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

Sending your Grandparents to university increases cognitive reserve: The Tasmanian Healthy Brain Project

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Abstract

Objective Increasing an individual's level of cognitive reserve (CR) has been suggested as a non-pharmacological approach to reducing an individual's 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 aged between 50-79. Participants underwent a comprehensive annual assessment of current CR, neuropsychological function and psychosocial factors over a four year period. The intervention group of 359 older adults (M = 59.61, SD = 6.67 years) having completed a minimum of 12 months part-time university study were compared against a control reference group of 100 adults (M = 62.49, SD = 6.24) who did not engage in further education**.**

Results Growth Mixture Modelling demonstrated that 44.3% of the control sample showed no change in CR whereas 92.5% 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.

Conclusions Increasing mental activity in older adulthood may be a viable strategy to improve cognitive function and offset cognitive decline associated with normal aging.

Introduction

One non-pharmacological 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 utilise pre-existing 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 supports 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 an individual displays.

CR is a theoretical construct, therefore, it is imperative to recognise 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 operationalise 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, 1992; Frisoni, Rozzini, Bianchetti, & Trabucchi, 1993; Jorm, Rodgers, Henderson, & Korten, 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, 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, Touradji, & Sanchez, 2004). Educational attainment is not only 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, Wilson, Schneider, & Evans, 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 typically utilises 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, pre-existing intellectual capacity, and five sub-scores from the Life Experience Questionnaire (Valenzuela & Sachdev, 2007). However, as CR theoretically develops in response to new life experiences throughout the lifespan, 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). While prior CR enables CR set earlier in life to be determined, current CR measure 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 a world first prospective study examining 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, aged 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 have engaged in later-life tertiary study with a control reference group who do not undertake further education. The THBP undertakes annual assessment of each participant examining cognitive reserve, neuropsychological/cognitive function, psychosocial function and genetic factors. This paper examines whether engaging healthy older adults in university-level education results in a measureable change in CR when accounting for pre-existing CR levels for each individual.

Methods

Participants

Data from participants in the THBP as of the 31 December 2014 was utilised for this study. The initial sample comprised 566 adults aged between 50 and 79 years enrolled in the THBP

(Summers et al., 2013). Of these, 19 cases were excluded from the analysis due to English being a second, rather than primary language. A further 41 cases were excluded from analysis 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. As 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 conditions. Participants 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 undergraduate or post graduate levels. The remaining 100 subjects in the control reference 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).

Materials

Participants in the THBP completed a comprehensive testing battery. For the full project protocol refer to Summers et al. (2013). The Dementia Rating Scale, 2nd edition (DRS-2; Jurica, Leitten, & Mattis, 2001) the Hospital Anxiety and Depression Scale (Snaith, 2003) and the Medical Health Status questionnaire (Summers et al., 2013) were administered 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 & Gironda, 2003) are self-report questionnaires and were administered 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) (The Psychological Corporation, 2001) to estimate baseline intellectual capacity; five sub-scores from the Life Experience Questionnaire (LEQ) (Valenzuela & Sachdev, 2007) (Young Adulthood Specific and Non-specific; and the Midlife Specific, Non-specific and Continuing Education Bonus) to quantify previous lifetime experience in education, occupation and leisure activities; and the Medical Health Questionnaire (Summers et al., 2013) to obtain each individuals total years of prior education.

Current CR

The tests used for the calculation of current CR as specified in Ward et al. (2015) were: the Wechsler Adult Intelligence Scale, 3rd 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, 4th 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 utilised to avoid learning effects (e.g. Form 1 at baseline, Form 2 at year 1 follow up).

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. The LEQ and WTAR IQ estimate were only collected once, at baseline. Retesting occurred at one year intervals (± one month). When available alternate versions of tests were used to minimise familiarity effects, for example, forms 1-4 of the WRAT were utilised. The full THBP took approximately four hours to complete and subjects 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 (Ward et al., 2015). The equation to calculate prior CR = .370 (WTAR FSIQ) + .408 (Prior education in years) + .567 (LEQ Young Adulthood Specific) + .565 (Young Adulthood Non-specific) + .630 (LEQ Midlife Non-specific) + .875 (LEQ Midlife Continuing Education Bonus) + 1.004 (LEQ Midlife Specific). The equation used to calculate current CR = .454 (WAIS-III-SF1) + .369 (WRAT-4-PMV Spelling LES) + .463 (WRAT-4-PMV Math Computation LES). As the regression based formula for prior CR and current CR are based on z-score transformed raw

scores; current CR scores for years 1, 2 and 3 (retesting) were z-transformed against the mean and SD of the entire sample at baseline (year 0). Therefore, positive CR scores represent an increase in CR relative to baseline CR scores.

Modelling approach

Growth Mixture Modelling (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 is characterised by classes of individuals with distinct patterns of change in current CR.

The procedure outlined by Jung and Wickrama (2008) for conducting GMM was followed. As 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 paramatised 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). As 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 squared error of approximation (RMSEA), standardised root mean square residual (SRMR) and comparative fit index (CFI). As a general rule a smaller chi-square indicates a better fit. A RMSEA value <.05 and a SRMR <.05 is seen to 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 Bayesian 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 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 (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, as 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 overtime.

[INSERT TABLE 1 HERE]

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, 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 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 (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 four year period (Figure 1 and Table 2). The effect of prior CR was consistent in both classes (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 if 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.

[INSERT FIGURE 1 HERE]

[INSERT TABLE 2 HERE]

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 four year period and the significant quadratic term suggests that CR change accelerated over time (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 (Figure 2 and Table 3). The negative quadratic term indicated the rate of increase decelerated over time, though this parameter was not significant (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 (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.

[INSERT FIGURE 2 HERE]

[INSERT TABLE 3 HERE]

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, while the remaining 7.5% generally maintained CR across the four year period. Among 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 four 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 50^{th} percentile of the baseline CR of the entire cohort.

These results indicate that the overwhelming majority of healthy older adults who engage in some degree of university level education for at least 12 months display a measureable 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 *SD* 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 non-educational 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 utilises a

multivariate estimation of both pre-existing 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 modelling approaches utilised 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 just reaches the minimum sample size of 100 which is typically preferred for latent growth modelling (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 dataset, where 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 re-examine the findings of the present analysis as the complete THBP participant pool completes assessment over all time points.

Although unavoidable due to the design of the present study, it is also important to note that 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 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 utilised 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 which could be achieved through the pursuit of mentally stimulating activities distinct from university level education.

To summarise, the findings of the present study indicate that engaging healthy older adults in university level education of a minimum of 12 months results in a measureable 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.

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Figure legends

Figure 1. Control group 2 class model estimated means adjusted for the effect of prior CR *(dotted horizontal line indicates the 50th percentile of current CR of the entire cohort at baseline).*

Figure 2. Intervention group 2 class model estimated means adjusted for the effect of prior CR *(dotted horizontal line indicates the 50th percentile of current CR of the entire cohort at baseline).*

Figure 1

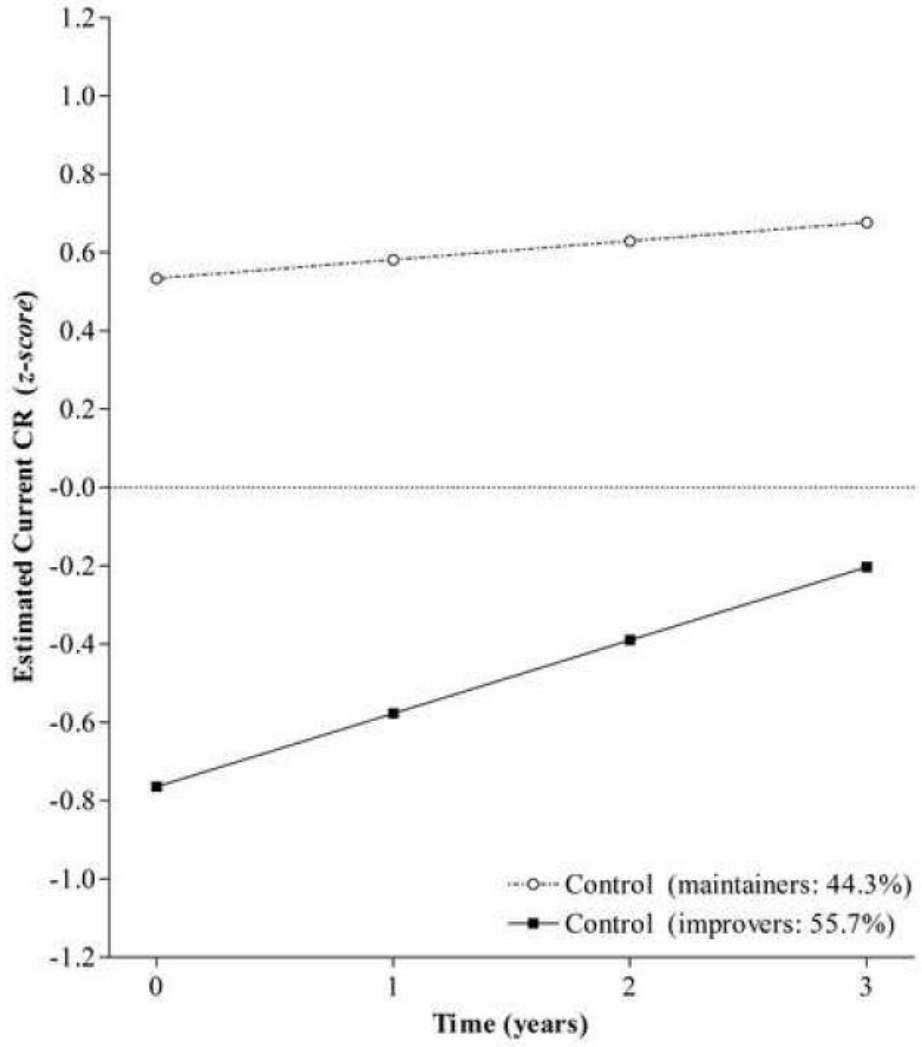
1.2
1.0
0.8
0.6
0.4
0.2
-0.0
-0.2
-0.4
-0.6
-0.8
-1.0
-1.2
Estimated Current CR (z-score)
0
1
2
3
Time (years)
Control (maintainers: 44.3%)
Control (improvers: 55.7%)

Figure 2

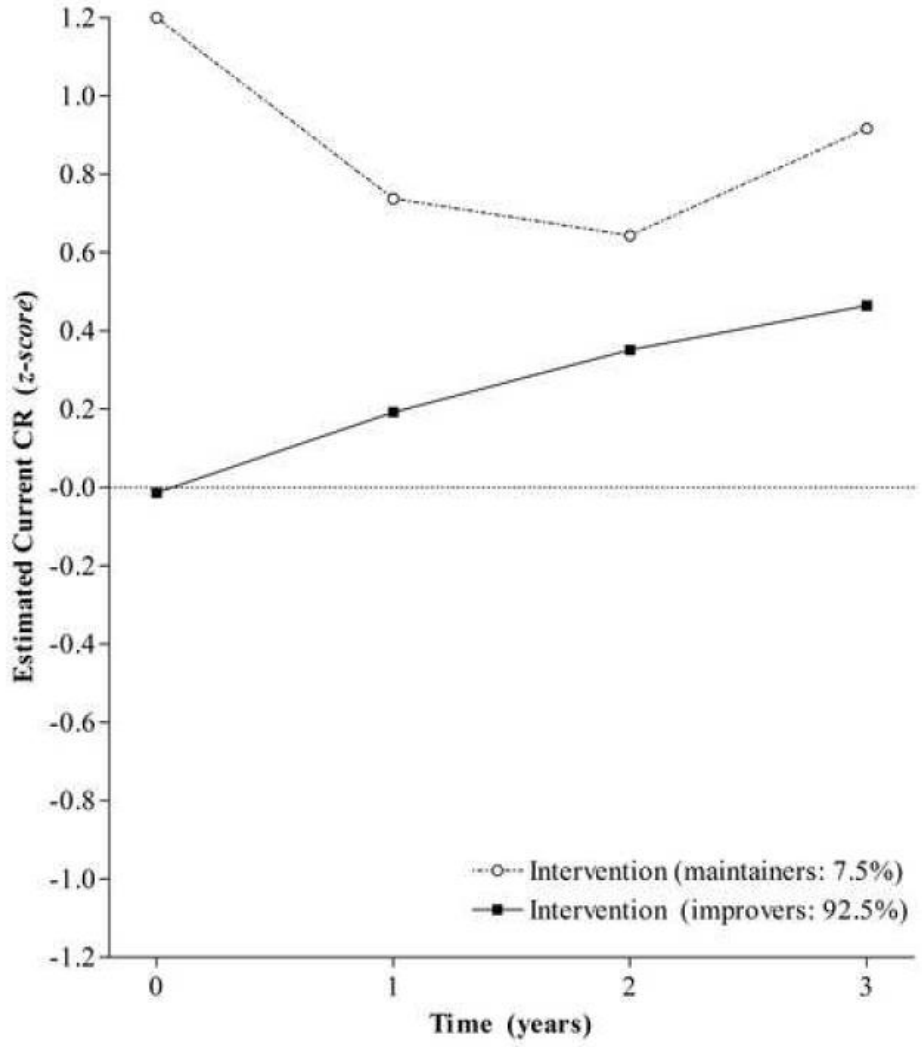
1.2
1.0
0.8
0.6
0.4
0.2
-0.0
-0.2
-0.4
-0.6
-0.8
-1.0
-1.2
Estimated Current CR (z-score)
0
1
2
3
Time (years)
Intervention (maintainers: 7.5%)
Intervention (improvers: 92.5%)

Table 1. *Sample demographic and CR as a function of group*

	Control *N* at T0 = 100 M *(SD)*	Intervention *N* at T0 = 359	*Independent samples t-test* *p.*	Obtained effect size (*d*)	Power
Female *N* (%)	64 (61%)	273 (69.5%)	(χ^2) = .10		
Baseline Age	62.62 *(6.34)*	59.48 *(6.69)*	< .001	.482	.828
DRS-2 AEMSS	11.81 *(2.27)*	11.96 *(2.07)*	.52	.069	.004
WTAR (est. FSIQ)	112.23 *(5.10)*	112.65 *(5.47)*	.47	.079	.005
HADS - Anxiety	5.51 *(2.91)*	5.24 *(3.15)*	.35	.090	.006
HADS - Depression	2.86 *(2.28)*	2.38 *(2.26)*	.05	.212	.076
Prior CR	-.36 *(2.27)*	.13 *(2.28)*	.06	.215	.081
Current CR					
T0 -Baseline	-.26 *(1.01)*	.07 *(.98)*	.002	.332	.354
T1	-.05 *(1.12)*	.32 *(1.05)*	.04	.341	.384
T2	.11 *(.97)*	.34 *(1.00)*	.11	.234	.108
T3	.22 *(1.11)*	.68 *(.98)*	.01	.439	.716

DRS-2 AEMSS = Mattis Dementia Rating Scale age and education corrected Mayo scaled score; WTAR (est FSIQ) = Wechsler Test of Adult Reading Scale estimated full scale IQ; HADS = Hospital Anxiety and Depression Scale; CR = cognitive reserve.

Table 2. *Estimates (S.E.) of class specific intercept parameters and the effect of prior CR on class specific growth terms for the control group*

	Class 1: Maintainers (*n* =43)	**Class 2: Improvers (*n* = 57)**	**Effect Size *d***
	Model estimates (*SE*)	**Model estimates (*SE*)**	
Initial status	.598 (.242)*	-.674 (.114)**	4.34
Linear growth rate	.040 (.044)	.185 (.052)**	1.67
Covariate			
Prior CR			
Initial status	.180 (.078)*	.253 (.058)**	0.62
Linear term	-.022 (.019)	-.004 (.018)	0.55

Note: * $p. < .05$, ** $p. < .01$.
$d = \beta_{11}(\text{time})/SD_{\text{pooled}}$ (Feingold, 2009)

Table 3. *Estimates (S.E.) of class specific intercept parameters and the effect of prior CR on class specific growth terms for the intervention group*

	Class 1: Maintainers (*n* = 15)	**Class 2: Improvers (*n* = 344)**	**Effect Size *d***
	Model estimates (*SE*)	**Model estimates (*SE*)**	
Initial status	1.227 (.229)**	-.038 (.053)	5.17
Linear growth rate	-.664 (.203)	.226 (.051)**	3.79
Quadratic growth rate	.189 (.072)**	-.022 (.018)	2.55
Covariate			
Prior CR			
Initial status	-.208 (.062)**	.182 (.022)**	3.89
Linear term	.133 (.082)**	.024 (.021)	1.13
Quadratic term	-.037 (.028)	-.005 (.008)	0.87

Note: * $p. < .05$, ** $p. < .01$.
$d = \beta_{11}(\text{time})/SD_{\text{pooled}}$ (Feingold, 2009)