Sending Your Grandparents to University Increases Cognitive Reserve: The Tasmanian Healthy Brain Project

Megan E. Lenehan
University of Tasmania

Mathew J. Summers
University of the Sunshine Coast and University of Tasmania

Nichole L. Saunders
University of Tasmania, Hobart

Jeffery J. Summers
University of Tasmania, and Liverpool John Moores University

David D. Ward
University of Tasmania, Hobart

Karen Ritchie
INSERM, Montpellier, France

James C. Vickers
University of Tasmania

Objective: Increasing an individual’s level of cognitive reserve (CR) has been suggested as a nonpharmacological approach to reducing the risk for Alzheimer’s disease. We examined changes in CR in older adults participating over 4 years in the Tasmanian Healthy Brain Project. Method: A sample of 459 healthy older adults between 50 and 79 years of age underwent a comprehensive annual assessment of current CR, neuropsychological function, and psychosocial factors over a 4-year period. The intervention group of 359 older adults (M = 59.61 years, SD = 6.67) having completed a minimum of 12 months part-time university study were compared against a control reference group of 100 adults (M = 62.49 years, SD = 6.24) who did not engage in further education. Results: Growth mixture modeling demonstrated that 44.3% of the control sample showed no change in CR, whereas 92.5% of the further education participants displayed a significant linear increase in CR over the 4 years of the study. These results indicate that older adults engaging in high-level mental stimulation display an increase in CR over a 4-year period. Conclusion: Increasing mental activity in older adulthood may be a viable strategy to improve cognitive function and offset cognitive decline associated with normal aging.

Keywords: aging, education, cognitive reserve, age-related cognitive decline

One nonpharmacological approach to reducing the risk of rapid age-related cognitive decline and Alzheimer’s disease is to increase cognitive reserve (CR). CR is a theoretical construct describing the capacity of an individual to utilize preexisting brain networks efficiently (neural reserve) as well as to enlist alternate brain networks (neural compensation) when under the duress of brain pathology (Stern, 2002; Tucker & Stern, 2011). Life experiences and innate intelligence are proposed to impart CR on individuals (Stern, 2002). Research evidence has supported the role of occupational attainment (Valenzuela & Sachdev, 2006), intelligence (Whalley et al., 2000), education (e.g., Anstey & Christensen, 2000), and involvement in cognitively stimulating activities (Scarmeas & Stern, 2003) in modifying an individual’s risk for dementia. It is inferred that the modification of an individual’s risk for dementia is a result of modifications to the level of CR that the person displays.

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Megan E. Lenehan, School of Medicine (Psychology), University of Tasmania; Mathew J. Summers, School of Social Sciences, University of the Sunshine Coast, and Wicking Dementia Research & Education Centre, School of Medicine, University of Tasmania; Nichole L. Saunders, Wicking Dementia Research & Education Centre, School of Medicine, University of Tasmania; Jeffery J. Summers, School of Medicine (Psychology), University of Tasmania, and Research Institute for Sport and Exercise Sciences, Liverpool John Moores University; David D. Ward, Wicking Dementia Research & Education Centre, School of Medicine, University of Tasmania; Karen Ritchie, U1061 Neuropsychiatry, INSERM, Montpellier, France; James C. Vickers, School of Medicine, and Wicking Dementia Research & Education Centre, University of Tasmania.

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Correspondence concerning this article should be addressed to Mathew J. Summers, School of Social Sciences (ML32), University of the Sunshine Coast, Locked Bag 4, Maroochydore DC, Queensland, Australia 4558. E-mail: msummers@usc.edu.au

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CR is a theoretical construct, and therefore it is imperative to recognize that what is measured (latent variable, observed score on a task or test, or physical property) is not the same thing as the construct (Zumbo, 2007). At best, attempts to operationalize and measure CR (Harrison et al., 2015) represent proxy measures with differing levels of construct validity. Various studies have used single-proxy measures to infer the impact of CR on cognitive performance and rate of age-related cognitive decline. For example, individuals with lower occupational status have shown lower performance on measures of global cognitive function in later life (Dartigues et al., 1992; Frisoni, Rozzini, Bianchetti, & Trabucchi, 1993; Jorm et al., 1998). Similarly, a socially engaged lifestyle in later life is associated with superior cognitive performance and a reduced rate of age-related cognitive decline (Barnes, Mendes de Leon, Wilson, Bienias, & Evans, 2004; Ertel, Glymour, & Berkman, 2008; Lövdén, Ghisletta, & Lindenberger, 2005).

A key contributor to CR is thought to be education. Education is seen as increasing CR through fostering the development of new cognitive strategies (Manly, Byrd, Tzourio, Sanchez, & Stern, 2004). Educational attainment not only is associated with a decreased risk of dementia (Valenzuela & Sachdev, 2006) but also modifies the association between a direct measure of brain pathology and performance on measures of cognitive function (Bennett et al., 2003; Dufouil, Alpérovitch, & Tzourio, 2003). Despite mixed results, higher levels of education in early adulthood have been associated with superior performance on measures of cognitive function (Anstey & Christensen, 2000; Lenehan, Summers, Saunders, Summers, & Vickers, 2015). Therefore, regardless of whether education influences the rate of normal age-related cognitive decline, enhancing an individual’s level of cognitive function has the potential of preserving normal cognitive function for a longer period of time in the presence of neuropathological changes in the brain.

A recent advancement in the area of CR research has been the development of a multidimensional proxy measure of CR (Ward, Summers, Saunders, & Vickers, 2015). Previous research has typically utilized a single proxy measure, such as years of education or occupational attainment, to infer an individual’s level of CR. However, this approach may not be accurate given that education, occupational attainment, and leisure activities differentially contribute to CR (Foubert-Samier et al., 2012). Acknowledging the multivariate nature of CR, we developed two factor-analysis-defined latent proxy measures of CR (Ward et al., 2015). Prior CR combines proxy measures traditionally associated with CR, including education, preexisting intellectual capacity, and five subscores from the Life Experience Questionnaire (Valenzuela & Sachdev, 2007). However, because CR theoretically develops in response to new life experiences throughout the life span, we developed a second proxy measure of CR designed to assess dynamic change in CR (Ward et al., 2015). This measure of current CR incorporates cognitive tests suitable for repeated assessment including current intellectual capacity and academic ability (Ward et al., 2015). Whereas prior CR enables CR set earlier in life to be determined, current CR enables possible increases in CR following an intervention to be quantified. University study typically involves complex mental and social stimulation that is increasingly being accessed by older populations.

The Tasmanian Healthy Brain Project (THBP) is the first prospective study in the world to examine the potential of university level of education in later life to reduce age-related cognitive decline (Summers et al., 2013). The THBP has recruited a sample of older adults, age 50–79 years at commencement in the study, from the island state of Tasmania, Australia. The THBP adopts a mixed-group longitudinal design, comparing older adults who engaged in later-life tertiary study with a control group who did not undertake further education. The THBP undertakes annual assessment of each participant, examining cognitive reserve, neuropsychological/cognitive function, psychosocial function, and genetic factors. This article examines whether engaging healthy older adults in university-level education results in a measureable change in CR when accounting for preexisting CR levels for each individual.

Method

Participants

Data from participants in the THBP as of December 31, 2014, were utilized for this study. The initial sample comprised 566 adults age 50–79 years enrolled in the THBP (Summers et al., 2013). Of these, 19 were excluded from the analysis due to English being a second, rather than primary, language. A further 41 were excluded due to having withdrawn from the project prior to any follow-up testing. Of the remaining 498 participants, a further 39 were missing data necessary to calculate prior CR score. Because prior CR was used as a covariate in the analysis, participants with missing data on this variable were excluded. The final sample used in the analysis consisted of 459 healthy older adults.

Participants were not randomly allocated to conditions but volunteered to participate in either the intervention or control condition. Those in the intervention group (N = 359) undertook a minimum of 12 months part-time or full-time university study, with a minimum study load of two units at the undergraduate or postgraduate level. The remaining 100 participants in the control group did not engage in any tertiary-level study. Participants who presented with a medical, neurological, or psychiatric disorder that could potentially influence neuropsychological test performance were precluded from entry into the THBP. The project was approved by the Human Research Ethics Committee (Tasmania) Network, and further details of the study protocol have been published elsewhere (Summers et al., 2013).

Measures

Participants in the THBP completed a comprehensive testing battery. For the full project protocol, refer to Summers et al. (2013). The Dementia Rating Scale–2 (DRS–2; Jurica, Leitten, & Mattis, 2001), the Hospital Anxiety and Depression Scale (HADS; Snaith, 2003), and the Medical Health Status questionnaire (Summers et al., 2013) were completed to ensure participants were free from dementia and of sound psychological and physical health. The Personal Wellbeing Index (PWI; International Wellbeing Group, 2006) and the 18-item version of the Lubben Social Network Scale (LSNS-18; Lubben & Girona, 2003) are self-report questionnaires and were completed to assess quality of life and perceived social support within the sample.
Prior CR. The tests included in the calculation of prior CR were as specified in Ward et al. (2015): the Wechsler Test of Adult Reading (WTAR; Wechsler, 2001) to estimate baseline intellectual capacity; five subscores (Young Adulthood Specific and Nonspecific; and the Midlife Specific, Nonspecific, and Continuing Education Bonus) from the Wide Range Achievement Test, Fourth Edition, Progress Monitoring Version (WRAT-4-PMV; Roid & Ledbetter, 2006) to assess current academic ability. The WRAT-4-PMV has four alternate versions of each test, which were utilized to avoid learning effects (e.g., Form 1 at baseline, Form 2 at Year 1 follow-up).

Current CR. The tests used for the calculation of current CR as specified in Ward et al. (2015) were: the Wechsler Adult Intelligence Scale, Third Edition, Short Form 1 (WAIS-III-SF1; Donnell, Pliskin, Holdnack, Axelrod, & Randolph, 2007) to estimate current intellectual capacity and the spelling and math computation subtests of the Wide Range Achievement Test, Fourth Edition, Progress Monitoring Version (WRAT-4-PMV; Roid & Ledbetter, 2006) to assess current academic ability. The WRAT-4-PMV has four alternate versions of each test, which were utilized to avoid learning effects (e.g., Forms 1–4 of the WRAT). The full THBP took approximately 4 hr to complete, and participants were encouraged to take short breaks as needed to avoid fatigue (Summers et al., 2013).

Procedure

The elements of the test battery used in the current analysis were as follows: WTAR, DRS-2, Medical Health Status, LEQ, WAIS-III-SF1, WRAT-4-PMV, HADS, PWI, and LSNS-18. The LEQ and WTAR IQ estimate were collected only once, at baseline. Retesting occurred at 1-year intervals (±1 month). When available, alternate versions of tests were used to minimize familiarity effects (e.g., Forms 1–4 of the WRAT). The full THBP took approximately 4 hr to complete, and participants were encouraged to take short breaks as needed to avoid fatigue (Summers et al., 2013).

Analysis

Calculating prior CR and current CR. Current CR and prior CR were calculated for each participant using factor analysis defined regression coefficients as developed and described by Ward and colleagues (2015). This equation was used to calculate prior CR: .370 (WTAR full-scale IQ) + .408 (prior education in years) + .567 (LEQ Young Adulthood Specific) + .565 (Young Adulthood Nonspecific) + .630 (LEQ Midlife Nonspecific) + .875 (LEQ Midlife Continuing Education Bonus) + 1.004 (LEQ Midlife Specific). This equation was used to calculate current CR: .454 (WAIS-III-SF1) + .369 (WRAT-4-PMV Spelling Level Equivalent Score [LES]) + .463 (WRAT-4-PMV Math Computation LES). Because the regression-based formula for prior CR and current CR are based on z-transformed raw scores, current CR scores for Years 1, 2, and 3 (retesting) were z-transformed against the mean and standard deviation of the entire sample at baseline (Year 0). Therefore, positive CR scores represent an increase in CR relative to baseline CR scores.

Modeling approach. Growth mixture modeling (GMM) was conducted using Mplus 7.0 (Muthén & Muthén, 1998–2012) maximum likelihood with robust standard errors estimation. GMM identifies unobserved, homogenous subgroups of individuals from larger heterogeneous populations on the basis of similar response patterns (Muthén & Muthén, 1998–2012). This is important, given research has shown that various subpopulations exist within a broader population and are differentially impacted by an intervention (Jackson & Sher, 2005). This is particularly relevant in the field of CR research, given that a potential increase in CR could depend on each individual’s untapped CR capacity. Taking this into account, the conventional latent curve growth approach to analysis could oversimplify and potentially underestimate change (Jung & Wickrama, 2008). As such, GMM was conducted on the control and intervention groups separately to examine whether each group was characterized by classes of individuals with distinct patterns of change in current CR. We chose to analyze each group separately (relative comparison) to enable an examination of differences between individuals high or low in CR in the rate of CR change over the 4-year period.

The procedure outlined by Jung and Wickrama (2008) for conducting GMM was followed. Because the number of unobserved groups is unknown to the investigator, the suggested procedure is to identify the best fitting single-class latent growth curve model (e.g., linear or quadratic) and then progressively test models with more classes until the model fit is no longer improved by the addition of extra classes (Jung & Wickrama, 2008). In all models time was paramatized with scores that represented years since study entry (0, 1, 2, 3 for the linear term and 0, 1, 4, 9 for the quadratic term). Initially, Mplus default parameters were used. The intercepts of the outcome variable at the four time points were fixed at zero. The intercepts, residual variances, and covariances of the growth factors were estimated and not held equal across classes. The model allowed for the effect of the covariates on the growth parameters for each class to be estimated. Incremental model changes such as fixing growth factor variance to zero were also investigated to find the best fitting model. In each group, initial status of the model represented mean current CR at baseline, the linear growth rate represented the annual rate of change in current CR, and the quadratic growth rate indicated the change in the rate of change (accelerating or decelerating change). Because the models included a covariate (conditional models), the intercepts describe the growth factors (i.e., initial starting point, linear term, and quadratic term) after taking into account the effect of covariates, so these are reported throughout.

Model evaluation. In the initial latent growth curve analysis (single class), model fit was assessed by considering a range of fit indices: the likelihood-ratio chi-square, the root-mean-square error of approximation (RMSEA), the standardized root-mean-square residual (SRMR), and the comparative fit index (CFI). As a general rule, a smaller chi-square indicates a better fit. An RMSEA value less than .05 and an SRMR less than .05 indicate a good-fitting model (Geiser, 2013). The CFI should be larger than .95. For GMM, the optimal number of classes was determined by considering both the Bayes information criteria (BIC) and the sample-adjusted BIC. As a general rule, the model with the smallest information criterion is preferred (Geiser, 2013). The interpretability of classes was also considered with reference to theory and prior research (Schaie, 1989).
Results

Descriptive Data

Data from a sample of 459 participants was included in this study. Participants at commencement in the study were 50–79 years of age, of average intelligence, free from dementia, and not clinically depressed or anxious (see Table 1). The control group was significantly older, \( t(496) = 4.32, p < .001 \), and had lower current CR at baseline, \( t(494) = -3.05, p < .01 \), compared to the intervention group. However, because there were no significant correlations between age and current CR at any time point in either the control group or the intervention group, the decision was made not to include age as a covariate in further analysis. There were no significant differences between the control and intervention groups across baseline measures of prior CR, global cognition, estimated premorbid IQ, level of anxiety, or level of depression. The mean scores of current CR of the control group were lower at baseline compared to the experimental group, but both groups appeared to increase current CR score over time.

In the control group, the best fitting single class model was a linear model with prior CR included as a time-invariant covariate, \( \chi^2(7, N = 100) = 23.00, p = .01 \). RMSEA = .15, confidence interval (CI) [.09, .22], SRMR = .04, CFI = .95. In the intervention group, the best fitting model was a quadratic model with prior CR included as a covariate, \( \chi^2(7, N = 359) = 26.45, p = .001 \). RMSEA = .09, CI [.05, .13], SRMR .04, CFI = .98. Zero variance in the linear and quadratic growth factors was specified to avoid an inadmissible model due to negative residual variances. These models were used to progressively test models with more classes in each of the control and intervention groups.

GMM control group. The lowest Adjusted Bayes Information Criterion (ABIC) corresponded to a two-class model. The entropy was calculated at .60, which indicated that the model had a reasonable classification of individuals into classes. Class 1 (maintainers) comprised 44.3% of the control group. In Class 1, the linear slope was not significant, indicating that linear change in current CR did not significantly differ from zero (see Figure 1 and Table 2). The remainder of the control group were in Class 2 (improvers; 55.7%). This class had a significant linear slope, suggesting progressive increase in CR over the 4-year period (see Figure 1 and Table 2). The effect of prior CR was consistent in both classes (see Table 2). Higher prior CR was associated with a higher current CR score at baseline. Prior CR did not have a significant association with the rate of linear change in current CR over time. The classes were examined to determine whether other demographic variables could account for class membership. However, there were no differences between decliners and improvers in sex, age, level of depression, level of anxiety, personal wellbeing, or social connectedness.

Intervention group. The lowest ABIC corresponded to a two-class model in the intervention group also, and the entropy value of .78 indicated good separation of individuals into classes. Class 1 (maintainers) constituted a minority of the intervention group (7.5%). In this class the significant negative linear growth term indicates that current CR score decreased over the 4-year period, and the significant quadratic term suggests that CR change accelerated over time (see Figure 2 and Table 3). The majority of the intervention group were in Class 2 (improvers; 92.5%). The significant linear growth term indicates that the current CR for this class increased over the 4-year period (see Figure 2 and Table 3). The negative quadratic term indicated the rate of increase decelerated over time, though this parameter was not significant (see Table 3). Within Class 1 (maintainers), higher prior CR was associated with lower current CR at baseline. However, within Class 2 (improvers), higher prior CR was associated with higher current CR at baseline. In both classes, prior CR had no association with the rate of linear or quadratic change in current CR over time (see Table 3).

The classes were examined to see whether other demographic variables could describe class membership. However, there were no differences between maintainers and improvers in sex, age,
level of depression, level of anxiety, personal wellbeing, or social connectedness.

**Discussion**

The hypothesis that individuals who receive an education intervention will display an increase in CR compared to a control group was supported by the results of the study. In both the control group and the intervention group, there appear to be two distinct subgroups of individuals. In the intervention group, approximately 92.5% of the sample displayed a significant increase in CR over time, whereas the remaining 7.5% generally maintained CR across the 4-year period. Among those in the intervention group, the maintainers displayed higher levels of CR at baseline relative to the improvers. In contrast, among the control group participants, 44.3% displayed no change in CR over time, with the remaining 55.7% displaying a significant increase in CR over the 4 years. The increase in CR seen in this subgroup of control participants was evident in those individuals who displayed below-average CR at baseline. Despite increasing over time, the level of CR of the control improvers remained below the 50th percentile of the baseline CR of the entire cohort.

**Table 2**

Estimates (and Standard Errors) of Class-Specific Intercept Parameters and the Effect of Prior CR on Class-Specific Growth Terms for the Control Group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model estimate (SE)</th>
<th>Effect size d</th>
<th>Class 1: Maintainers (n = 43)</th>
<th>Class 2: Improvers (n = 57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial status</td>
<td>.598 (.242)*</td>
<td></td>
<td>- .674 (.114)**</td>
<td>- .185 (.052)**</td>
</tr>
<tr>
<td>Linear growth rate</td>
<td>.040 (.044)</td>
<td></td>
<td>.185 (.052)**</td>
<td>1.67</td>
</tr>
<tr>
<td>Prior CR covariate</td>
<td>.180 (.078)*</td>
<td></td>
<td>.253 (.058)**</td>
<td>0.62</td>
</tr>
<tr>
<td>Initial status</td>
<td>-.022 (.019)</td>
<td></td>
<td>-.004 (.018)</td>
<td>.55</td>
</tr>
</tbody>
</table>

*Note. CR = cognitive reserve; d = β_{11}(time)/\text{SD}_{\text{pooled}} (Feingold, 2009). *p < .05. **p < .01.*
These results indicate that the overwhelming majority of healthy older adults who engaged in some degree of university-level education for at least 12 months displayed a measurable increase in CR over a 4-year period. The small number of participants who displayed no change in CR over time while attending university already had higher than average CR at baseline (~1.2 SDs above the cohort at baseline). This tentatively suggests that individuals with already high levels of current CR may lack the capacity for further increases in current CR. This finding should be interpreted with caution, however, due to the small sample size for this group (n = 15).

The findings of the present research are consistent with other investigations reporting benefits from cognitive training programs (Ball et al., 2002) and physical activity (Kramer et al., 1999) on cognitive function, presumably through the positive effect these activities have on building CR. The proportion of the control group who showed improvement in current CR despite not receiving the intervention is comparable to that shown in other studies. For example, up to 37% of the no-contact control group in the study by Ball and colleagues (2002) showed increases on a range of cognitive measures despite not receiving a cognitive training program. That 55.7% of the control group in the present study displayed an increase in CR may reflect unreported involvement in mentally complex and stimulating activities outside of the THBP. It would have been informative to have an ongoing measure of noneducational life experiences and activities, beyond baseline, in order to explain control group growth.

For three of the groups, prior CR tended to be associated with higher current CR at baseline. This finding suggests that prior life experience, such as education, promotes higher levels of CR in later life. However, in the intervention-maintainers group, prior CR was associated with lower current CR at baseline. Due to the small sample size of this group (n = 15), such associations must be treated with caution. There was no association between prior CR and the rate of linear or quadratic change over time. Thus, prior CR predicts initial levels of current CR for the majority of participants but is not predictive of the rate or degree of change in CR that occurs following exposure to university-level education.

Though the benefit of early-life education on late-life cognitive function is well reported (Anstey & Christensen, 2000; Lenehan et al., 2015), this research is the first to investigate the potential benefit of a period of formal education in later life to enhance CR. It also utilizes a multivariate estimation of both preexisting and current CR in order to provide an accurate evaluation of the potential benefit associated with the education intervention (Ward et al., 2015). However, it is important to note that the modeling approaches utilized rely on extrapolation from an incomplete dataset. The THBP is an ongoing study, and it will be interesting to see whether these findings are robust once the full sample proceeds through all of the time points in future years. There are a number of limitations that should be noted in interpreting the results of the present study. Noticeably, the control group reaches just the minimum sample size of 100, which is typically preferred for latent growth modeling (Curran, Obeidat, & Losardo, 2010). The total number of person-by-time observations influences statistical power (Curran et al., 2010). Additionally, due to the progressive recruitment of participants into the THBP over a 4-year period, the models estimated are based on extrapolation from an incomplete data set, in which some individuals have only one or two observations over time. This may result in increased within-group variability, as indicated by a larger standard error of the mean, which is more evident in the control group and therefore less power to detect significant intercept and slopes. Future research will need to reexamine the findings of the present analysis once the complete THBP participant pool finishes assessment over all time points.

It is also important to note that although unavoidable due to the design of the present study, the recruitment of voluntary participants into the THBP may result in a self-selection bias of older adults with an interest in pursuing further education and a history of higher level secondary school education required for entry into University-level study. Therefore the participants in the THBP are likely to have a higher level of prior education and a greater interest in education than WOULD the wider community. However, it is important to note that the THBP is designed to determine whether increased mental activity in later life is beneficial to cognitive function in an aging population. As such, the THBP has utilized higher education as the tool for stimulating mental activity. A finding of increased cognitive capacity would be evidence of an effect of increased mental activity that could be achieved through the pursuit of mentally stimulating activities distinct from university-level education.

To summarize, the findings of the present study indicate that engaging healthy older adults in university-level education FOR a minimum of 12 months results in a measurable and significant increase in cognitive reserve. Future research is planned to determine whether this increase in cognitive reserve is sufficient to offset age-related cognitive decline and, further, whether this increase in CR mitigates the risk for degenerative conditions such as dementia or delays the onset of clinical symptoms of dementia in those at risk of dementia.

References


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