or in the adequate assessment of specific cognitive domains (Lezak *et al.*, 2012). The MMSE also lacks the sensitivity to robustly assess non-memory domains (Alladi *et al.*, 2006), such as processing speed, a function which demonstrates significant decline in late adulthood (Hedden and Gabrieli, 2004). Research examining age-related cognitive decline highlights differential trajectories of deterioration for specific cognitive functions (Hedden and Gabrieli, 2004). Consequently, there is a need for research to focus on specific cognitive functions in order to explore the potential protective effects of education. The MMSE may also be insensitive to change among high-functioning or well-educated adults (Jacqmin-Gadda*, et al.*, 1997). Due to these factors, the findings from studies utilising global cognitive screening measures should be interpreted with caution. Interpreting the results from neuropsychological tests with

established sensitivity and specificity in assessing specific cognitive domains is more informative in this context.

Specific Cognitive Functions

The majority of studies reviewed do not report significant differences in the rate of cognitive decline between lower and more highly educated individuals on measures of verbal memory (Christensen*, et al.*, 2001; Der*, et al.*, 2010; Seeman*, et al.*, 2005; Van Dijk*, et al.*, 2008; Zahodne*, et al.*, 2011), visual memory (Proust-Lima*, et al.*, 2008), processing speed (Christensen*, et al.*, 2001; Tucker-Drob*, et al.*, 2009; Van Dijk*, et al.*, 2008; Zahodne*, et al.*, 2011), spatial ability (Cullum*, et al.*, 2000; Seeman*, et al.*, 2005), abstract thought/reasoning (Cullum*, et al.*, 2000; Der*, et al.*, 2010; Tucker-Drob*, et al.*, 2009), attention/calculation (Cullum*, et al.*, 2000) or interference control (Van Dijk*, et al.*, 2008). Such findings suggest that education does not reduce the rate of age-related cognitive decline in specific cognitive domains. These findings support a *passive* model of *reserve* (Stern, 2002). The theory of *passive cognitive reserve* or *brain reserve* maintains that it is individual differences in brain anatomy, including brain size and number of neurons and synaptic connections, that determines task performance (Stern, 2009). The passive cognitive reserve model posits that age-related cognitive decline will occur at a similar rate regardless of the amount of education an individual attains throughout their life (Figure 1a). However, of the ten reviewed studies, four report results that contradict passive cognitive reserve explanations.

Bosma*, et al.* (2003) report that a lower level of education was associated with more rapid decline in measures of processing speed and verbal memory. Similarly, Cullum*, et al.* (2000)

report that age-related decline in memory was associated with lower levels of educational

attainment. These findings support the notion of a *neural cognitive reserve,* which posits that

higher levels of educational attainment lead individuals to process cognitive tasks more

effectively and as such the structural changes associated with an aging brain are associated

with reduced rates of cognitive decline relative to individuals with a lower level of education

(Figure 1b). Interestingly, the associations found by Bosma*, et al.* (2003) disappeared when

the influence of mental workload of current job and intellectual abilities were controlled,

leading the researchers to suggest that accelerated cognitive decline could be due to a lack of

mental stimulation at work among people with lower levels of educational attainment.

Conversely, two studies reported that a higher level of education was associated with an

increasingly rapid decline in cognitive function, evident on measures of verbal memory

(Alley*, et al.*, 2007), as well as processing speed and verbal fluency (Proust-Lima*, et al.*,

2008). These findings are in keeping with the *neural compensation* model of *cognitive*

reserve (Stern, 2009), which posits that it is individual differences in the ability to enlist

alternate brain structures or networks when faced with brain pathology that underlie task

performance. In line with this explanation, individuals with a higher level of educational

attainment may deal with normal age-associated decline in some cognitive functions by

utilising other intact cognitive domains, effectively reducing the rate of cognitive decline

until these secondary functions too begin to decline (Figure 1c).

[INSERT FIGURE 1 HERE]

Other Considerations

As with prior research in this field, studies differ on a number of methodological factors; some of which may account for the inconsistent findings between studies, including: treatment of education as a dependent variable; duration of longitudinal study; statistical analytical techniques used; and sample characteristics.

Education as a dependent variable: categorical or continuous

Whether education was considered a categorical variable or a continuous variable did not appear to influence the results. An effect of education on rate of cognitive decline was found in studies using education as a categorical variable (Cullum, *et al.*, 2000; Proust-Lima, *et al.*, 2008), as a continuous variable (Alley, *et al.*, 2007), or as a mix of both continuous and categorical variables (Bosma, *et al.*, 2003). In contrast, no effect of education on rate of cognitive decline was found in studies using education as a categorical variable (Seeman, *et al.*, 2005; Van Dijk, *et al.*, 2008), as a continuous variable (Der, *et al.*, 2010; Tucker-Drob, *et al.*, 2009), or as a combination of categorical and continuous variables (Christensen, *et al.*, 2001; Zahodne, *et al.*, 2011).

Length of follow up and number of assessments

Age-related cognitive decline is a progressive long-term process with some cognitive functions showing minimal decline over a 5-10 year period (see Hedden and Gabrieli, 2004).

For this reason, studies that assess participants at multiple time points over extended time periods are better placed to differentiate between genuine cognitive change and measurement error, random variation, and familiarity or learning effects associated with repeated exposure to tests (Morris*, et al.*, 1999). While the majority of studies reviewed assessed participants on at least three occasions for a period of up to 15 years, the studies conducted by Bosma*, et al.* (2003) and Cullum*, et al.* (2000) involved testing participants on only two occasions over three and four years, respectively. This may not be a sufficient time period over which to accurately model rates of cognitive change.

Statistical analytical techniques

Related to the number of assessment occasions and study length, is the analytical method chosen to analyse the results. Traditionally, studies with two assessments have tended to adopt regression analysis or analysis of variance techniques. More recent research tends to adopt more sophisticated statistical approaches, such as growth curve modelling (e.g. Zahodne*, et al.*, 2011), linear mixed modelling (e.g. Van Dijk*, et al.*, 2008) and non-linear latent process modelling (e.g. Proust-Lima*, et al.*, 2008). These approaches are statistically powerful and highly flexible in terms of the ability to manage both missing data and unevenly spaced assessment time points, which are common occurrences in longitudinal research, in comparison to traditional analytic methods (Curran *et al.*, 2010). All of the studies reviewed utilised these more sophisticated methods of analysis with the exception of Bosma*, et al.* (2003), who used ordinary least squares regression, and Cullum*, et al.* (2000), who used logistic regression. Additionally, Bosma*, et al.* (2003) adjusted for cognitive function at

baseline, which may have contributed to an inaccurate association between education and cognitive change (Glymour, *et al.*, 2005).

Analytical techniques may also account for the discrepancy evident between the research conducted since 2000 and the findings of pre-2000 research, which tended to rely on these more rudimentary analysis methods and report a protective effect of education on rates of cognitive decline over time (e.g. a reviewed in Anstey and Christensen, 2000). In the analyses of cognitive change between time one and time two data (see Christensen, *et al.*, 1997), which utilised regression, an education effect was found. However, when three time points were analysed using latent growth modelling (Christensen, *et al.*, 2001) this protective effect of education was no longer evident.

Sample Characteristics

Age

Prior research (Lyketsos, *et al.*, 1999) in this field has also raised questions as to whether education may have a differential impact across older age groups. For example, while Alley, *et al.* (2007) found that verbal memory declined faster in adults with higher education aged over 70 years, the authors acknowledged the possibility that the lower educated group may have shown more decline before the age of 70, suggesting a delayed onset of cognitive decline in the highly educated. However, other studies with a broader age-range, including both the young-old (<70 years) and old-old (>70 years) age groups, do not provide evidence to support this hypothesis (Van Dijk, *et al.*, 2008; Zahodne, *et al.*, 2011).

Education

The finding of no effect of education or otherwise in the reviewed research could be due in part to either an insufficient number of participants with low levels of education (low levels of cognitive reserve), or an insufficient sample of individuals with very high levels of education (high cognitive reserve). For example, a sample that is mostly high-functioning at baseline could limit the statistical power of an analysis because initial test scores are higher at baseline. Although age-related cognitive decline will be apparent, greater declines may be evident in a more educationally representative sample. Previous research focusing specifically on a sample with lower levels of education found that while having 8 years of education was associated with a reduced rate of decline compared to those with <8 years of schooling, having ≥9 years of education provided no additional protective effect (Lyketsos*, et al.*, 1999).

Unfortunately, most of the research reviewed does not clearly specify the number of participants at the lower and higher extremes of education. Of the studies reviewed, a number include a substantial proportion of participants with lower levels of education (Christensen*, et al.*, 2001; Seeman*, et al.*, 2005; Van Dijk*, et al.*, 2008), providing evidence contradictory to the claim of Lyketsos*, et al.* (1999). However, as the majority of research in this field examines participant samples with an average of >10 years educational attainment, there remains scope for further research into how education effects cognitive decline in lower education groups (see Table 1).

Health

Physical health status and, in particular, certain diseases are known to interfere with normal cognitive function. As such, two types of studies were selected for this review: studies that had a physically healthy sample; and/or studies that statistically controlled for the effect of state of physical health (i.e. used health as a covariate). Whether the study included only a healthy sample to begin with, or whether the study controlled for health status post-hoc, affected outcome. Of the studies which only included a physically healthy sample, two studies (Seeman*, et al.*, 2005; Zahodne*, et al.*, 2011) failed to identify a protective effect of education on older age cognitive decline, and one study (Proust-Lima*, et al.*, 2008) found that the highly educated declined faster on some cognitive functions. In studies that statistically controlled for health status, four reported no evidence of protective effects of education (Christensen*, et al.*, 2001; Der*, et al.*, 2010; Tucker-Drob*, et al.*, 2009; Van Dijk*, et al.*, 2008), and one found that education was related to rate of decline in some functions (Alley*, et al.*, 2007). Importantly, Van Dijk*, et al.* (2008) highlighted the necessity of including health factors in examining the role of education in age-related cognitive decline. Van Dijk*, et al.* (2008) compared the impact of both including and excluding a measure of health status in their analyses of education effects. The results showed that the inclusion of measures of health status as covariates decreased the amount of variance explained by education and its interaction with time.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

IMPLICATIONS AND CONCLUSIONS

This review demonstrates that there is little consistent evidence to support the assumption that education moderates age-related cognitive decline across any cognitive domain(s). The limited evidence supporting this association must be interpreted with caution due to current methodological constraints, including short study duration and the statistical analysis technique used. Substantial evidence exists indicating that individuals with higher levels of educational attainment will continue to perform at a higher level of cognitive functioning when compared to their lower educated peers. Such results support a passive model of cognitive reserve. In this sense, education is beneficial because more highly educated individuals will continue to perform at a higher level of cognitive functioning as they age and may withstand neurodegenerative pathology for a longer period of time before functional or clinical impairment is reached. However, there appears to be no decrease in the rate of age-related cognitive decline over time attributable to increased levels of education.

Another consideration neglected in existing research is measures of effect size. Effect sizes are useful in distinguishing trivial results from those with practical or clinical significance (Tabachnick and Fidell, 2013). This is particularly important in the context of what are often large sample sizes in population based aging research. In studies involving large sample sizes, statistical significance may have little practical meaning (Lantz, 2013). The research reviewed does not explicitly report effect sizes, and, in many cases, does not report the data necessary to calculate effect sizes. An analysis of the magnitude of particular significant education effects may reveal only small effect sizes with little practical utility. This may help to explain the inconsistency evident in the findings of different studies.

Cohort effects may also help to explain the lack of association between education and

reduced age-associated cognitive decline found in the most recent studies. Historically,

educational attainment has steadily increased in developed counties such as the United States

of America since the early 1900s (Hester *et al.*, 2004). If cognitive reserve is enhanced with

education and life experience, it is possible that with increasing levels of educational

attainment as the norm, the majority of the population may attain maximum cognitive reserve

capacity. If this occurs, the capacity to detect the effect of increased education on cognitive

reserve may dissipate in the future as variance in educational attainment disappears.

The effect of education among lower educated groups (<8 years) remains under-researched.

Further investigations are required to determine if lower levels of education are associated

with greater rates of age-associated cognitive decline. If this is the case, low-level educational

subpopulations may benefit most from education-based intervention approaches. The effect

of education in later stages of adulthood remains to be explored. Future research should

examine the effect beyond that attained during a person's initial schooling. This approach

could also assist in the development of interventions designed to target those groups most at

risk of rapid age-related cognitive decline.

CONFLICT OF INTEREST

Dr. M. Summers reports personal fees from Eli Lilly (Australia) Pty Ltd, grants from

Novotech Pty Ltd, outside the submitted work.

DESCRIPTION OF AUTHOR ROLES

ML: conducted the research and prepared the manuscript

MS: co-project leader, co-authored the paper

NS: assisted with writing the paper

JS: assisted with writing the paper

JV: co-project leader, assisted with writing the paper.

ACKNOWLEDGEMENTS

References

Albert, M. S., Jones, K., Savage, C. R., Berkman, L. F., and et al. (1995). Predictors of cognitive change in older persons: MacArthur studies of successful aging. *Psychology and Aging, 10*(4), 578-578.

Alladi, S., Arnold, R., Mitchell, J., Nestor, P. J., and Hodges, J. R. (2006). Mild cognitive impairment: Applicability of research criteria in a memory clinic and characterization of cognitive profile. *Psychological Medicine, 36*(4), 507-515.

Alley, D., Suthers, K., and Crimmins, E. (2007). Education and cognitive decline in older Americans: Results from the AHEAD sample. *Research on Aging, 29*(1), 73-94.

Anstey, K., and Christensen, H. (2000). Education, activity, health, blood pressure and apolipoprotein E as predictors of cognitive change in old age: A review. *Gerontology, 46*(3), 163-177.

Arbuckle, T. Y., Maag, U., Pushkar, D., and Chaikelson, J. S. (1998). Individual differences in trajectory of intellectual development over 45 years of adulthood. *Psychology and Aging, 13*(4), 663-675.

Bennett, D. A., Wilson, R. S., Schneider, J. A., and Evans, D. A. (2003). Education modifies the relation of AD pathology to level of cognitive function in older persons. *Neurology, 60*(12), 1909-1915.

Bosma, H., van Boxtel, M. P. J., Ponds, R. W. H. M., and Houx, P. J. (2003). Mental work demands protect against cognitive impairment: MAAS prospective cohort study. *Experimental Aging Research, 29*(1), 33-45.

Brayne, C., *et al.* (2010). Education, the brain and dementia: neuroprotection or compensation?: EClipSE Collaborative Members. *Brain, 133*(8), 2210-2216.

Carmelli, D., Swan, G. E., LaRue, A., and Eslinger, P. J. (1997). Correlates of change in cognitive function in survivors from the Western Collaborative Group Study. *Neuroepidemiology, 16*(6), 285-295.

Christensen, H., Henderson, A. S., Griffiths, K., and Levings, C. (1997). Does ageing inevitably lead to declines in cognitive performance? A longitudinal study of elite academics. *Personality and Individual Differences, 23*(1), 67-78.

Christensen, H., Hofer, S. M., Mackinnon, A. J., Korten, A. E., Jorm, A. F., and Henderson, A. S. (2001). Age is no kinder to the better educated: Absence of an association investigated using latent growth techniques in a community sample. *Psychological Medicine, 31*(1), 15-28.

Christensen, H., Korten, A. E., Jorm, A. F., and Henderson, A. S. (1997). Education and decline in cognitive performance: Compensatory but not protective. *International Journal of Geriatric Psychiatry, 12*(3), 323-330.

Colsher, P. L., and Wallace, R. B. (1991). Longitudinal application of cognitive function measures in a defined population of community-dwelling elders. *Annals of Epidemiology, 1*(3), 215-230.

Cullum, S., Huppert, F. A., McGee, M., and Dening, T. (2000). Decline across different domains of cognitive function in normal ageing: Results of a longitudinal population-based study using CAMCOG. *International Journal of Geriatric Psychiatry, 15*(9), 853-862.

Curran, P. J., Obeidat, K., and Losardo, D. (2010). Twelve frequently asked questions about growth curve modeling. *Journal of Cognition and Development 11*(2), 121-136.

Der, G., Allerhand, M., Starr, J. M., Hofer, S. M., and Deary, I. J. (2010). Age-related changes in memory and fluid reasoning in a sample of healthy old people. *Aging, Neuropsychology, and Cognition, 17*(1), 55-70.

Dufouil, C., Alpérovitch, A., and Tzourio, C. (2003). Influence of education on the

   relationship between white matter lesions and cognition. *Neurology, 60*(5), 831-836.

Evans, D. A., *et al.* (1993). Level of education and change in cognitive function in a

   community population of older persons. *Annals of Epidemiology, 3*(1), 71-77.

Folstein, M. F., Folstein, S. E., and McHugh, P. R. (1975). "Mini-mental state". A practical

   method for grading the cognitive state of patients for the clinician. *Journal of

   Psychiatric Research, 12*(3), 189-198.

Galasko, D., Klauber, M. R., Hofstetter, C. R., Salmon, D. P., Lasker, B., and Thal, L. J.

   (1990). The mini-mental state examination in the early diagnosis of Alzheimer's-

   Disease. *Archives Of Neurology, 47*(1), 49-52.

Glymour, M. M., Weuve, J., Berkman, L. F., Kawachi, I., and Robins, J. M. (2005).

   When is baseline adjustment useful in analyses of change? An example with

   education and cognitive change. *American Journal of Epidemiology, 162*(3), 267-278.

Hedden, T., and Gabrieli, J. D. (2004). Insights into the ageing mind: a view from cognitive

   neuroscience. *Nature Reviews Neuroscience, 5*(2), 87-96.

Hester, R. L., Kinsella, G. J., and Ong, B. E. N. (2004). Effect of age on forward and

   backward span tasks. *Journal of the International Neuropsychological Society, 10*(4),

   475-481.

Hultsch, D. F., Hertzog, C., Dixon, R. A., and Small, B. J. (1998). *Memory change in the

   aged*. Cambridge: Cambridge University Press.

Jacqmin-Gadda, H., Fabrigoule, C., Commenges, D., and Dartigues, J. F. (1997). A 5-

   year longitudinal study of the Mini-Mental State Examination in normal aging.

   American Journal of Epidemiology, 145(6), 498-506.

Jones, R. N., Manly, J., Glymour, M. M., Rentz, D. M., Jefferson, A. L., and Stern, Y.

(2011). Conceptual and Measurement Challenges in Research on Cognitive Reserve.

Journal of the International Neuropsychological Society, 17(4), 593-601.

Kramer, F., Bherer, L., Colcombe, S. J., Dong, W., and Greenough, W. T. (2004).

Environmental Influences on Cognitive and Brain Plasticity During Aging. *The*

Journals of Gerontology, 59A(9), 940-957.

Lantz, B. (2013). The large sample size fallacy. *Scandinavian Journal of Caring Sciences,*

27(2), 487-492.

Lezak, M. D., Howieson, D. B., Bigler, E. D., and Tranel, D. (2012). *Neuropsychological*

Assessment (5th ed.). Oxford: Oxford University Press.

Lyketsos, C. G., Chen, L., and Anthony, J. C. (1999). Cognitive decline in adulthood: An

11.5-year follow-up of the Baltimore Epidemiologic Catchment Area study. *The*

American Journal of Psychiatry, 156(1), 58-65.

Manly, J. J., Byrd, D., Touradji, P., and Sanchez, D. (2004). Literacy and cognitive

change among ethnically diverse elders. *International journal of psychology, 39*(1),

47-60.

Monroe, T., and Carter, M. (2012). Using the Folstein Mini Mental State Exam (MMSE) to

explore methodological issues in cognitive aging research. *European Journal of*

Ageing, 9(3), 265-274.

Morris, M. C., Evans, D. A., Hebert, L. E., and Bienias, J. L. (1999). Methodological

issues in the study of cognitive decline. *American Journal of Epidemiology, 149*(9),

789-793.

Proust-Lima, C., Amieva, H., Letenneur, L., Orgogozo, J.-M., Jacqmin-Gadda, H., and

Dartigues, J.-F. (2008). Gender and Education Impact on Brain Aging: A General

Cognitive Factor Approach. *Psychology and Aging, 23*(3), 608-620.

Rentz, D. M., Locascio, J. J., Becker, J. A., and Moran, E. K. (2010). Cognition, Reserve, and Amyloid Deposition in Normal Aging. *Annals Neurology, 67*(3), 353-364.

Schaie, K. W. (1989). The Hazards of Cognitive Aging. *Gerontologist, 29*(4), 484-493.

Seeman, T. E., Huang, M.-H., Bretsky, P., Crimmins, E., Launer, L., and Guralnik, J. M. (2005). Education and APOE-e4 in longitudinal cognitive decline: MacArthur Studies of Successful Aging. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 60*(2), P74-P83.

Shichita, K., Hatano, S., Ohashi, Y., Shibata, H., and Matuzaki, T. (1986). Memory changes in the Benton Visual Retention Test between ages 70 and 75. *The Journals of Gerontology, 41*, 385-386.

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society, 8*(03), 448-460.

Stern, Y. (2009). Cognitive reserve. *Neuropsychologia, 47*(10), 2015-2028.

Tabachnick, B. G., and Fidell, L. S. (2013). *Using multivariate statistics* (6th ed.). United States of America: Pearson Education.

Tucker-Drob, E. M., Johnson, K. E., and Jones, R. N. (2009). The cognitive reserve hypothesis: A longitudinal examination of age-associated declines in reasoning and processing speed. *Developmental Psychology, 45*(2), 431-446.

Valenzuela, M. J., and Sachdev , P. (2006). Brain reserve and dementia: A systematic review. *Psychological Medicine, 36*(04), 441-454.

Van Dijk, K. R. A., Van Gerven, P. W. M., Van Boxtel, M. P. J., Van der Elst, W., and Jolles, J. (2008). No protective effects of education during normal cognitive aging: Results from the 6-year follow-up of the Maastricht aging study. *Psychology and Aging, 23*(1), 119-130.

Zahodne, L. B., *et al.* (2011). Education does not slow cognitive decline with aging: 12-Year

evidence from the Victoria Longitudinal Study. *Journal of the International*

Neuropsychological Society, 17(06), 1039-1046.

Table 1.

Studies examining the association between education and age-related cognitive decline.

Author & Date	n	Sample	Age range Years at baseline	Education Categorical or continuous	Education Mean Years (*SD*) (When available)	Study design and analysis	Cognitive Functions	Findings
Cullum et al. (2000)	135	Subsample of the Cambridge City Over-75 Cohort	75-85+	Categorical <15 years (64%) >15 years (36%)		2 assessments over 4 years Logistic Regression	The Cambridge Cognitive Examination (CAMCOG) subscales: memory, attention/calculation (combined), perception, orientation, praxis, abstract-thought and language.	Less education associated with decline in memory subscale only. Declines occurred in all other functions but were not associated with education.
Christensen et al. (2001)	887	Canberra Longitudinal Study, community sample drawn from electoral roll	70-93	Continuous & <10 (*N*=68) 10-12 (*N*=127) >12 (*N*=99)		3 assessments over 8 years *1. Latent growth curve modelling* 2. ANOVA and Regression analyses on survivors for whom complete data available (*N*=294)	Crystallised intelligence (vocabulary, similarities & NART); memory (word recognition, recall of three items, address recall); speed (SLMT); general cognitive function (MMSE)	1. Education significantly related to level of CIQ, memory and speed; education level not associated with differences in rates of decline on any cognitive measure. 2. Education associated with better performance in CIQ, speed and MMSE, but not memory. Decline evident across 8 year period for speed, memory, and MMSE but not CIQ; no differences in rate of decline as a function of level of education for any function.
Bosma et al. (2003)	708	Maastricht Aging Study longitudinal data (MAAS) drawn from a registration network of general practices	50-80	Continuous & 3 categories ranging from primary education to university education		2 assessments over 3 years Ordinary least squares regression	Processing speed (modified Stroop-Colour-Word Test); verbal memory (Verbal Learning Test); general cognitive function (MMSE)	Low educational level associated with faster decline in speed, memory and general cognitive function when compared to a high educational level. The associations lose statistical significance when controlling for mental workload and intellectual abilities.

| Seeman et al. (2005)	895	MacArthur Successful Aging Study data, subsample drawn on the basis of age and physical and mental health	70-79	0-8 years (reference group) (29.1%) 9-11 years (25.5%) 12 years (24%) 13+ years (21.5%)	Overall *M*=10.64 (*3.43*)	3 assessments over 7 years Mixed models	Memory (sum of delayed incidental recall and delayed spatial recognition); abstraction (4 items of Similarities); language (modified BNT); spatial ability (figures); global cognition (sum of scores on 5 tests listed above)	Higher education associated with better performance on all 5 cognitive measures. No significant differences in rates of decline as a function of education level across any function. For those with 13+ and 9-11 years education the APOE e4 allele was associated with faster decline in global cognition over time, similar trend observed for those with 12 years education though *p*>.05.
Alley et al. (2007)	6651	Asset and Health Dynamics of the Oldest Old (AHEAD) data, community sample	70+	Continuous	*M* = 11.1 (3.5)	4 assessments over 7 years Growth curve modelling	Verbal memory (delayed and immediate recall); working memory (Serial 7's); general mental status (Telephone Interview for Cognitive Status)	Higher education related to better performance on all three cognitive tests. Higher education was associated with slower decline in general mental status, faster decline in verbal memory and was unrelated to rate of decline in working memory.
Van Dijk et al. (2008)	872	MacArthur Successful Aging Study data, subsample drawn on the basis of age and cases with no missing data	49-81	Categorical Low (primary & lower vocational, ≤10 years) or High (secondary education or university)	Low: *M* = 8.3 (1.6) High: *M* =11.3 (2.9) Total sample: *M*=9.9 (2.8)	3 assessments over 6 years Linear mixed modelling	Verbal learning (The Verbal Learning Test); long-term memory (delayed recall modified RAVLT); attention switching (modification of Trail Making); semantic fluency (verbal fluency test); phonemic fluency (verbal fluency test)' interference control (Stroop Colour-Word Test); mental speed (Letter Digit Substitution Test); general cognitive status (MMSE).	Higher education related to better performance on all cognitive tests. Rate of decline did not differ depending on educational level on any of the cognitive tests.
Proust-Lima et al. (2008)	1800	Personnes Agées QUID (PARQUID) data, subsample without dementia	65+	Categorical Low (no primary school diploma) ~≤6 years of education (*N*=453) High (primary school diploma)~≥6 years education (*N*=1347)		8 assessments over 15 years Non-linear latent process models	Global cognitive performance (MMSE); verbal fluency (Isaacs Set Test); verbal memory (recognition form of the Benton Visual Retention Test); psychomotor speed (Digit Symbol Substitution Test); Latent cognitive factor (the common factor of the four psychometric tests)	Linear mixed models showed that subjects with higher education performed better on visual memory and psychomotor speed tasks but there were no significant differences between education groups on MMSE or verbal fluency score. Subjects with higher education declined at a faster rate for measures of global cognitive function and psychomotor speed. Non-linear models revealed that higher education was associated with faster decline in verbal fluency and psychomotor speed. There were no significant differences in rate of decline between performance on the MMSE or visual memory task.

Author	N	Study	Age	Education type	Education	Assessments / Analysis	Cognitive measures	Findings
Tucker-Drob et al. (2009)	690	Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE), subsample no-contact control group	65-94 years	Continuous	Range: 6-20 years M=13.4 (2.7)	5 assessments over 5 years Latent growth curve modelling techniques	Reasoning (Letter Series, Word Series and Letter Sets); processing speed (three tasks from the field-of-view measure); vocabulary (a test from the Kit of Factor Referenced Cognitive Tests). Composite test scores representing reasoning and speed were also computed.	Education was related to cognitive performance but not associated with rates of cognitive decline over time, both before and after controlling for baseline education
Der et al. (2010)	398	Healthy Old People in Edinburgh (HOPE) study, subsample based on completion of cognitive tests	70+	Continuous	M=10.9 (2.6) at baseline	3 assessments over 9 years Linear mixed effects modelling	Fluid intelligence/non-verbal inductive reasoning (Raven's Standard Progressive Matrices) and verbal declarative memory (Logical Memory).	Participants with higher education had a higher mean score on both cognitive outcomes at baseline. There were no interaction effects between age and education suggesting there are no differences between rates of cognitive decline between those with lower or higher education levels.
Zahodne et al. (2011)	1014	Victoria Longitudinal Study, two subsamples based on follow up period	54-95	Continuous & categorical ≤13 years or ≥14 years education	Range 6–20 years. Sample 1 M=13.4 years Sample 2 M=14.7 years Entire sample M=14.1 (3.1) years	Up to 5 assessments over 12 years Unconditional and conditional growth models and	Verbal processing speed (lexical decision and sentence verification); working memory (sentence construction and two span tests); verbal fluency (three tests from the Kit of Factor Referenced Cognitive Tests: controlled associates, opposites and figures of speech); verbal episodic memory (immediate recall from two word list learning and two story memory tasks).	After controlling for age at baseline and gender, higher education was related to better performance in all cognitive domains, especially verbal fluency. The effect of education was the smallest for the processing speed domain. However, higher education was not associated with reduced rate of decline in any cognitive domain. Considering education as a dichotomous variable did not alter this pattern of results. Excluding the covariate of baseline age and running separate models in subgroups of younger (<70 years) and older (>70 years) still revealed no association between education and the trajectory of cognitive decline.

Figure 1

Trajectories of age-related cognitive decline according to three theories of cognitive reserve
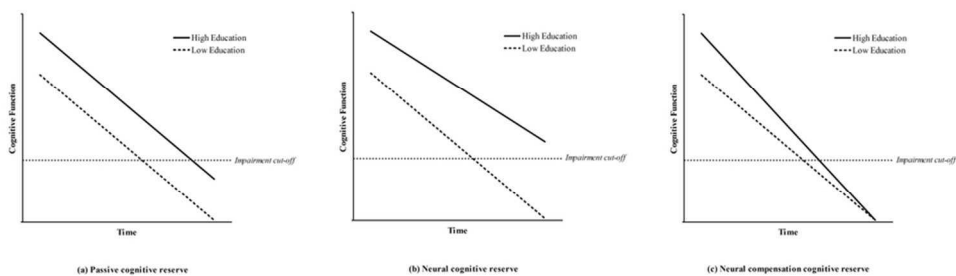
Trajectories of age-related cognitive decline according to three theories of cognitive reserve
84x26mm (300 x 300 DPI)