Cognitive Reserve Capacity: Construct Validity and Modifiability in Healthy Ageing

A thesis presented to Dublin City University for the Degree of Doctor of Philosophy

By

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Declaration

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List of Abbreviations

AD	Alzheimer's Disease
AIC	Akaike Information Criterion
aMCI	Amnestic Mild Cognitive Impairment
aMCI-AD	Amnestic Mild Cognitive Impairment to Alzheimer's Disease
APOE ε4	Apolipoprotein E-*ε*4
BRC	Brain Reserve Capacity
BRI	Behavioural Regulation Index
CANTAB	Cambridge Neuropsychological Test Automated Battery
CAPI	Computer Assistant Personal Interviewing
CCE	Cumulative Cognitive Enrichment
CDCR model	Cognitive Domains and Cognitive Reserve model
CFA	Confirmatory Factor Analysis
CFA	Confirmatory Factor Analysis
CFI	Comparative Fit Index
CI	Confidence Interval
CMA	Complex Mental Activity
CR	Cognitive Reserve
CRIq	Cognitive Reserve Index Questionnaire
CRT	Choice Reaction Time
CST	Concept Shifting Test
CTT	Colour Trails Task
DESCRIPA	Development of Screening Guidelines and Diagnostic Criteria for Predementia Alzheimer's disease

DF	Degrees of Freedom
DSST	Digit Symbol Substitution Test
EF	Executive Function
EF/PR	Executive Function/Processing Resources
EFA	Exploratory Factor Analysis
Est	Unstandardised Parameter Estimate
Est/SE	Test Statistic (z-value)
FLU	Verbal Fluency Test
FP7	7th Framework Programme for Research and Technological Development
FU	Follow-Up
GEC	Global Executive Composite
GIT	Groningen Intelligence Test
HDL	High-density lipoprotein
In-MINDD	Innovative Midlife Interventions for Dementia Deterrence
IQ	Intelligence Quotient
ISI	Inter-stimulus interval
ISSDA	Irish Social Science Data Archive
K-S	Kolmogorov-Smirnov Test
LDMT	Letter-Digit Modalities Test
LDT	Letter Digit Task
LOA	Level of Occupational Attainment
MAAS	Maastricht Ageing Study
MCI	Mild Cognitive Impairment

MFQ	Memory Functioning Questionnaire
MI	Metacognition Index
ML	Maximum Likelihood
MLR	Robust Maximum Likelihood
MMSE	Mini Mental State Examination
MS	Multiple Sclerosis
NA	Noradrenaline
PEBL	Psychology Experiment Building Language
POMS	Profile of Mood States
PR	Processing Resources
PRMQ	Prospective and Retrospective Memory Questionnaire
pSTROOP	Primed Stroop Task
RCL	Recall
RCT	Randomised Controlled Trial
RMSEA	Root Mean Square Error of Approximation
RNH	Registration Network of Family Practices
SART	Sustained Attention to Response Task
SD	Standard Deviation
SE	Standard Error
SEM	Structural Equation Modelling
SMEM	Subjective Memory
SPC	Semi Partial Correlations
SPSS	Statistical Analysis Software Package
SR	Structural Regression

SRMR	Standardised Root Mean Square Residual
STD	Standardised Parameter Estimate
STDYX	Completely Standardised Parameter Estimate
STR	Stroop Colour Word Test
TBI	Traumatic Brain Injury
TC	High Serum Total Cholesterol
TIA	Transient Ischemic Attack
TILDA	The Irish Longitudinal Study on Ageing
TLI	Tucker-Lewis Index
TMT	Trail Making Task
VaD	Vascular Dementia
VIF	Variance Inflation Factor
WAIS	Wechsler Adult Intelligence Scale
WLLT	Word List Learning Test
WLSMV	Robust Weighted Least Squares (Means and Variances Adjusted)
WLT	Verbal Learning Task
WM	Working Memory
WRMR	Weighted Root Mean Square Residual

Abstract

Cognitive Reserve capacity: Construct validity and modifiability in healthy ageing

– Lisa M. McGarrigle

Cognitive Reserve (CR) capacity can be viewed as the maximum processing potential of neural systems that support adaptive cognitive performance in age-related cognitive decline. CR is a complex construct that cannot be directly measured as it refers to processing efficiency of standard, and non-standard networks. Proxy factors such as psychosocial/lifestyle and cognitive variables are therefore used but are in need of construct validation; and importantly, the cognitive factors potentially involved in CR capacity, such as executive function (EF), may be modifiable. The research objectives were to investigate in healthy adults (a) the validity of an a priori model of CR capacity and cognitive outcomes, and (b) the modifiability of the construct of CR capacity through adaptive EF training. Firstly, the construct validity of Satz et al.'s (2011) four-factor CR capacity model was explored using data from the Maastricht Ageing Study (MAAS) (study 1). Exploratory and confirmatory factor analysis established a two-factor model comprised of executive function/processing resources (EF/PR) and cumulative cognitive enrichment (CCE), which was validated using data from the Irish Longitudinal Study on Ageing (TILDA) (study 2). Predictive relationships between this model and global cognition/memory outcomes were also explored (study 3) and replicated (study 4), providing support for a strong, positive predictive relationship between CR capacity and outcomes at baseline and follow-up. Healthy older adults with variable memory concerns (aged ≥50) were profiled to further investigate relationships between the CR capacity model parameters and global cognition/memory (study 5). EF/PR was again found to be predictive of global cognition/memory scores. The effects of a targeted novel response inhibition training intervention (active control vs. experimental) aimed at boosting a formative component of CR capacity (EF/PR) were investigated (study 6). Both levels of training were found to have direct and near transfer effects following five weeks of training. However, effects did not generalise to far transfer measures (e.g., global cognition/memory outcomes). Overall, this novel approach to modelling CR suggests that control processes are an important contributor to CR capacity, are modifiable, and therefore represent a promising target for future interventions aimed at improving cognitive function in healthy ageing.

Chapter 1: Introduction to the Research Programme

1.1 Background

1.1.1 Brief Background: Innovative Midlife Interventions for Dementia Deterrence (In-MINDD)

This PhD project was embedded within a larger European study entitled Innovate Midlife Interventions for Dementia Deterrence (In-MINDD). In-MINDD was an FP7 funded project that aimed to confirm modifiable risk factors in dementia through the formulation and validation of a multi-factorial model of dementia risk and protection. Focusing on the modifiable factors associated with dementia risk offers a way to profile 'at-risk' individuals and tailor interventions before the clinical phase of disease trajectory. Based on meta-analysis and a Delphi expert study, a comprehensive list of risk/protective factors in dementia was established and validated in two ageing datasets, the Maastricht Ageing Study (MAAS) and a multicentre dataset consisting of eight European population based cohorts - Development of Screening Guidelines and Diagnostic Criteria for Predementia Alzheimer's disease (DESCRIPA). Risk/protective factors included lifestyle variables such as diet, exercise, smoking, depression and cognitive activity (Deckers et al., 2015). These findings were used to construct a risk prediction algorithm that quantified an individual's risk of developing dementia. In-MINDD also aimed to translate this risk prediction model into an online tool (In-MINDD profiler) for use in primary care to help assess if a person's lifestyle supports long-term brain health. The In-MINDD profiler was purposely designed and developed to generate a profile of how at-risk/protected individuals in midlife (aged 40-60 years) are of developing dementia. In a feasibility study, the In-MINDD profiler was used to generate an individualised risk score and a personalised plan for individuals participating in the study aimed at helping them take actions to reduce their risk of/increase their protection against developing dementia in later life (O'Donnell et al., 2015). Analysis of pre- and post-risk scores suggest a small but statistically significant difference in risk following the In-MINDD intervention. In the coming years, the predicted increase in the elderly population in Ireland will result in a significant increase in the number of people with dementia. This will impact on both family caregivers and the general health and social care system as they come under increasing pressure to provide and maintain adequate levels of care. Identifying and modifying risk and protective factors may delay onset of dementia and significantly reduce the number of dementia diagnoses (Alzheimer Society, 2010). It has been estimated that delaying onset of Alzheimer's disease (AD) by five years would reduce the overall prevalence rate by 50%, profoundly reducing caregiver burden and institutional care and enhancing quality of life (Thal et al., 1997).

1.1.2 PhD Research Programme

This PhD project complemented the overall goals of In-MINDD through its focus on identification of modifiable protective factors in age-related cognitive decline (Profile goal) and developing a targeted intervention aimed at boosting protection (Modification goal). The PhD programme was developed under a protection or 'cognitive reserve' (CR) framework. CR has been defined as an active process that involves efficiency of cognitive networks/capacity and the recruitment of alternative networks in protection against the impact of brain changes (Y. Stern, 2009), and can be considered core to protection in age-related decline. The programme was divided into two sections reflective of the two key research objectives. The first objective (Section I) was to develop a protective model of cognitive/lifestyle factors in healthy ageing using data from the longitudinal Maastricht Ageing Study (MAAS) (study 1). The factors involved in CR are not clearly understood, therefore the first objective of the research programme involved exploration of the construct validity of the CR concept. This objective also involved validation of a measurement model of CR capacity in a secondary ageing dataset, the Irish Longitudinal Study on Ageing (TILDA) (study 2). Longitudinal modelling was also conducted using the MAAS data to explore the predictive relationships between this measurement model of CR capacity and cognitive measures that are sensitive to age-related decline (study 3). These models were then replicated using TILDA data to confirm the generalisability of the relationships (study 4).

The second objective of the research programme (Section II) mapped onto the modification goal of In-MINDD. This objective concerned the modifiability of a construct of CR capacity and involved the design and implementation of a novel cognitive training intervention in healthy older adults aged 50 years or over with varying subjective memory concerns. Firstly, pre-intervention data was used to further validate the CR capacity/outcome model relationships found in Section I as well as to explore CR relationships that were beyond the scope of the modelling studies. Pre-intervention data was also used to profile CR capacity model measures as a function of a subjective measure of memory ability (study 5). Individuals with memory concerns are worthy of study as subjective memory complaints may be a marker of objective memory decline. Secondly, the effects of a novel, adaptive cognitive training task on CR model parameters was investigated following five weeks of online training (study 6) (see Appendix A for DCU REC approval for the aforementioned studies).

In sum, the research programme focuses on the identification of the factors involved in CR and their potential for modification. Developing a clearer understanding of the cognitive mechanisms involved in building CR capacity and their modifiability could have important implications for health policy and primary prevention. For instance, clarification of the multidimensional factors involved in CR capacity and a greater understanding of how these factors interact with each other in healthy ageing could inform the development of simple and clear public messages about what kinds of activities are likely to make a difference to cognitive health. This research could compliment current European initiatives concerned with increasing the societal impact of health research, such as Hello Brain which provides easy to understand scientific information to the public about brain health.

1.1.3 Summary of the Research Programme

The following provides a summary of the chapter content of the research thesis:

- ❖ Chapter 2 broadly reviews the literature on risk and protective factors in dementia and cognitive decline before outlining the CR theoretical framework, issues surrounding measurement and construct validity of CR, and the modifiability of the factors hypothesised to be involved in CR capacity.

Section I: Modelling CR Capacity

- Chapter 3 (study 1) describes the use of exploratory and confirmatory factor analysis to probe the underlying relationships in an a priori four-factor CR capacity model proposed by Satz, Cole, Hardy and Rassovsky (2011). Convergent and discriminant validity of the model across age-groups is assessed in healthy adults using data from the Maastricht Ageing Study (MAAS; *n*=1823).
- Chapter 4 (study 2) describes the validation of the measurement model in Irish healthy older adults using data from a secondary ageing dataset – the Irish Longitudinal Study on Ageing (TILDA; *n*=8504).
- Chapter 5 (study 3) outlines the development a structural model of CR capacity based on the findings outlined in Chapters 3 and 4. Multivariate modelling is used to investigate the predictive relationships between the CR capacity factors and global cognition/memory outcomes in healthy older adults at baseline, six- and 12-year follow-up in MAAS.
- Chapter 6 (study 4) describes the replication of the structural model of CR capacity and global cognition/memory outcomes in healthy older adults using TILDA data. The model was replicated using baseline data and data from two-year follow-up assessments.

Section II: Modifiability of CR Capacity

- Chapter 7 (study 5) further validates the CR capacity model relationships established in Section I in a small sample of healthy Irish older adults, pre-intervention. The chapter also outlines CR capacity relationships with additional parameters that were beyond the scope of the modelling studies. CR capacity (as modelled in Section I) is profiled as a function of subjective memory concerns.
- Chapter 8 (study 6) explores the modifiability of CR capacity through a targeted cognitive training intervention in this sample of healthy Irish older adults.

- ❖ Finally, Chapter 9 synthesises the research findings across Sections I and II, before discussing the theoretical and practical implications of the research and future directions for research in the field.

Chapter 2: Literature Review

2.1 Risk and Protection in Dementia and Cognitive Decline

Dementia can be viewed as the clinical manifestation of disease processes in the brain and is characterised by symptoms such as disturbed memory and comprehension, speech and language difficulties and behavioural changes beyond that expected in healthy ageing (Alzheimer Society of Ireland, 2013b). Underlying disease processes can be varied, with Alzheimer's disease (AD) being the most common form of dementia. AD is a degenerative brain syndrome characterised by protein abnormalities (plaques and tangles) in the brain and accounts for 60-80% of dementia cases (Thies & Bleiler, 2011). Other forms of dementia include vascular dementia (VaD) caused by decreased blood flow to parts of the brain, and dementia with lewy bodies characterised by abnormal protein deposits (Alzheimer Society of Ireland, 2013a). Additionally, dementia may develop in people who have progressive brain diseases such as Parkinson's Disease (Thies & Bleiler, 2011). It follows that dementia is a complex disorder and many factors contribute to its pathogeneses including genetics, oxidative stress and inflammation, as well as features such as amyloid plaques, neurofibrillary tangles and synaptic and neuronal depletion (Sultana & Butterfield, 2010). Related to dementia is the concept of cognitive decline in healthy ageing, or normative cognitive decline. Objective cognitive decline can be viewed as reduced information processing capacity and efficiency as a result of healthy ageing (Ramscar, Hendrix, Shaoul, Milin, & Baayen, 2014). Subjective cognitive decline, on the other hand, can be viewed as memory concerns, or other cognitive concerns, experienced by an individual despite having intact cognitive performance (Jessen, 2014). While the expression and trajectory of cognitive decline can vary widely among older adults, it is likely that by the age of 70 years, the majority of people will experience significant, but manageable, decline in cognitive functioning compared to their cognitive functioning in middle-age (Gow & Gilhooly, 2003). Distinguishing between decline as a result of pathology and decline as a result of healthy ageing is not always straightforward as brain changes due to dementia are often found in healthy older adults, and many of the risk factors implicated in dementia have also been found to increase the risk of cognitive decline in healthy ageing (Deary et al., 2009).

When considering dementia and cognitive decline, both risk and protective factors must be taken into account. However, there is little consistency or clarity in epidemiological research with regard to the definition and use of the terms ‘risk factor’ and ‘protective factor’. For the purposes of this review a risk factor is defined as an exposure that is statistically related to a negative outcome (Burt, 2001). A protective factor has the reverse effect of statistically enhancing the likelihood of a positive outcome, or lessening the negative consequences associated with risk exposure (Jessor, Turbin, & Costa, 1998). With regard to dementia and cognitive decline, protective factors can be viewed as delaying disease onset and/or slowing the rate of decline for at-risk individuals. In this way, risk and protective factors can often be viewed as interdependent. It is likely a focus on the identification of modifiable risk/protective factors in dementia and cognitive decline is necessary if effective preventive strategies are to be implemented. A recent review of modifiable risk and protection in dementia combined findings from a systematic review and a Delphi expert consensus study and concluded that vascular, cognitive and lifestyle factors were implicated in risk and protection (Deckers et al., 2015). These findings may have important implications, as the ageing population in the developed world is on the rise leading to a corresponding increase in the number of adults with long-term conditions such as dementia as well as age-related cognitive decline. The population of those aged 65 and over in Ireland currently represents 11% of the total population and this figure is expected to double by 2031 (Cahill, O’Shea, & Pierce, 2012).While the majority of these individuals will not develop dementia, a greater understanding of the mitigating factors in cognitive decline in healthy ageing could help to improve cognitive function and quality of life for this group (Harada, Love, & Triebel, 2013).

2.1.1 Risk Factors, Dementia, and Cognitive Decline

A number of biological, vascular and behavioural factors that influence an individual’s risk of developing dementia have been identified. Biological risk factors are non-modifiable and include age, genetic factors and gender. There is evidence to support an association between vascular risk factors, such as hypertension, cholesterol, diabetes and obesity, and the development of AD. Research of particular interest to the current research programme has also identified several behavioural and lifestyle factors associated with dementia risk.

Evidence for these risk factors is outlined below and critically assessed in light of recent literature.

Biological Risk Factors and Dementia

Age is the most significant dementia risk factor. The incidence and prevalence of Alzheimer's Disease doubles every five years after the age of 65 (McCullagh, Craig, McIlroy, & Passmore, 2001). After the age of 85, risk increases to almost fifty percent (Alzheimer's Association, 2014). However, dementia should be viewed as age-related rather than age-dependent and development of dementia in later life is not an inevitable part of the ageing process (Gao, Hendrie, Hall, & Hui, 1998).

Genetic variations have also been found to play an important role in the development of dementia. A genetic factor in late-onset AD is apolipoprotein E-*ε*4 (*APOE ε*4). *APOE ε*4 is one of three common forms (*ε*2, *ε*3 and *ε*4) of the APOE gene which provides instructions for a protein that carries cholesterol in the bloodstream (Thies & Bleiler, 2011). A Swedish twin study found that 60-80% of late-onset AD can be attributed to genetic effects (Pedersen, Gatz, Berg, & Johansson, 2004). Carriers of the *APOE ε*4 gene have an increased risk of developing AD than those who inherit the *ε*2 and *ε*3 forms of the *APOE* gene (Thies & Bleiler, 2011).

Research suggests that the prevalence of AD is higher in women than in men (Andersen et al., 1999; J.-H. Chen, Lin, & Chen, 2009; Fratiglioni et al., 1997) while the incidence of vascular dementia (VaD) is higher in men than women (Ruitenberg, Ott, Van Swieten, Hofman, & Breteler, 2001). It remains unclear whether this difference is due to biology, female longevity or behavioural sex differences across the life-span. It may be the case that these findings can be explained by the protective effects of oestrogen in pre-menopausal women, and earlier death for men from cardiovascular disease (Andersen et al., 1999).

Vascular Risk Factors and Dementia

Hypertension has been identified as a potentially modifiable risk factor for dementia. A number of systematic reviews have examined the association between hypertension and increased risk of AD and dementia (Kennelly, Lawlor, & Kenny, 2009; Kloppenborg, Van den

Berg, Kappelle, & Biessels, 2008; Qiu, Winblad, & Fratiglioni, 2005). The relationship between blood pressure and dementia risk is complex and appears to differ as a function of age (Qiu et al., 2005). Hypertension in midlife is consistently associated with higher risk of AD and dementia in later life, whereas hypertension in late life is not consistently associated with AD and dementia. In fact, it appears that hypotension is associated with increased risk of AD and dementia in late life (Kennelly et al., 2009; Kloppenborg et al., 2008). While there are some inconsistencies in the literature regarding vascular risk factors and dementia as a function of age, a recent review by Barnes and Yaffe (2011) provides strong evidence from epidemiological studies and randomised controlled trials (RCTs) that midlife, but not late life, hypertension is associated with an increased risk of AD and dementia.

Additionally, high serum total cholesterol (TC) values in midlife have been found to increase risk of late-life AD (Whitmer, Sidney, Selby, Johnston, & Yaffe, 2005). However, the effect of TC on dementia risk does not appear to occur in late-life and there may also be different cardiovascular risk factor profiles for AD and VaD (Anstey, Lipnicki, & Low, 2008). The association between diabetes mellitus, a metabolic disorder resulting from defects in insulin secretion, and an increased risk of dementia has been inconsistent. However, a number of studies have linked type II diabetes with an increased risk of VaD (Bruce et al., 2003; Luchsinger, Tang, Stern, Shea, & Mayeux, 2001; Stewart & Liolitsa, 1999).

Obesity, which is related to vascular disorders, may also be linked with dementia. Recently, strong evidence in the form of meta-analyses have reported a statistically significant association between obesity and increased risk of AD (Beydoun, Beydoun, & Wang, 2008; Profenno, Porsteinsson, & Faraone, 2010). Research suggests that this association may be age-dependent. A recent study found that obesity in midlife is associated with a significantly increased risk of dementia, whereas in late life, obesity is associated with reduced dementia risk. Being underweight in late life is also associated with increased risk of dementia (Fitzpatrick et al., 2009). Furthermore, research has shown that health status as indexed by a measure of frailty, is a risk factor in AD and vascular dementia for older adults (Solfrizzi et al., 2013; Song, Mitnitski, & Rockwood, 2011).

Behavioural Risk Factors and Dementia

Environmental and behavioural factors such as depression, stress, smoking and alcohol consumption have demonstrated links with dementia risk. There is a large body of evidence to indicate that people with a history of depression have an increased risk of developing dementia (Barnes & Yaffe, 2011; Buntinx, Kester, Bergers, & Knottnerus, 1996; Dal Forno et al., 2005; Fernández Martínez et al., 2008; Jorm, 2001; Ownby, Crocco, Acevedo, John, & Loewenstein, 2006). A meta-analysis of 13 studies found that people with a history of depression have about a two-times increased risk of dementia compared to those with no history of depression (Jorm, 2001). These findings have been supported by a more recent systematic review and meta-analysis that found similar results (Ownby et al., 2006). There has also been some evidence suggesting that an individual’s reactivity to stress results in subsequent risk of dementia. A study by Crowe, Andel, Pedersen and Gatz (2007) found that greater reactivity to stress predicted higher risk of dementia when controlling for age, education, sex, occupational status, alcohol use, and smoking status. Co-twin control analyses also revealed that dementia probands were more likely to be highly reactive to stress than their non-demented co-twins (Crowe, Andel, Pedersen, Johansson, & Gatz, 2003).

Initial case-control studies indicated that smoking was associated with a reduced risk of AD (Almeida, Hulse, Lawrence, & Flicker, 2002). However, more recent longitudinal research indicates that the risks of AD and dementia increase with smoking (Anstey, Von Sanden, Salim, & O’Kearney, 2007). It has been estimated that nearly 14% of AD cases worldwide and 11% in the USA are potentially attributable to smoking (Barnes & Yaffe, 2011). Cognitive impairment is frequently observed in heavy drinkers as excessive alcohol consumption can lead to alcohol related brain damage (Peters, Peters, Warner, Beckett, & Bulpitt, 2008). Binge drinking in midlife has also been associated with an increased risk of dementia (Järvenpää, Rinne, Koskenvuo, Räihä, & Kaprio, 2005). Some studies have shown that heavy alcohol consumption is associated with an increased risk of dementia in patients with mild cognitive impairment or in men carrying the *APOE ε*4 allele (Mukamal et al., 2003; Xu et al., 2009).

Risk factors associated with Cognitive Decline

Risk factors associated with cognitive decline are considered to be the same as those involved in dementia risk. For instance, Singh-Manoux et al. (2012) investigated the relationship between age and cognitive decline healthy adults aged 45 to 70 years old over a ten-year period. It was found that scores in memory, reasoning and fluency declined for all participants, but there was evidence for a faster decline in older individuals. The authors concluded that cognitive decline is already evident in middle age (45-49 years of age) and this finding may have implications for interventions aiming to alter cognitive ageing trajectories, as they may be more effective if applied when an individual is first experiencing decline. Recent research, in an Irish population aged over 50 years, explored the relationship between frailty (defined as the physical inability to respond adequately to external stressors) and cognitive functioning in an ageing population (D. A. Robertson, Savva, Coen, & Kenny, 2014). It was found that weakness and walking speed were linked to poorer cognition across multiple domains, while exhaustion was linked with both objective and subjective measures of memory. These findings suggest that frailty may be a risk factor in both objective and subjective decline outcomes in later life. Metabolic risk factors such as obesity, hypertension, and low high-density lipoprotein (HDL) levels, have also been identified as risk factors in cognitive decline, as well as dementia (Yaffe et al., 2004). Modification of these factors through behavioural and/or medical treatment could potentially delay brain changes that occur with normal ageing (Rodrigue et al., 2013).

Summary and Evaluation of Risk Factors in Dementia and Cognitive Decline

Overall, research has provided strong evidence for a number of risk factors in dementia and cognitive decline in the form of observational studies, systematic reviews, and meta-analyses. These factors range from non-modifiable biological risk factors such as age and genetics, to potentially modifiable behavioural and lifestyle factors, such as depression and smoking. Of particular interest to researchers is the degree to which modifiable risk factors are related to protective factors that prevent or delay the expression of dementia, or cognitive decline in healthy ageing. As outlined at the beginning of this review, risk and protective factors can be viewed as interrelated, with protective factors having the reverse effect of risk factors by statistically enhancing the likelihood of positive outcomes, or reducing the negative effects associated with risk exposure (Jessor et al., 1998). Therefore, modification of risk can be viewed as a means of increasing protection by preventing or delaying symptom expression. However, there have been few RCTs conducted to investigate the effect of risk factor modification on the prevalence of dementia and cognitive decline in the general population (Barnes & Yaffe, 2011).

2.1.2 Protective Factors, Dementia, and Cognitive Decline

As acknowledged above, there exists an interrelationship between risk and protective factors in the sense that increasing protection can be viewed as reducing the negative effects of exposure to risk (Jessor et al., 1998). There is extensive epidemiological and experimental evidence for the protective effects of a number of lifestyle and cognitive factors that may potentially delay dementia onset and/or slow the rate of cognitive decline. The following section outlines and critically evaluates the current evidence for a range of lifestyle and cognitive protective factors in dementia and cognitive decline.

Lifestyle Protective Factors and Dementia

Lifestyle factors such as diet and physical activity have been suggested as having a protective effect against dementia. There is evidence to indicate that certain nutritional factors have links with lower dementia risk. For example, dietary habits may play an important role in protecting against dementia: however, research results are mixed. Epidemiologic research has suggests that higher dietary intake of antioxidants, vitamins B_6, B_{12}, and folate, unsaturated fatty acids, and fish are related to lower risk of AD (Luchsinger, Noble, & Scarmeas, 2007; Nourhashémi et al., 2000). Modest to moderate alcohol intake (wine in particular) and adherence to the Mediterranean diet is protective against dementia (Scarmeas et al., 2009). The Mediterranean diet is characterized by high intake of fish, vegetables, legumes, fruits, cereals and unsaturated fatty acids; and low intake of dairy products, meat and saturated fatty acids; as well as a regular but moderate intake of alcohol (Scarmeas, Stern, Mayeux, & Luchsinger, 2006; Scarmeas, Stern, Tang, Mayeux, & Luchsinger, 2006). However, randomized clinical trials of the effects of vitamins E, B_{12}, B_6 and folate have not demonstrated significant cognitive benefit and RCTs for other nutrients or diets are not available (Luchsinger et al., 2007). A protective effect of light to moderate alcohol consumption has been observed in a number of studies with a recent meta-analysis indicating that alcohol consumption may be protective for AD (Peters et al., 2008). This protective effect may well be the result of several mechanisms such as an increased level of high-density lipoprotein (HDL) cholesterol leading to lower platelet aggregation and possibly lower risk of stroke/ischemia (Agarwal, 2002). It has also been put forward that the antioxidant properties of the flavonoids in wine prevent the oxidative damage implicated in dementia (Peters et al., 2008).

The link between physical activity and cognitive health has been the focus of a great deal of research suggesting that being physically active may help to preserve cognitive function and protect against dementia. Research on a community sample selected from the Canadian Study of Health and Ageing, a prospective cohort study of dementia, identified significant trends for increased protection against dementia with greater physical activity and concluded that regular physical activity could represent an important protective factor for dementia and cognitive decline in elderly individuals (Laurin, Verreault, Lindsay, MacPherson, & Rockwood, 2001). These findings have been supported by a number of observational studies (Abbott et al., 2004; Karp et al., 2006; Podewils et al., 2005; Yaffe, Barnes, Nevitt, Lui, & Covinsky, 2001). Results from a recent systematic review indicate that physical activity is inversely associated with dementia risk, however the optimal dose of physical activity remains unclear (Hamer & Chida, 2009). The protective effect of physical activity might be due to reduced vascular risk and obesity, lower levels of inflammatory markers, enhanced fitness, and neuronal creation and function (Barnes, Whitmer, & Yaffe, 2007). While there have been some inconsistencies in findings, these may be explained by the use of different measurements of cognition, varied lengths of study period, and different participant characteristics being used to evaluate the effect of physical activity on the risk of dementia and cognitive decline (J.-H. Chen et al., 2009). Also, it may be the case that genetic factors mediate the effects of physical activity on dementia risk. Podewils et al. (2005) conducted a large prospective cohort study of community-dwelling older adults and identified an inverse association between physical activity and dementia risk for *APOE ε*4 non-carriers, but no association was identified for carriers of the *APOE ε*4 allele.

Cognitive Protective Factors and Dementia

Participation in cognitively stimulating activities across the lifespan has been associated with reduced incident dementia in later life (Bosma et al., 2002; Crowe et al., 2003; Scarmeas, Levy, Tang, Manly, & Stern, 2001; Wilson et al., 2013). Activities that require cognitive effort, such as reading, doing crosswords or puzzles, or learning a new language, have been linked with protection against developing dementia in later life (Crowe et al., 2003; Helzner, Scarmeas, Cosentino, Portet, & Stern, 2007; Hughes, 2010; Sattler, Toro, Schönknecht, & Schröder, 2012; Valenzuela et al., 2011; Wilson et al., 2002). A similar effect has been observed for social connectedness and participation in social activities, as high levels of these activities have been linked with reduced risk of developing dementia (Wang, Karp, Winblad, & Fratiglioni, 2002). The Kungsholmen Project, a Swedish community-based study, also found that a rich social network had a protective effect against dementia (Fratiglioni, Wang, Ericsson, Maytan, & Winblad, 2000).

Large-scale epidemiological studies have also indicated that high levels of education, occupational complexity and cognitively stimulating leisure activities are protective against dementia (Valenzuela & Sachdev, 2006). Education level in particular is a widely acknowledged protective factor in dementia and cognitive decline. However, in recent years the evidence for the protective effects of education has been mixed. For instance, a 6-year longitudinal study by Alley et al. (2007) found that higher educated adults showed slower rates of decline on a measure of global cognition, but not on measures of verbal recall and working memory. Furthermore, a 6-year longitudinal study by van Dijk et al. (2008) found that education had no significant effect on changes on cognition over time. Anstey and Christensen (2000) suggest that findings in relation to the protective effects of education must be interpreted with caution due to methodological limitations and the possibility of publication bias.

In relation to participation in stimulating leisure activities, a longitudinal cohort study by Wilson et al. (2002), with a mean follow-up of 4.5 years, was conducted on 801 cognitively healthy older catholic nuns, priests and brothers in the United States. Frequency of participation in common cognitive leisure activities (such as reading a newspaper) were rated at baseline. A proportional hazards model controlling for age, sex, and education found that a one-point increase in cognitive activity score was associated with a 33% reduction in risk of AD (hazard ratio, 0.67; 95% confidence interval, 0.49-0.92)A systematic review investigating the role of cognitive leisure activities examined 13 observational studies, the majority of which were cohort design. Meta-analysis was deemed inappropriate due to a number of factors including the heterogeneity of interventions, the study design, participant groupings, and the different stages of life at which they were measured. It was found that five out of six studies demonstrated a positive association between participation in cognitive activities and a reduced risk of developing AD and other dementias when interventions occurred in midlife. Moreover, six out of seven studies indicated a positive association for late life participation. There was some evidence to suggest that certain activities may be more beneficial than others (such as reading), however, this must be interpreted cautiously due to the subjective nature of activity inclusion across studies and the absence of RCTs in the review (C. Stern & Munn, 2010).

Protective Factors associated with Cognitive Decline

As with risk factors in cognitive decline, protective factors in decline are in line with those of dementia. For instance, lifestyle protective factors such as physical activity have also been shown to be protective against both objective and subjective decline in healthy ageing. A meta-analysis evaluating the role of physical activity in cognitive decline in healthy ageing, predominantly indicated by scores on a measures of global cognition, found that high levels of physical activity were significantly protective against decline at follow-up, and even low to moderate levels of physical activity were found to have a protective effect (Sofi et al., 2011). Furthermore, a randomised controlled trial of a 24-week physical activity intervention conducted between 2004 and 2007 found that physical activity provided a modest improvement in cognition in adults with subjective memory impairment over an 18-month follow-up period (Lautenschlager et al., 2008). Cognitively stimulating activities have also been linked with protection against decline in older adults. For instance, a study investigating the effects of playing a musical instrument and cognitive ageing found that older adults with at least ten years' experience playing a musical instrument performed better on tasks of non-verbal memory, naming, and executive processes, compared to controls (Hanna-Pladdy & MacKay, 2011). Similarly, high levels of social involvement and maintaining numerous personal relationships have been associated with better cognitive performance in later life (Crowe et al., 2003; Fritsch et al., 2005) and have been linked to prevention of cognitive decline in community-dwelling elderly persons (Bassuk, Glass, & Berkman, 1999). More recently, a review examined observational studies focusing on cognitive activity and reported a series of mixed effects models that included both baseline activity and change in cognitive activity and their predictive relationships with cognitive outcomes over 21 years using data from four longitudinal ageing studies (M. B. Mitchell, Cimino, et al., 2012). Consistent evidence for cross-sectional relationships between cognitive activity level and cognitive test performance were observed. Results suggest that individuals with a decrease in cognitive activity over time relative to their baseline levels are at an increased risk of cognitive decline. Results also suggest that increases in cognitive activity from baseline levels are associated with improved cognitive performance. However, it was found that baseline activity at younger age was not predictive of rates of decline later in life; thus, not supporting the argument that early life engagement in cognitive activities increases the ability to mitigate future age-related cognitive decline. Conversely, change in activity was found to be associated with changes in cognitive performance on neuropsychological tests, suggesting that change in cognitive activity from an individual's previous level is associated with improved cognitive performance measured at the same time point. The authors acknowledge that these effects may be transitory, however.

Summary and Evaluation of Protective Factors in Dementia and Cognitive Decline

Overall, there is strong evidence for a number of lifestyle/cognitive protective factors in both dementia and cognitive decline in healthy ageing. Protective factors related to lifestyle and cognitive activity can be considered modifiable and therefore subject to targeted interventions aimed at increasing protection by preventing or delayed symptom expression.

While it is clear from the literature that risk and protective factors are related concepts, what remains unclear is the degree to which modifiable factors thought to reduce risk/increase protection may overlap and interact with each other, and together influence cognitive outcomes over time. What is also unclear from the literature on risk and protection is the nature of the underlying cognitive mechanisms that facilitate protection from dementia and cognitive decline. The protective effects of lifestyle and cognitive activity can be characterised as “cognitive reserve”, and questions regarding the interactions between protective factors and the mechanisms by which protection operates can be addressed within this framework.

In sum, the literature outlined in this section gives a broad overview of both non-modifiable (e.g., age, genetic factors) and potentially modifiable (e.g., lifestyle/cognitive variables) risk and protective factors. Following on from the goals of In-MINDD, where the focus was on modifiable risk in healthy mid-life individuals, this research programme places the emphasis on the related concept of protection in healthy ageing populations. The development of a predictive model of protection can be addressed within a “cognitive reserve” framework whereby lifestyle/cognitive activity are viewed as protective with regard to cognitive outcomes.

2.2 Cognitive Reserve: Characterising the Protective Effects of Lifestyle/Cognitive Activity

Cognitive reserve has traditionally been defined as the hypothesised capacity of the brain to cope with brain damage in order to minimise clinical manifestations (Y. Stern, 2009). The concept of reserve was proposed following the observation that the severity of neuropathological manifestations did not always correlate with brain damage severity (Solé-Padullés et al., 2009). For instance, post-mortem examinations have found high rates of Alzheimer’s disease neurodegeneration in individuals who did not display neurocognitive clinical manifestations of the disease (Katzman et al., 1988). In this sense, risk and protection can be characterised from a reserve framework in that risk factors in dementia and cognitive decline have been shown to be predictive of neural changes/atrophy, but this does not always result in the expression of cognitive deficits, possibly due to the buffering effect of protective factors such as lifestyle and cognitive activity. Therefore, risk analyses in relation to dementia and cognitive decline needs to take protective factors that influence disease expression into account. Research has consistently demonstrated a significant protective effect of cognitive leisure activities, and findings suggest that early as well as late life activity have the potential to significantly moderate the risk of AD by increasing reserve (Karp et al., 2006; Scarmeas et al., 2001; Verghese et al., 2003; Wilson et al., 2002). The concept of reserve has also been used to explain variability in behaviour indicative of cognitive decline in healthy ageing, especially under increased load/stress (Zihl, Fink, Pargent, Ziegler, & Bühner, 2014). As follows, reserve can be broadly viewed as a protective mechanism against decline in both healthy ageing and in the face of pathology. Furthermore, reserve can be viewed as an explanatory construct with regard to the frequently observed discrepancy between neural changes and expected cognitive function outcomes.

The mechanisms underlying the association between lifestyle/cognitive activity and effects on cognition are not clearly understood (Marioni et al., 2012; Wilson et al., 2013). Two proposed mechanisms to explain how cognitive activity protects brain function from neuropathology include disease modification and compensation. Disease modification suggests a decreased risk for developing neuropathology, or a slower rate of the expression of pathology, while compensation indicates a better ability to cope with underlying brain damage (Marioni et al., 2012). Mechanisms by which cognitive activity protects healthy brains from age-related changes and cognitive decline may include variability in the efficiency of cognitive processing in healthy brains (Y. Stern, 2002). All of these mechanisms characterise reserve. Furthermore, reserve should not be viewed as a fixed trait which is determined early in life but as something that may be actively enhanced by an individual's lifestyle (Sattler et al., 2012). However, interventions aimed at enhancing reserve may be impeded due to operationalisations of the concept of reserve differing across studies (see *Table 1* for a glossary of selected definitions). This definitional variability highlights a need for clarification of the reserve concept, its measurement, and underlying neural mechanisms if effective interventions are to be developed.

Table 1. Definitional complexity of the cognitive reserve concept

Author(s)	Conceptual Definition	Operationalisation/Measurement	Neural Mechanism(s)
Jones et al., 2011; Scarmeas et al., 2003; Singh-Manoux et al., 2011; Solé-Padullés et al., 2009; Y. Stern, 2002; Reed et al., 2011; Zahodne et al., 2013	CR can be viewed as the observed discrepancy between the level of brain pathology and the clinical expression of that pathology	Cognitive activity/lifestyle proxies such as education level, occupational attainment, social and mental activity, crystallised IQ; Variance in cognition that is not explained by a specific set of known brain variables	Disease modification/compensation
Y. Stern, 2009; Tucker-Drob, Johnson, & Jones, 2009	Individual differences in cognitive networks underlying task performance in healthy populations (i.e., more efficient networks may result in greater capacity and/or flexibility, which may facilitate coping in the face of brain pathology)	Cognitive tasks measuring speed and executive abilities that reflect efficiency of functioning.	Greater efficiency/capacity in brain networks in healthy ageing and/or disease
I. H. Robertson, 2013, 2014	The ability of the brain to adapt to pathology and maintain function. Cognitive mechanisms that assist adaptations to age-related changes and pathology (networks for arousal, novelty, attention, awareness, and working memory) may be facilitated by noradrenergic (NA) function	Cognitive activity/lifestyle proxies; NA activity	Disease modification/compensation; maintenance of structural and functional integrity and connectivity of NA system in healthy ageing and disease.
Zihl, Fink, Pargent, Ziegler, & Bühner, 2014	The brain's capacity to cope with challenge (e.g., brain injury/dysfunction; age-related decline)	Improvement in cognitive performance (gain) in a complex testing-the-limits paradigm, the digit symbol substitution test (DSST).	Greater efficiency/capacity in brain networks in healthy ageing and/or disease

2.2.1 Paradigmatic Approaches to Reserve

Paradigmatic approaches to CR differ in terms of whether they view reserve as a passive process, or view the brain as actively attempting to cope with cognitive decline as a result of healthy ageing, or compensate for pathology (Y. Stern, 2002). Passive models define reserve in terms of the amount of brain damage that can be sustained before reaching a clinical expression threshold. The brain reserve capacity (BRC) construct depends on a passive threshold model of reserve (Katzman, 1993). It asserts that reserve derives from brain size or number of synapses. Under this model it is hypothesised that larger brains can sustain more neuropathology before clinical deficit can be observed. The BRC construct presupposes that once BRC is depleted past a fixed critical threshold, clinical deficits emerge (Y. Stern, 2009). It also predicts that rates of cognitive decline will be slower for high BRC individuals who have not yet surpassed their neuropathological threshold, even if their rate of degradation is similar to that of a low BRC individual (Tucker-Drob, Johnson, & Jones, 2009). Thus, more BRC can be considered a protective factor, while less BRC would leave an individual more vulnerable to the effects of pathology (Y. Stern, 2002). There has been research to support the threshold model of BRC as several studies have found that individuals with a larger brain size or head circumference experience reduced severity of AD pathology, or are less likely to develop AD (Graves et al., 1996; Schofield, Logroscino, Andrews, Albert, & Stern, 1997). Arguably, such individuals with a larger brain size would have more synapses to lose before they reach the critical threshold for AD (Y. Stern, 2002). Nevertheless, this view is problematic with regard to normal age-associated declines as the cognitive effects of ageing are continuous across the lifespan rather than abrupt (Salthouse, Berish, & Siedlecki, 2004). Threshold models such as the BRC model also fail to account for individual differences in how brains affected by neurodegeneration process cognitive or functional tasks (Y. Stern, 2009).

Active models of reserve are similar to the concept of BRC in that they present a potential mechanism for coping with cognitive decline or brain pathology. Active models, such as cognitive reserve (CR), propose that the brain actively attempts to cope with brain damage and age-related decline by using pre-existing cognitive processes or by recruiting compensatory processes (Y. Stern, 2002). Stern (2002) argues that CR is a normal process that can be observed in healthy ageing as well as in brain damaged populations, and modulation of the same brain networks is evident in both groups. Two individuals may have the same amount of BRC, however, the person with more CR may be able to tolerate more extensive pathology than the other before clinical impairment is apparent. Thus, an active model differs from a passive model as it does not assume that there is a fixed threshold at which functional impairment will be observed. Stern (2009) proposes two subtypes of CR – neural reserve and neural compensation. Neural reserve refers to cognitive processing differences between healthy brains. Neural compensation refers to variability in the ability to compensate for brain pathology's disruption of standard processing networks by recruiting alternative brain structures or networks not normally used by individuals with healthy brains. Functional neuroimaging studies have found that CR modulates brain activity when faced with cognitive demands (Bosch et al., 2010). In this sense CR can be defined as the ability to compensate for advancing brain pathology and minimise symptomatology both in healthy participants and in brain damaged patients (Scarmeas et al., 2003). There is a general consensus that active and passive models are not mutually exclusive and both may play a role in how the brain protects itself when faced with neurodegeneration (Y. Stern et al., 2005). Strictly speaking, the CR model must also have a basis in physiology in that the brain ultimately mediates all cognitive function. The key difference between passive and active approaches lies in the level of analysis – BRC implies that the quantity of available neurons will vary, whereas, CR implies anatomic variability in terms of brain networks. Also, many of the lifestyle factors associated with increased CR, such as cognitively stimulating activities, will directly affect the brain. There has been research to suggest that individuals with higher IQ and individuals who partake in cognitively stimulating activities have larger brain volume (Kesler, Adams, Blasey, & Bigler, 2003). Similar findings have emerged from studies into the effects of exercise in promoting neurogenesis (Cotman & Berchtold, 2002; van Praag et al., 2002). Furthermore, research has highlighted the role of biological mechanisms in CR , such as the repeated activation of the noradrenergic (NA) system in response to environmental influences (I. H. Robertson, 2013). The research hypothesises that traditional CR proxies, such as education level and premorbid IQ, involve upregulation of NA, a system negatively affected by ageing, which in turn reduces risk of cognitive decline and dementia. In order to give a thorough account of CR it is necessary to combine the complex interactions between genetics, the environmental influences on brain reserve and pathology, and the ability to actively compensate (Y. Stern, 2009).

2.2.2 Measuring CR

While BRC is generally measured using neuronal/synaptic count and brain volume measures, CR is not measured directly (Jones et al., 2011). In research on cognitive decline and dementia, regularly used proxies of CR include educational attainment, occupational level, premorbid intelligence quotient, social and leisure activities, and cognitive/mentally stimulating activities (Valenzuela & Sachdev, 2006). Several studies have provided epidemiologic evidence for the differential susceptibility to age-related memory changes and dementia associated with these CR proxies (Hughes, 2010; Sattler et al., 2012; Valenzuela et al., 2011). High educational and occupational attainment has been found to contribute independently to increased CR (Evans et al., 1993; Mortel, Meyer, Herod, & Thornby, 1995; Y. Stern et al., 1994). Tucker-Drob et al. (2009) found that education and vocabulary knowledge, as markers of CR, are associated with higher levels of functioning in old age. Similarly, a study by Snowden et al. (1997) found that linguistic ability among nuns at a mean age of 22 years was predictive of their cognitive performance and the risk of Alzheimer's disease approximately 58 years later. Further evidence comes from a study by (Scarmeas et al., 2001), where they observed that individuals who consistently engaged in leisure activities had 38% less risk of developing dementia. Thus, as measured by these proxies, CR can be viewed as a dynamic process that develops with age and has crucial implications for cognitive function in the later stages of life (Sánchez, Torrellas, Martín, & Barrera, 2011).

Several of these proxies are often gathered in a customised questionnaire to be administered to research participants, with a high score generally indicating high CR (Solé-Padullés et al., 2009). A critique put forward by (Jones et al., 2011) states that a major limitation to using proxy measures of CR is that they may be linked to neuropsychological test performance via several alternative paths, and not just via the hypothesised 'reserve' mechanisms. This means there is a possibility that any single measure of CR may be predictive of cognitive ageing for reasons other than protection from expression of brain pathology. This limitation has motivated an interest in multiple-indicator methods for measuring CR, in which the shared variance between several CR indicators is used to infer a latent CR variable. Advantages of this approach include avoiding bias from non-CR pathways (i.e., those pathways are only relevant for one of the multiple indicators), providing a more accurate measure of CR than could be obtained by any single indicator, and enabling use of a single coefficient to summarise the relationship between CR and cognitive function instead of presenting several coefficients across different scales. As there is currently no direct measure of CR, it may be more appropriate to consider latent variable data analysis approaches that might be capable of testing theories regarding the role of CR (Jones et al., 2011).

Another approach to measuring CR was outlined in a research paper by Reed et al. (2010) who used a latent variable approach to investigate a novel method for measuring how CR reduces the impact of brain pathology on cognitive function. Key to this method is defining CR as differences between the cognitive performance predicted by an individual's level of brain pathology and that individual's actual cognitive performance. Going by this definition, individuals whose measured cognitive performance is better than predicted by their brain pathology can be said to have high CR, whereas individuals who perform worse than predicted have low CR. A latent variable model was applied to data from a diverse ageing population and the variance in a measure of episodic memory was decomposed into three separate components. The first component was predicted by demographics, the second was predicted by pathology as measured by structural MRI, and the third was a 'residual' or 'reserve' term that encompassed all the remaining variance. This residual component was then tested as an operational measure of CR and several predictions about the effects of this measure were generated from a general conceptual model of CR. The results indicated that CR, as measured by this decomposition approach, modifies rates of conversion from mild cognitive impairment to dementia, modifies rates of longitudinal decline in executive functioning, and also attenuates the effect of brain pathology on cognitive decline. A more recent study by Zahodne et al. (2013) replicated these methods in a large community-based sample with results supporting this operational measure of CR. This method of decomposing the variance in cognitive function scores is a promising and novel approach in the measurement and study of CR.

More recently, discussion has centred on the construct of executive function (EF) as a CR proxy given that it is highly related to a construct of CR comprised of proxy indicators reflecting lifestyle (Siedlecki et al., 2009), and therefore may present another novel approach to measuring CR. EF refers to the ability to inhibit impulsive responses, update and monitor incoming information, and mental flexibility (Miyake et al., 2000). Response inhibition is an EF concerning the ability to deliberately inhibit dominant, automatic or prepotent responses when necessary, and it has been linked with dementia outcomes (Balota et al., 2010). During the Stroop task, a task frequently used to measure response inhibition, participants are required to inhibit or override the tendency to produce a more dominant or automatic response (Miyake et al., 2000). Stroop errors on colour incongruent trials have been shown to be predictive of conversion to Alzheimer's disease (Balota et al., 2010). However, the exact role of EF in CR is not clearly understood and requires further research if it is to be considered as a potential measure of CR.

2.2.3 Construct validity of CR

A review paper by Satz, Cole, Hardy, and Rassovsky (2011) has questioned the construct validity of the CR concept. The review addresses the various conceptualisations of reserve and their application in research. The authors proposed four constructs that represent potential proxies of CR: EF, Processing Resources (PR), Complex Mental Activity (CMA), and intelligence (IQ). These constructs characterise CR status as a function of cumulative experience in various domains, as well as emphasising the importance of cognitive domains in determining CR. CMA is reflective of the protective effects of cognitive activity and it is comprised of traditional CR indicators such as education, occupation, and mental engagement. However, CR may not be a unidimensional construct and therefore cognitive constructs such as EF, PR, and IQ have been put forward as potential CR measures as these cognitive domains may be involved in protection against the expression of pathology/age-related decline. It remains unclear whether these constructs are separate or are subject to some degree of overlap. Neuroanatomical evidence points to the prefrontal cortices as the primary locus of EF (Miller & Cohen, 2001), and these areas are selectively vulnerable to the effects of healthy ageing (for example, grey matter atrophy and degradations in white matter structural integrity, Raz et al., 1997). Cognitive constructs such as PR and IQ have also been proposed as potential measures of CR and may be subject to some degree of overlap. For instance, Salthouse and Davis (2006) empirically investigated the convergent and discriminant validity of a latent cognitive construct (18 cognitive abilities measuring IQ, memory and speed) and a latent executive construct (9 neuropsychological variables measuring executive abilities) on 3,400 individuals ranging in age from 5 to 93 years. Indicators for both constructs showed convergent validity. With regard to discriminant validity, results showed extremely high correlations between EF, fluid abilities and speed. These overlapping correlations call into question the discriminant validity of the EF, PR and IQ constructs. With regard to the CMA factor, a study on the construct validity of CR demonstrated a strong overlap between a construct of EF and a construct of CR comprised of lifestyle factors (Siedlecki et al., 2009). Empirically testing a comprehensive model of CR, such as that proposed by Satz et al. (2011), could help to clarify the status of these hypothesized constructs in terms of convergent and discriminant validity.

Although Satz et al. (2011) propose a four-factor CR capacity model, they only provide a definition for “CR”, rather than “CR capacity”. Therefore, for the purposes of this research, CR capacity will be interpreted in a similar way to Baltes (1987) who defines CR capacity as the overall learning potential or plasticity of an individual’s cognitive system. Building on this interpretation, while also considering Stern’s (2009) definition of neural reserve, CR capacity can be viewed as the cognitive processing potential of neural systems that support adaptive cognitive performance in the face of age related decline. In this sense, CR capacity can be understood as being predictive of cognitive performance over time in healthy ageing.

2.3 Modifiable Risk and Protection

The prospect of older adults being able to modify their risk of cognitive decline is appealing given the predicted rise in the ageing population in the coming decades (Hughes, 2010). In a meta-analysis of longitudinal studies it was found that CR, as indexed by variables such as education, occupation, and premorbid IQ was associated with lower risk of incident dementia (Valenzuela & Sachdev, 2006). These variables, as well as other CR proxies such as social engagement, have also been associated with increased protection against cognitive decline in healthy ageing (Ardila, Ostrosky-Solis, Rosselli, & Gómez, 2000; Zunzunegui, Alvarado, Del Ser, & Otero, 2003). These variables may operate independently or in cooperation with each other and other variables such as EF, PR, and IQ (Satz et al., 2011). CR has not yet been empirically tested under the four-factor CR capacity framework proposed by Satz et al. (2011). The relationship between traditional proxy CR measures and measures of cognitive function such as EF offers a promising approach to modifying certain protective factors in cognitive decline. For instance, research has suggested that cognitive control processes such as EF may be modifiable through brain training interventions. Furthermore, healthy ageing can lead to deficits in EF, which is strongly correlated with other cognitive abilities such as fluid intelligence, mental capacity and memory (Verhaeghen & Salthouse, 1997). This lends support to the idea that an intervention based on EF training may in turn impact on CR in terms of a positive change in current CR status, thus strengthening the brain's capacity to sustain cognitive abilities in the face of healthy ageing/neuropathology.

2.3.1 Brain Training Interventions in Healthy Ageing

The concept of neuroplasticity, the brain's ability to change neural structure and function in response to experiences or environmental stimulation, is fundamental to brain training interventions (Rabipour & Raz, 2012). There has been evidence to suggest that the adult brain is neuroplastic, with the greatest brain changes occurring through repeated practice of a skill over a prolonged period of time (Cannonieri, Bonilha, Fernandes, Cendes, & Li, 2007; Maguire, Woollett, & Spiers, 2006). A randomized controlled trial conducted by Ball et al. (2002) investigated whether three cognitive training interventions improve mental abilities and daily functioning in healthy older adults aged 65 to 94. Participants were randomly assigned to one of four groups: memory training; reasoning training; speed of processing training; or a no-contact control group. Results indicated that each intervention improved the targeted cognitive ability compared with baseline and effects were observed for up to two years. No training effects were detected on everyday functioning at two years indicating that effects of cognitive training were not generalizable to daily living. However, the results provide strong evidence for the effectiveness and durability of the cognitive training interventions in improving targeted cognitive abilities. A recent review on brain training in healthy elderly concluded that plasticity is key to the long-term retention and transferability of training gains (Buitenweg, Murre, & Ridderinkhof, 2012). The authors suggest that maximal benefit can be achieved if not just one, but multiple cognitive functions are engaged during training tasks. Targeting higher order cognitive abilities such as EF may potentially meet these criteria. There has been evidence to suggest that age effects diminish after extensive training on a cognitive switching task (Kramer, Hahn, & Gopher, 1999). It has also been suggested that training in task switching might potentially have transfer gains as a study found that elderly who grew up as bilinguals, thus constantly needing to switch between the two languages during their lifetime, were found to have greater inhibitory control compared to monolingual elderly (Bialystok, Craik, & Ryan, 2006). A systematic review investigating the efficacy of brain training interventions in individuals with mild cognitive impairment found moderate-sized effects on memory performance and global cognition measures following training. The effect sizes and generalizability of benefits were stronger for computer-based cognitive exercise interventions compared to memory strategy training. Cognitive exercise involving multiple cognitive domains also demonstrated greater efficacy than uni-modal memory strategy training. However there is a need for further RCT research before firm conclusions can be made (Gates, Sachdev, Fiatarone Singh, & Valenzuela, 2011). A more recent systematic review of RCTs and clinical studies investigating cognitive interventions in healthy elderly and MCI found that cognitive training can be effective in improving memory performance, EF, processing speed, attention and fluid intelligence (Reijnders, Van Heugten, & Van Boxtel, 2013).

2.4 Conclusion

In summary, a number of risk and protective factors in dementia and cognitive decline have been identified through epidemiological research. Viewing risk and protection in terms of CR may provide a sensitive explanatory framework for observed discrepancies between brain changes/atrophy and the cognitive expression of these changes. The theory of CR characterizes the protective effects of cognitive activity in relation to cognitive decline in healthy ageing as well as decline due to pathology. However, CR is difficult to measure directly and proxy indicators such as education and occupation are frequently used in research. A recommended approach to the measurement of CR uses multiple-indicator methods in which the shared variance between several CR indicators is used to infer a latent CR variable. In this way, bias from non-reserve pathways (i.e., those pathways are only relevant for one of the multiple indicators), can be avoided (Jones et al., 2011). A priori groupings of variables purported to represent CR are in need of construct validation to clarify the underlying structure of, and relationships between, the hypothesized CR constructs. This issue of construct validity is dealt with in section I of the research programme. There is also evidence to suggest that cognitive protective factors potentially involved in CR, such as EF, may be modifiable through cognitive training interventions, and this issue is addressed in section II of the research programme. However, prior to embarking on intervention studies, clarification of the factors involved in CR is necessary.

Section I: Construct Validity of CR Capacity

Section I of the research programme is focused on modelling CR in healthy senior adults with a focus on moving from a conceptual to a measurement definition of CR. An active approach to modelling CR focuses heavily on lifetime enrichment factors, such as education and occupation, as proxies predictive of neural reserve and compensatory reserve. However, this approach does not address two fundamental questions: (1) Should other candidate reserve capacity proxies such as EF be considered alongside the traditional lifetime enrichment factors when modelling reserve capacity? Here we are considering if reserve capacity can be additionally modelled by cognitive function; and (2) How statistically valid is such a multidimensional reserve capacity model?

An additional next step will include modelling the measurement and predictive relationship between CR and cognition over time. As outlined in Chapter 2, research has identified a multitude of indicators that may contribute to CR and in turn confer protection against cognitive decline in healthy ageing as well as in the face of pathology. One important candidate proxy, EF, is of particular significance as this function is not immutable, and therefore could present one potential route to altering reserve capacity, and thereby affect cognitive function. However, agreement on an organisational structure in which to group these indicators, including EF, is needed before predicting cognitive function based on reserve capacity. We address this next step by longitudinally modelling reserve capacity in two data sets, as this approach can be useful in helping to refine the definition of CR and determine which CR indicators may be more robust than others in contributing to CR capacity (Harrison et al., 2015).

Using data-driven empirical testing, study 1 seeks to optimise the measurement of CR through exploration and confirmation of the organisational structure of indicators hypothesised to contribute to CR capacity using data from the longitudinal Maastricht Ageing Study (MAAS). Study 2 seeks to further confirm this organisational structure using data from a secondary dataset, the Irish Longitudinal Study on Ageing (TILDA). Studies 3 and 4 focus on the predictive relationships between CR capacity and cognitive outcome measures over time based on data from two large longitudinal ageing studies –MAAS and TILDA. Specifically, study 3 is based on MAAS data, up to 12-year follow-up, and it explores the predictive relationships between a model of CR capacity and cognitive outcomes over time, while study 4 is based on TILDA data, up to two-year follow-up, and seeks to replicate the findings from study 3 in an Irish sample.

Chapter 3: Study 1 - Exploring a Four-Factor Model of Cognitive Reserve Capacity

3.1 Introduction

The concept of protection from dementia and cognitive decline is referred to as 'cognitive reserve' (CR) and has traditionally been put forward as a potential explanation for individual variability in the relationship between brain pathology and symptomatology (Y. Stern, 2002). Threshold models of CR, such as brain reserve capacity (BRC), that assert that those with larger brain sizes have more synapses to lose before they reach a critical threshold for disease expression, fail to take into account normal age-associated declines in cognition (Salthouse et al., 2004). They are also unable to account for individual differences in how cognitive or functional tasks are processed by brains affected by neurodegeneration (Y. Stern, 2009). Conversely, active models of CR do not assume there is a fixed threshold at which functional impairment occurs. Rather, CR can be viewed as the use of differential brain networks or alternative cognitive strategies in order to maximise performance (Y. Stern, 2002). This definition suggests that CR is evident in both healthy individuals and individuals with varying degrees of brain damage. Thus, an active model of CR may be better placed to account for individual differences in cognitive decline in healthy ageing. In particular, Stern's (2009) "neural reserve" subtype of active CR emphasises the role of individual differences in efficiency of cognitive networks/capacity and the recruitment of alternative networks in protection against the impact of brain changes. The "neural compensation" subtype refers to instances where brain pathology interferes with cognitive networks and requires the recruitment of additional compensatory networks. In this sense, CR can be viewed as the brain's capacity to actively compensate for advancing brain pathology and minimise symptom expression in both healthy ageing and dementia.

CR is recognised as a latent construct, meaning that it cannot be directly measured (Whalley, Deary, Appleton, & Starr, 2004). It is traditionally measured by environmental enrichment factors such as educational attainment, occupational level, premorbid IQ, and social and mental engagement and has been associated with a lower dementia risk (Valenzuela & Sachdev, 2006). The assertion that these traditional proxy measures have a protective role with regard to cognitive decline and dementia may be questionable as these observations may also be the result of differences in functioning that have existed since earlier adulthood and have persisted into later life (Tucker-Drob et al., 2009). Jones et al. (2011) also warn that there is ambiguity surrounding the use of a single indicator as a proxy for CR in that any individual measure may predict cognitive ageing for reasons other than protection from expression of neuropathology. Instead, the authors recommend a multiple indicator method, in which the shared variance between a number of candidate CR measures is used to infer a latent CR variable. Additionally, broadening the scope of CR beyond simple demographic proxies to include cognitive functions may prove informative in developing a comprehensive model of CR that is empirically testable to determine construct validity (Siedlecki et al., 2009).

3.1.1 CR Measurement Paradigms

There are a number of paradigmatic frameworks for measuring CR that are conceptually similar, but have varying assumptions regarding the mechanisms of protection against age-related changes in the brain and pathology (acquired/progressive). While threshold models of CR such as BRC are frequently measured using brain volume or neuronal/synaptic count, active CR is not measured directly (Jones et al., 2011). CR, as measured by proxies such as education level, occupational complexity, crystallised IQ, and mental engagement, can be viewed as a dynamic process that develops across the lifespan and has considerable implications for cognitive functioning in the later life (Sánchez et al., 2011). Such active models predict that individuals with high levels of education or crystallised IQ, and thus high levels of knowledge, can delay the clinical expression of age-related brain changes or brain pathology (Tucker-Drob et al., 2009). Possible mechanisms by which increased levels of knowledge can offer protection include superior organisational structuring of information, enhanced problem solving skills, and more efficient and reliable algorithms to reduce processing requirements (Salthouse, 2003). To further illustrate this point, Stern (2002) puts forward the example of a mathematics expert, who is able to draw from a large array of alternative networks when solving a problem, whereas a less experienced individual may be more limited in their ability to generate a solution. Similarly, mental exercise through a stimulating occupation or participation in cognitively stimulating hobbies and activities may result in new connections being formed between neurons, which in turn leads to more efficient and flexible cognitive networks (Salthouse, 2006).

Brain imaging research has tested the relationship between CR level as predictive by proxies such as education, and activation of standard networks supporting task function in both healthy individuals and those with varying levels of brain pathology. One brain imaging study investigated the relationship between proxy CR measures (education, occupation, crystallised IQ, social and mental activities) and cerebral measures and found that higher levels of CR were related to larger brain volumes and reduced activity during cognitive processing in healthy older adults (Solé-Padullés et al., 2009). This suggests that these individuals are using standard brain networks more efficiently than those with low CR levels, which links in with Stern's (2009) neural reserve subtype of CR. Conversely, the study found that higher CR levels were associated with lower brain volumes and increased use of brain networks in individuals with MCI and AD. This suggests that when neuropathology is present, compensatory mechanisms can be recruited in high CR individuals to support task function. Again, this can be interpreted as Stern's (2009) proposed neural compensation arm of CR.

In a review of the various approaches to conceptualising and measuring CR, Barulli and Stern (2013) compared the various models of reserve such as BRC, CR, and its subtypes of neural reserve and compensation, and conclude that while the concepts may differ in some important respects, they are complementary to each other as opposed to competing. The key conceptual difference between BRC and active models of CR lies in their measurement, whereby BRC implies varying quantities of neurons, whereas CR implies variability in terms of brain networks (Y. Stern et al., 2005). Both, however offer explanations for how the brain protects itself in the face of age-related decline or pathology. As imaging methods become increasingly advanced, CR can guide the direction toward subtler BRC measures, resulting in BRC and CR growing more interconnected (Barulli & Stern, 2013). Additionally, neural reserve encompasses elements of both BRC and CR as it refers to the cognitive networks that have developed due to both cognitively enriching experiences as well as innate capacity. In summary, active CR offers a promising paradigmatic approach to the understanding and measurement of CR, although the precise nature of the interrelationships between purported indicators of an active CR construct are in need of clarification.

3.1.2 Construct Validity of the CR Concept

Although an active paradigmatic approach to conceptually understanding CR offers a strong theoretical solution to the problem of CR measurement, it does not necessarily address the fact that many proxies of 'active' CR are used interchangeably. It follows that the construct validity of CR has been questioned due to the myriad reserve indicators used across studies and the lack of an organisational structure in which to group these indicators (Jones et al., 2011; Satz et al., 2011). Few studies have directly investigated the construct validity of CR. If CR is to be viewed as a valid latent construct, it is necessary to establish that its candidate indicators are correlated with each other (Siedlecki et al., 2009). Traditionally, the candidate indicators are cognitive enrichment measures such as education level (Scarmeas et al., 2003; Y. Stern et al., 1994; Tucker-Drob et al., 2009). However, Barulli and Stern (2013) note that one of the outstanding questions in CR research is the extent to which CR is based on acquired knowledge (e.g., crystallised abilities) versus cognitive processes (e.g., fluid abilities). Stern's theory of neural reserve posits that more efficient cognitive networks can protect against the impact of brain changes as a result of ageing or pathology. This highlights the potential role of higher order executive processes in CR as neural reserve operates by allowing greater flexibility in network selection, an ability believed to be captured by EF tasks (Tucker & Stern, 2011). Along with the traditional lifestyle-based proxy indicators of CR, such as education and participation in cognitively stimulating activities, Satz and colleagues (2011) have proposed three other cognitive domains that represent potential proxy candidates of CR: EF, PR, and IQ, and their interrelationships are discussed below.

A Four-Factor Model of CR Capacity

Numerous studies have demonstrated the predictive power of traditional CR proxies in cognitive decline and dementia outcomes (Crowe et al., 2003; Fratiglioni, Paillard-Borg, & Winblad, 2004; Hughes, 2010; Sattler et al., 2012; Scarmeas et al., 2001; Valenzuela & Sachdev, 2006; Wilson et al., 2002). However, the measurement of CR requires refinement and construct validation. Jones et al. (2011) have been critical of research using only a single indicator of CR (e.g., education) in predictive models as any individual measure may be predictive of cognitive decline/dementia for reasons other than the buffering effect of CR against pathology. Instead, a multiple indicator method is recommended, in which the shared variance between a number of candidate CR proxies is used to infer a CR latent variable. Additionally, as there is a large body of evidence for a significant overlap and fluidity between these proxy measures and cognitive functions such as EF, PR, and IQ, and these interrelationships are discussed below. These cognitive constructs must also be included in models of CR and empirically tested, as convergent and discriminant validity remains unclear.

According to Satz et al., instead of arguing a priori in support of a hypothetical model of CR, it is necessary to establish its construct validity through empirical testing. The aim of this study was to investigate the construct validity of a four-factor model, representing CR capacity, using factor analytic techniques. The four-factor model proposed by Satz et al. comprises four hypothetical subcomponents that contribute to CR capacity (see *Figure 1*):

(1) Executive Function (EF): Response inhibition, fluency, error monitoring, selective attention, cognitive switching, and reasoning;

(2) Processing Resources (PR): Divided attention, processing speed, and working memory;

(3) Complex Mental Activity (CMA): Engagement in cognitively stimulating activities, social networks, education, literacy, and occupation;

(4) Intelligence (IQ): Fluid and crystallised IQ.

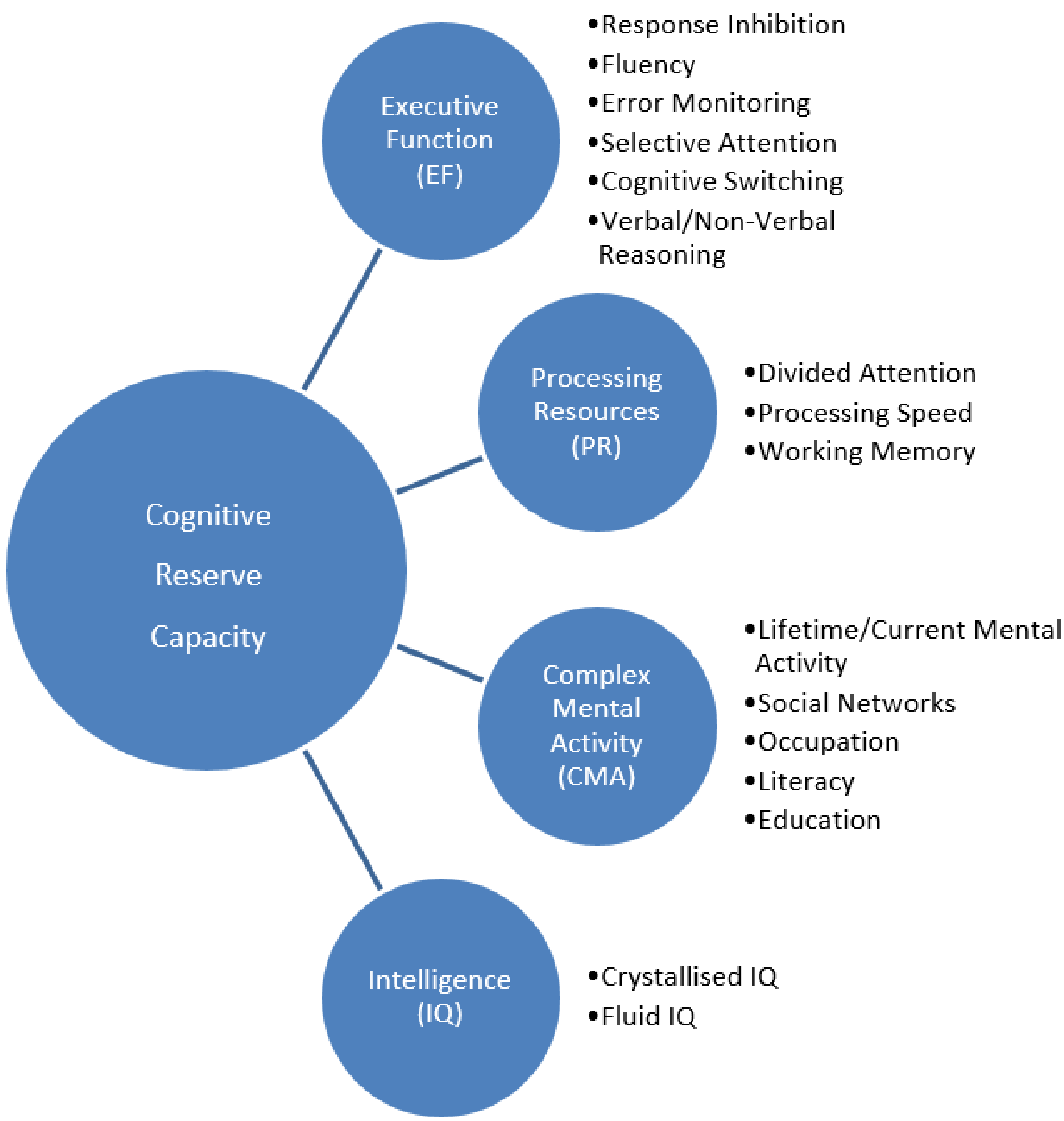


Figure 1. Satz et al.'s (2011) four-factor model of CR capacity

Relationships Between EF, PR, and IQ

Previous research suggests that EF may not represent a unique cognitive dimension. Salthouse and colleagues (Salthouse, Atkinson, & Berish, 2003; Salthouse & Davis, 2006) found that EF highly correlated with the constructs of crystallised and fluid intelligence. Bryan and Luszcz (2000) also showed that among healthy older adults, tasks purported to tap EF did not load on a common factor and any association between performance on these tasks could be accounted for by a common loading with intelligence. Furthermore, Miyake et al. (2000) examined the distinctiveness of the three commonly postulated EFs (mental set shifting, information updating, and inhibition of prepotent responses) and found that while they were moderately correlated with each other, latent variable analysis indicated they were also separable. These findings suggest that there are different types of EF, each measuring unique aspects of EF, but with some overlapping variance (Delis, Kaplan, & Kramer, 2001). In addition, an investigation into the relationships between these EF components and IQ found that updating was highly correlated with a measure of fluid IQ, whereas inhibition and shifting were not (Friedman et al., 2006). The same study found that all of the component EFs were correlated with crystallised IQ, but updating was more highly correlated than inhibition and shifting. It must be noted, however, that this study was conducted in a sample of young adults for whom fluid abilities likely strongly influence the acquisition of knowledge (crystallised abilities). In an older population with reduced frontal integrity it would be expected that fluid intelligence would show more EF involvement than crystallised IQ, as crystallised IQ may be less affected by frontally related EF dysfunction (Duncan, Burgess, & Emslie, 1995).

Speed of information processing and working memory (WM), the ability to control attention and actively maintain information to facilitate quick retrieval, are considered to be highly related, as processing information through encoding, transforming or retrieving within WM is dependent on time (Conway, Cowan, Bunting, Therriault, & Minkoff, 2002). However, whether or not these abilities represent a distinct “PR” construct is questionable, as both processing speed and WM have been linked to fluid abilities like EF and fluid IQ. Research has shown that EF variables are strongly related to reasoning and perceptual speed abilities, which raises questions not only about the extent to which EF tests measure a distinct dimension, but also the extent to which PR represents a construct distinct from EF (Salthouse, 2005). For instance, although it has been well established that performance on a variety of reaction time and processing speed tests declines with increasing age (Bryan, Luszcz, & Crawford, 1997; Salthouse, 1994), there is an argument against viewing processing speed as a marker of generalised ageing as brain imaging research has linked performance on processing speed tasks (verbal and non-verbal measures) with frontal-parietal association areas similar to the substrates of EF (Kennedy & Raz, 2009), indicating a potential overlap between processing speed and EF abilities.

Executive processes are also generally considered to play an important role in WM. For instance, under Miyake et al.'s (2000) EF framework, monitoring and updating of working memory representations is considered one of the core EFs along with shifting of mental sets and inhibition of prepotent responses. Furthermore, Engle, Tuholski, Laughlin and Conway (1999) demonstrated that WM span tasks had a predictive relationship with general fluid ability. Later studies supported and built on this finding, with WM capacity found to be related to both general fluid intelligence and executive attention (Conway, Kane, & Engle, 2003; Engle, 2002). Similarly, a study by Kyllonen and Christal (1990) investigated the relationship between WM and reasoning, an ability closely related to EF (Salthouse, 2005). Using structural equation modelling the study demonstrated a near unity between WM capacity and reasoning ability, again calling into question the distinctiveness of EF and PR. These findings were supported in a study by Süß, Oberauer, Wittmann, Wilhelm and Schulze (2002) who found a correlation of similar magnitude between WM and reasoning ability. Overall, these findings highlight the large degree of overlap between these cognitive constructs, which has implications for the divergent validity of EF, PR and IQ.

Relationships between CR proxy indicators and EF, PR, and IQ

There is evidence to suggest that traditional CR proxies are highly related to measures of EF, PR and IQ. Mitchell, Shaughnessy, Shirk, Yang and Atri (2012) examined the factor structure of typical proxy CR indicators (years of education and premorbid IQ) in relation to other cognitive functions in order to validate a model of cognitive domains and cognitive reserve (CDCR model). A priori, CR was considered distinct from other cognitive domains in the model. The four-factor model was comprised of the following factors: Memory/language (logical memory subtests of the Wechsler Memory Scale-Revised, the Free and Cued Selective Reminding Test, the Boston Naming Test, and Semantic Fluency); processing speed/executive function (Trail Making Test, and Digit Symbol Coding subtest of the Wechsler Adult Intelligence Scale-Revised); attention (Digit Span Forward and Backward subtests of the Wechsler Memory Scale-Revised); and CR (years of education and the American version of the National Adult Reading Test – AMNART). The model was tested using confirmatory factor analysis in a group of cognitively healthy older adults and a group of older individuals with memory impairment along the spectrum of amnestic mild cognitive impairment to Alzheimer's disease (aMCI-AD). Results supported the construct validity of a CR factor as distinct from indicators of PR and EF. However, there was a moderate positive correlation between the two factors in both healthy adults (r=0.431) and those with aMCI-AD (r=0.433). Similar results were found in a study by Siedlecki et al. (2009) in which the construct validity of CR (education level, vocabulary, literacy) was evaluated using four structural equation models that represented progressively more stringent tests of construct validity. The latent variable models compared neuropsychological indicators and CR indicators on the constructs of memory, processing speed, EF and CR. In general, findings supported CR as a construct distinct from measures of memory and processing speed based on convergent validity and moderate discriminant validity. However, the results from the most demanding model suggested a strong relationship between the CR and EF measures, which calls into question the discriminant validity of the traditional CR construct in relation to EF. Although Siedlecki et al. conclude that, based on their overall findings, it is reasonable to describe CR as a distinct construct, they advise that the relationship between CR and EF must also be acknowledged, and go on to suggest that the CR construct be revised to include EF indicators as CR may be highly related to fluid executive abilities (p. 567).

In relation to PR, Bennett, Schneider, Tang, Arnold and Wilson (2006), and Boyle et al. (2008), have shown that years of education and social network size, commonly used environmental enrichment proxies of CR, have strong mediating effects on cognitive performance in individuals with Alzheimer's disease in areas such as perceptual speed and working memory. Traditional proxy indicators of CR have also been found to overlap with measures of IQ. Research has demonstrated a strong relationship between level of education and measures of general, as well as crystallised, intelligence (Sternberg, Grigorenko, & Bundy, 2001). Furthermore, Schooler, Mulatu, and Oates (1999) investigated the relationship between occupational complexity, another frequently used proxy of CR, and cognitive functioning, and found that intellectual flexibility in early life was associated with occupational complexity later in life. The association between occupational complexity and fluid IQ suggests that fluid abilities may be driving the protective relationship between high occupational complexity and better cognitive performance in later life. The apparent overlap between traditional environmental enrichment CR proxies and the other candidate CR constructs of EF, PR and IQ highlights the need for further investigation into the exact nature of these relationships (Satz et al., 2011).

In sum, it remains unclear whether these factors are separate or are subject to some degree of overlap. The approach recommended by Satz et al. is the data-driven use of exploratory factor analysis to establish groupings of indicators and the theory-driven approach of confirmatory factor analysis that relies on hypothesis testing of potential models. Empirically testing this four-factor model of CR capacity could help to clarify the status of these hypothesized constructs in terms of convergent and discriminant validity.

3.2 Method

3.2.1 Participants

The sample was selected from the Maastricht Ageing Study (MAAS), a 12-year longitudinal study on the determinants of cognitive ageing (Jolles, Houx, Van Boxtel, & Ponds, 1995). Access to the MAAS dataset was granted though the In-MINDD study. The baseline sample consisted of 1,823 participants, aged 24 to 82 years, who were chosen at random from the Registration Network of Family Practices (RNH; Metsemakers, Höppener, Knottnerus, Kocken, & Limonard, 1992), a patient register of general practices in the province of Limberg, the Netherlands. Prior to selection, all participants were screened for medical problems that may interfere with cognitive functioning. This screening process was conducted through examination of health data acquired by the RNH, such as a history of dementia, Parkinson's disease, cerebrovascular disease, nervous system disorders, epilepsy, schizophrenia, and psychosis. Additional screening was conducted though semi-structured interviews to check for exclusion criteria that was not acquired by the RNH: history of transient ischemic attacks (TIA), brain surgery, renal failure, and use of psychotropic medication. Any participants that met the above criteria were excluded from the sample frame. Participants were stratified according to age, sex and level of occupational achievement. All participants were Caucasian and native Dutch speakers. MAAS was approved by the Medical Ethics Committee of the University Hospital Maastricht and all participants gave their written informed consent. Two hundred and thirty-six individuals whose education and occupation were unknown were excluded. A further nine participants who converted to dementia during the course of the 12-year study were excluded. The final sample involved 1,578 individuals, of which 860 were male and 718 were female.

3.2.2 Measures of Cognitive Reserve Capacity

The MAAS ageing dataset contained a range of demographic, biological, and neuropsychological variables believed to be involved in cognitive ageing. In order to determine which specific measures could address the research questions in this study, a range of indicators were identified that were potentially reflective of the four cognitive domains specified by Satz et al. (2011). These were further refined through examination of measures typically used in studies measuring similar cognitive constructs, and discussion with In-MINDD partners in Maastricht regarding suitability (see *Table 2* for a summary of the CR capacity indicators and selected MAAS measures).

EF Indicators

The *Stroop Colour-Word Test* (Stroop, 1935; van der Elst, van Boxtel, van Breukelen, & Jolles, 2006d) was used to measure selective attention, response inhibition, and error monitoring. Card 1 depicts colour words in a random order (red, blue, yellow, and green) printed in black ink. Card 2 shows patches of solid colour in one of these four colours. Card 3 displays colour words printed in an incongruous ink colour (e.g., the word blue printed in yellow ink). Participants were instructed to read the words (card 1), name the colours (card 2), and name the ink colour of the printed words (card 3). Speed and accuracy were recorded. Participants' selective attention (str3) was measured as the total time taken to complete the colour-word card (card 3) in seconds. Participants' response inhibition (STR-int) was calculated as the time needed to complete the colour-word card (card 3) minus the average time needed to complete the word card (card 1) and the colour card (card 2). Many participants spontaneously corrected themselves when they noticed an error so the number of spontaneous corrections made was used as a measure of error monitoring.

The *Fluency* test measures strategy-driven retrieval of information from semantic memory (Lezak, Loring, & Howieson, 2004; van der Elst, van Boxtel, van Breukelen, & Jolles, 2006a). Participants were required to produce as many animal names as possible in one minute. The number of correct responses was taken as a measure of semantic fluency.

The *Concept Shifting Test* (CST) (van der Elst, van Boxtel, van Breukelen, & Jolles, 2006b; Vink & Jolles, 1985) is a modified version of the Trail Making Test (Reitan, 1958). The test comprises three cards with 16 small circles grouped in a larger circle. The small circles contain digits (CST A), letters (CST B) or both digits and letters (CST C). Participants were required to cross out the digits as quickly as possible in ascending order (CST A), the letters in alphabetical order (CST B), and the digits and letters in alternating order (CST C). A measure of set shifting (CST-Int) was calculated by subtracting the time in seconds needed to complete CST A and CST B from the time needed to complete CST C.

PR Indicators

The *Letter-Digit Modalities Test* (LDMT) is an adapted version of the Digit-Symbol Substitution Test (A. Smith, 1968). Participants were instructed to replace random letters with the appropriate digits according to a given key. The number of correctly completed letters in 90 seconds served as a measure of processing speed.

The *Verbal Learning Test* (Brand & Jolles, 1985; van der Elst, van Boxtel, van Breukelen, & Jolles, 2005) is a modified version of the word-list learning test by Rey (1958). In five consecutive trials, a list of 15 monosyllabic words were presented. Immediately after presentation participants were asked to recall these words. This test of immediate recall is believed to tap short term memory. According to Kane and Engle (2002), the representational components of short term memory plus a general executive attention component are involved in working memory capacity. Although “span” tasks are frequently used as measures of working memory, these types of tasks may be limited as they predominantly appeal to the representational component of working memory rather than the executive attention component (van Gerven, van Boxtel, Meijer, Willems, & Jolles, 2007). However, as this immediate recall task was the closest proxy of working memory administered to the full MAAS sample, the total number of correctly recalled words after the five trials was used as a measure of immediate working memory. This is in line with previous research using MAAS data, where the verbal learning test was used as a measure of passive working memory (van Gerven et al., 2007).

CMA Indicators

Level of education was determined by categorising formal education according to a scale used in the Netherlands (De Bie, 1987). The scale is comparable to the International Standard Classification of Education (United Nations Educational Scientific and Cultural Organisation, 1976). The levels of education were defined as follows: 1 (*primary education*), 2 (*lower vocational education*), 3 (*intermediate general secondary education*), 4 (*intermediate* *vocational education*), 5 (*higher general secondary education*), 6 (*higher vocational education*), 7 (*higher professional education*), and 8 (*university education*).

Level of Occupational Attainment (LOA) was based on a seven-point scale that estimates the highest level of professional activity (Directoraat-Generaal voor de arbeidsvoorziening, 1989). Information for this classification was derived from the reported occupation and a description of the work performed. LOA was defined as follows: 1 (*work requiring little or no insight and thought*), 2 (*work requiring some insight and thought*), 3 (*work requiring insight and thought*), 4 (*work requiring considerable experience*), 5 (*work requiring considerable theoretical knowledge as well as considerable experience*), 6 (*work requiring extensive and thorough theoretical knowledge*), and 7 (*work requiring scientific knowledge of scientific work*).

IQ Indicators

The *Groningen Intelligence Test* (GIT) is a test of general intelligence used as frequently as the Wechsler Adult Intelligence Scale (WAIS) in the Netherlands (Luteijn & Van der Ploeg, 1983). The vocabulary subtest of the GIT (GIT2) is a multiple choice test where participants are instructed to indicate which of five alternative words is exactly synonymous with a given word. The total score on the GIT2 was used as a measure of crystallised IQ (vocabulary). The mental rotation subtest of the GIT (GIT3) requires participants to indicate which two-dimensional shapes from a larger set are needed to fill a given space on a test page. This requires participants to mentally rotate each of the shapes as they are not presented in proper orientation. This test typically measures fluid abilities and the total score was used as a measure of fluid IQ.

It was not possible to include measures for five of the CR capacity indicators specified in the Satz et al. (2011) four-factor model. Measures for both lifetime/current mental activity and social networks were unavailable in baseline data, and measures for divided attention, reasoning and literacy were administered to a very small proportion of the total participant pool and were therefore not suitable for the subsequent analysis.

Table 2. CR model indicators and MAAS measures

CR Model Indicator	MAAS Measure	Description
Executive Function		
Response Inhibition	Stroop Colour-Word Test (STR-Int)	The mean RT (in seconds) difference between the incongruent and congruent conditions: STR-Int=STR3 - (STR1+STR2)/2)
Fluency	Verbal Fluency Test – animals (FLU)	Number of correct animal names listed within one minute
Error Monitoring	Stroop Spontaneous Correction (STR3SC)	Number of spontaneous corrections made during STR3
Selective Attention	Stroop Colour-Word Test (STR3)	Time to complete STR3 in seconds
Cognitive Switching	Concept Shifting Test (CST-Int)	CST-Int=CSTC – (CSTA + CSTB)/2)
Reasoning	No appropriate measure in selected MAAS sample	-
Processing Resources		
Divided Attention	No appropriate measure in selected MAAS sample	-
Processing Speed	Letter-Digit Modalities Task (LDMT)	Number of correct items after 90 seconds for the written version of the LDMT
Working Memory	Verbal Learning Test (WLT)	Total reproduction on learning trials 1-5
Complex Mental Activity		
Lifetime/current mental activity	No appropriate measure in selected MAAS sample	-
Social Networks	No appropriate measure in selected MAAS sample	-
Occupation	Level of Occupational Attainment (LOA)	Seven-point scale that estimates highest level of professional activity
Literacy	No appropriate measure in selected MAAS sample	-
Education	Level of Education	Eight-point scale of formal education
Intelligence		
Crystallised IQ	Groningen Intelligence Test (GIT2 - Vocabulary)	Total score on GIT2
Fluid IQ	Groningen Intelligence Test (GIT3 - Mental Rotation)	Total score on GIT3

3.3 Analysis

Exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) were used to investigate the construct validity of Satz et al.'s (2011) CR capacity model. EFA, also known as common factor analysis, is used to understand the relations among a set of measured variables in terms of underlying latent variables (Floyd & Widaman, 1995). The empirical objectives of this analysis are in accord with the common factor model as the aim is to reproduce the intercorrelations of this set of indicators with a smaller number of latent dimensions while recognising the existence of measurement error in the observed measures (Brown, 2006). Confirmatory factor analysis (CFA) was conducted to confirm the factor structure that emerged from the EFA. CFA is typically used in construct validation after the underlying structure has been tentatively established through EFA and also on theoretical grounds (Brown, 2006). The appropriateness of the MAAS data for factor analysis was considered in terms of the following attributes put forward by Tinsley and Tinsley (1987): (1) Sample size – A general rule of thumb is that approximately ten participants are required per variable analysed. The MAAS dataset has sufficient sample size to meet this criterion; (2) Independence of measures - Any dependency in the measurement of the variables may artificially increase their correlations, thus causing them to appear together in the same factor. Dependency can occur when component scores and their composite scores are included in the same factor analysis. In this dataset the measure for response inhibition (STR-int) was derived from an equation using the measure for selective attention (str3), therefore, str3 was removed from the analysis. Prior to analyses, outlying values greater than three standard deviations beyond the mean were removed for each variable. Kolmogorov-Smirnov (K-S) tests of normality were conducted on all measures. From these tests, it appeared that most measures deviated from the normal distribution (*p*s<.001) (see Appendix B for MAAS K-S test statistics). Therefore, an estimator robust to the effects of non-normality was used (WLSMV).

3.3.1 EFA Analysis

Analysis was conducted using Mplus Version 7.3 (L. K. Muthén & Muthén, 2011). The analysis used Robust Weighted Least Square extraction (WLSMV) and the solution was rotated using oblique rotation (promax with Kaiser normalisation) in order to achieve simple structure. The WLSMV estimator is appropriate when categorical variables are included in the analysis and has been shown to be effective with various sample sizes, model complexities and non-normal data (Flora & Curran, 2004). Oblique rotation was warranted in this case as upon running the analysis, the factor correlation matrix revealed a correlation greater than 0.32 between the factors (Tabachnick & Fidell, 2006). Ten CR indicators were subjected to WLSMV extraction to assess the dimensionality of the data. Factor retention was determined based on eigenvalues (factors with EV's >1 were retained) and examination of a scree plot. As per the guidelines proposed by Tabachnick and Fidell (2006), items with high loadings (≥.4) on more than one factor (cross-loadings) and items with small loadings (<.4) on all factors were eliminated from the analysis. Initial analysis revealed that there were two variables with small loadings on all factors, Stroop Spontaneous Corrections and Groningen Intelligence Test – Mental Rotation (GIT3). The GIT3 also cross-loaded on both factors, although the factor loadings were less than .4. These variables were removed and analysis was re-run for a more refined solution (Pett, Lackey, & Sullivan, 2003).

3.3.2 CFA Analysis

Analysis was conducted using Robust Weighted Least Squares estimation (WLSMV). The software package used for the analyses was Mplus version 7.3 (L. K. Muthén & Muthén, 2011). The model that emerged from the EFA was tested to confirm its structure. As per the guidelines proposed by Brown (2006), the acceptability of the model was evaluated by examining overall goodness of fit, specific points of ill fit using standardised residuals and modification indices, and the interpretability and statistical significance of the resulting parameter estimates.

Goodness of fit was evaluated using the χ^2 index of absolute model fit, the weighted root mean square residual (WRMR), root mean square error of approximation (RMSEA) and its 90% confidence interval (90% CI), comparative fit index (CFI), and the Tucker-Lewis index

(TLI). The WRMR is used when assessing categorical data and is similar to the residual-based fit index the Standardised Root Mean Square Residual (SRMR) (L. K. Muthén & Muthén, 2002). According to Barrett (2007), in order for the χ^2 index of absolute model fit to indicate good model fit the results must be insignificant at a threshold of 0.05. b and Mueller (2013) state that a WRMR value less than 1.0 indicates good model fit. Browne and Cudeck (1993) suggest that values of RMSEA in the range of .05 to .08 are indicative of reasonable fit. Hu and Bentler (1999) recommended that RMSEA no larger than around .06 indicates good fit. Bentler and Bonett (1980) suggest that CFI and TLI values above 0.90 indicate acceptable fit. Multiple indices were used as they provide different information about model fit and, used together, provide a more conservative and reliable evaluation of the solution. Absolute fit indices such as the χ^2 index of absolute model fit, RMSEA and WRMR measure how well a model fits in comparison to no model at all (Hooper, Coughlan, & Mullen, 2008). Comparative fit indices, or relative fit indices, such as CFI and TLI compare the hypothesized model with a more restricted baseline model that presumes all variables are uncorrelated (Bentler & Bonett, 1980).

3.4 Results

3.4.1 Descriptive Statistics

Table 3 contains details of the descriptive statistics at baseline for the sample participants on demographic and neuropsychological measures. The mean age of participants was 50.12 years. There were 860 male and 718 female participants. The mean level of education was 'intermediate vocational education' and the mean level of occupational attainment was 'work requiring considerable experience'. The two-tailed correlation of all indicators with age was investigated in order to not make direct assumptions about directionality. Inspection of the table indicates that all of the EF and PR variables were significantly negatively correlated with age. The two variables that measured reaction time (Stroop Colour Word Test and Concept Shifting Test) were reflected in order for a high score to represent better performance and these reflected measures also have negative correlations with age. This reflection was conducted for ease of interpretation of results as high scores equate to better performance on all measures, however the descriptive statistics for the variables prior to reflection are also reported below. The relationship between the IQ variables and age was mixed with a significant negative correlation for fluid IQ and a non-significant relationship for crystallised IQ (vocabulary). The relationship between demographic variables and age was also mixed. Education level was significantly negatively correlated with age whereas the relationship between occupation level and age was non-significant.

Table 3. Descriptive statistics of CR capacity measures and their correlations with age

	N	**Mean**	**Range**	***SD***	**Age *r***
Age	1578	50.12	24.00-82.00	16.10	-
EF Indicators					
Stroop Colour Word Test	1500	43.32	7.30-107.30	17.57	.514**
Stroop Colour Word Test (Reflected)	1500	66.23	2.25-102.25	17.57	-.514**
Stroop (Spontaneous Corrections)	1536	1.42	0.00-7.00	1.56	.090**
Stroop (Spontaneous Corrections) (Reflected)	1536	6.57	1.00-8.00	1.56	-.090**
Fluency (animals)	1568	24.18	6.00-43.00	6.25	-.304**
Concept Shifting Test	1528	10.92	-9.80-46.30	8.40	.366**
Concept Shifting Test (Reflected)	1528	36.38	1.00-57.10	8.40	-.366**
PR Indicators					
Letter Digit Modalities Test	1568	49.16	16.00-83.00	11.51	-.635**
Verbal Learning Test	1554	45.82	18.00-71.00	9.69	-.486**
CMA Indicators					
Education Level	1578	3.73	1.00-8.00	1.86	-.292**
Level of Occupational Attainment (LOA)	1578	3.86	1.00-7.00	1.61	.013
IQ Indicators					
Groningen Intelligence Test (Vocabulary)	1561	13.71	5.00-20.00	2.90	.024
Groningen Intelligence Test (Mental Rotation)	1576	10.92	2.00-20.00	3.47	-.366**

Note. * $p<.05$, two-tailed; ** $p<.01$, two-tailed; Age *r*=correlation with age; Scores for Stroop Colour Word Test, Stroop Spontaneous Corrections, and the Concept Shifting Test were reflected so that high scores represent better performance.

3.4.2 Exploratory Factor Analysis

In keeping with convention and simplicity, the pattern matrix was interpreted (Tabachnick & Fidell, 2006) and results are summarised in *Table 4*. Two factors were extracted: Factor 1 included five associated measures – the Letter Digit Modalities Test, Verbal Learning Test, Stroop Colour Word Test, Concept Shifting Test, and Fluency (animals); Factor 2 included three associated measures – the Groningen Intelligence Test (vocabulary), Education Level and Level of Occupational Attainment (LOA). The correlations between variables and factors are presented in the structure matrix (*Table 5*) with moderate correlations (>.4) highlighted in bold. These factors appear to represent a distinction between two types of cognition outlined by Salthouse (2006), that of *process* measures that reflect efficiency of process and function at the time of assessment (Factor 1), and *product* measures that reflect the cumulative products of processing over the lifespan (Factor 2). As the EF and PR indicators loaded on Factor 1, this suggests together they represent an **Executive Function/Processing Resources (EF/PR) factor**, similar to the EF/PR factor modelled by Mitchell et al. (2012) in relation to CR. The CMA indicators (education level and level of occupational attainment) and IQ indicator (crystallised IQ) loaded on Factor 2, and these can be viewed as experiential resources that enrich cognition throughout the lifespan, therefore representative of a **Cumulative Cognitive Enrichment (CCE) factor**. The factor correlation matrix revealed a correlation of 0.482 between these factors.

Table 4. Heuristic factor pattern matrix rotated to the promax criterion

Variable	**EF/PR**	**CCE**
Letter Digit Modalities Test	**.852**	-.007
Verbal Learning Test	**.670**	-.040
Stroop Colour Word Test	**.681**	-.022
Concept Shifting Test	**.462**	.129
Fluency (animals)	**.488**	.126
Groningen Intelligence Test (vocabulary)	.078	**.554**
Level of Occupational Attainment (LOA)	-.141	**.773**
Education Level	.136	**.854**

Note. Coefficients greater than .4 are highlighted in bold and retained for that factor.

Table 5. Heuristic factor structure matrix rotated to the promax criterion

Variable	**EF/PR**	**CCE**
Letter Digit Modalities Test	**.849**	**.404**
Verbal Learning Test	**.651**	.283
Stroop Colour Word Test	**.670**	.306
Concept Shifting Test	**.524**	.352
Fluency (animals)	**.549**	.361
Groningen Intelligence Test (vocabulary)	.345	**.592**
Level of Occupational Attainment (LOA)	.232	**.705**
Education Level	**.548**	**.920**

Note. Coefficients greater than .4 are highlighted in bold and retained for that factor.

Tables 4 and 5 depict the factor pattern matrix and factor structure matrix, respectively. According to Tabachnick and Fidell (2006), the pattern matrix represents unique relationships (uncontaminated by correlation between factors) between each factor and each observed variable. The matrix produces regression-like weights which are used to estimate the contribution of each factor to the variance of each variable. If the values in the pattern matrix are squared they represent the unique contribution of each factor to the variance of each variable. The structure matrix, on the other hand, estimates the correlations between variables and the correlated factors. These values represent the unique relationship between the variable and the factor when taking into account the relationship between the variable and the correlated factors. Following oblique rotation, the pattern matrix is interpreted in order to ascertain the meaning of the factors. This is because the correlations between variables and factors in the structure matrix are inflated due to overlap of factors and this can make interpretation difficult. In the pattern matrix the set of variables that comprise a factor is usually easier to decipher. Overall, the structure matrix supports the pattern matrix interpretation.

3.4.3 Confirmatory Factor Analysis

A two-factor model was specified in which processing speed (Letter Digit Modalities Test), working memory (Verbal Learning Test), response inhibition (Stroop Colour Word Test), cognitive switching (Concept Shifting Test), and fluency (Fluency - Animals) loaded onto the latent variable of EF/PR. Crystallised IQ (Groningen Intelligence Test - vocabulary), Education (Education Level), and Level of Occupational Attainment (LOA) loaded onto the latent variable CCE. By default, Mplus selected the first indicator on each latent variable as a reference or marker indicator. Processing speed and crystallised IQ were used as marker indicators for EF/PR and CCE, respectively. It was decided against overriding this default selection as both of these measures are reliable and valid. Their regression coefficients were fixed to ‘1’ to minimise the number of parameters estimated in the model. The measurement model contained no double-loading indicators. All measurement error was presumed to be uncorrelated, with the exception of education level and level of occupational attainment. The model was specified to account for the relatively high correlation between these variables (*r*=.618, *p*<.001). Theoretically, allowing these measures to correlate is prudent as they were both measured on a similar Likert scale and may therefore display common method variance (Brown, 2006). The latent factors were allowed to be correlated based on prior evidence of a relationship between these dimensions. Accordingly, the model was overidentified with 18 degrees of freedom (*df)*.

Results are summarised in *Table 6*. The χ^2 index of absolute model fit indicates that the model does not fit the data well as the sample variance-covariance matrix does not equal the predicted variance-covariance matrix (S≠∑) (χ^2(18)=159.997, *p*<.001). The WRMR value of 1.177 supports this finding. However, all other goodness-of-fit indices examined suggest that the two-factor model fits the data reasonably well: RMSEA=0.071, 90% CI [0.061, 0.081], TLI=0.946, CFI=0.965. Inspection of standardised residuals and modification indices indicated several points of ill fit in the solution. However, as parameters should not be freed with the sole intention of improving model fit (Brown, 2006), no re-specifications were made. Additionally, the CFA was re-run separately for male and female participants to ensure the factor structure held for both. For the full age range, model fit was good for both males and females. When broken out into age groups, on the whole, fit remained good for both males and females, therefore the dual-factor structure was retained (see Appendix C for fit statistics). The goodness-of-fit indices are in line with previous studies in the field that concluded reasonable fit (Courtney et al., 2012; M. B. Mitchell, Cimino, et al., 2012). The completely standardised parameter estimates from this solution are presented in *Figure 2* (standard errors of the estimates are provided in *Table 7*). All freely estimated unstandardised parameters were statistically significant (*p*s<.001). Factor loading estimates revealed that the indicators were moderately to strongly related to their purported latent factors (range of R^2s=0.264–0.890). Furthermore, estimates from the two-factor solution indicate a moderate to strong relationship between the dimensions of EF/PR and CCE (.595).

Table 6. Fit statistics for a two-factor CFA model of EF/PR and CCE

Statistic	Result
χ^2	159.997
df	18
p	.000
RMSEA (90% CI)	0.071 [0.061, 0.081]
CFI	0.965
TLI	0.946
WRMR	1.177

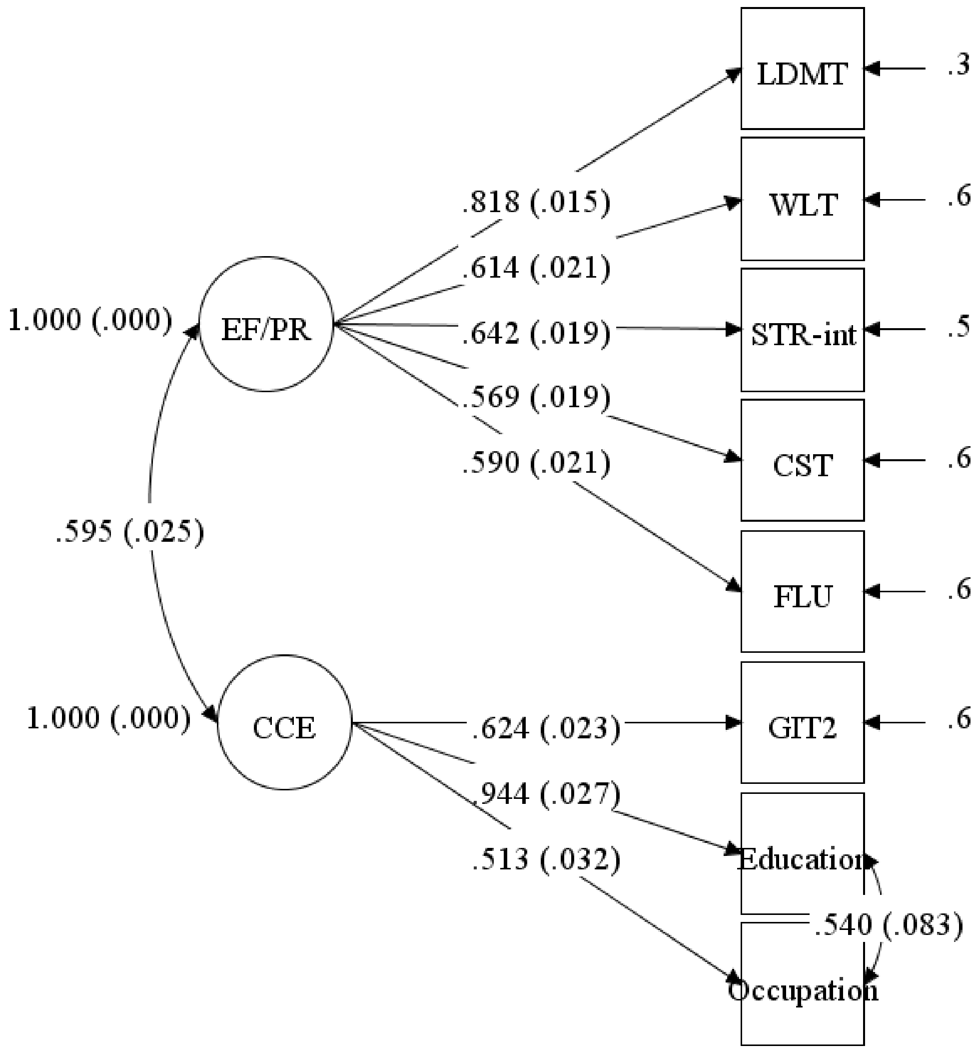


Figure 2. Two-factor model of CR capacity including standardised parameter estimates

Note. EF/PR=Executive Function/Processing Resources; CCE=Cumulative Cognitive Enrichment; LDMT=Letter-Digit Modalities Task (Processing Speed); WLT=Verbal Learning Test (Immediate Working Memory); STR-int=Stroop Colour Word Test (Response Inhibition); CST=Concept Shifting Test (Cognitive Switching); FLU=Fluency (Verbal Fluency); GIT2=Groningen Intelligence Test (Crystallised IQ); Education=Level of Education; Occupation=Level of Occupational Attainment; Standard errors of the estimates for the completely standardised solution are reported in parentheses.

Table 7. Parameter estimates from the two-factor CFA Model of EF/PR and CCE

	Estimates	S.E.	Est./S.E.	Std	StdYX	R^2
EF/PR						
Processing Speed	1.00	0.00	999.00	9.40	0.82	0.67
Immediate Working Memory	0.63	0.03	20.32	5.95	0.61	0.38
Response Inhibition	1.20	0.06	21.23	11.28	0.64	0.41
Cognitive Switching	0.51	0.03	19.57	4.78	0.57	0.32
Fluency	0.39	0.02	19.20	3.69	0.59	0.35
CCE						
Crystallised IQ	1.00	0.00	999.00	1.81	0.62	0.39
Education Level	0.52	0.03	15.30	0.94	0.94	0.89
Level of Occupational Attainment	0.28	0.02	11.74	0.51	0.51	0.26
Covariance of EF/PR and CCE	10.12	0.82	12.41	0.60	0.60	-

Note. Estimates=unstandardised parameter estimate; S.E.=standard error; Est./S.E.=test statistic (*z* value); Std=standardised parameter estimate; StdYX=completely standardised parameter estimate; R^2=square of the completely standardised parameter estimate.

3.4.4 Cognitive Reserve Capacity as a Function of Age

The two-factor structure of the CR capacity model was further investigated as a function of age. This was in order to investigate if the same structure holds across young, middle and old age. Due to individual differences in genetics and lifestyle, ageing cannot be viewed as a uniform process (Levine, 2013). However, conventionally, older age has been defined as being aged 65 years or older (Orimo et al., 2006; WHO, 2010). Middle age is often defined as being aged between 45 and 64 years, although this range varies across studies. However, as research has shown that decrements in cognitive performance are increasingly evident from the age of 50 years onwards (Albert & Heaton, 1988; De Luca et al., 2003), middle aged can be defined as those aged between 50 and 64 years. The full sample (*n*=1,578) was divided into three age-groups reflective of young, middle and older age: 24-49 years (*n*=801), 50-64 years (*n*=393), and 65-82 years (*n*=384). Analysis was conducted following the same procedure as above (WLSMV estimation; Mplus version 7.3). The acceptability of the model for each age group was evaluated by examining overall goodness of fit, specific points of ill fit, and evaluation of parameter estimates.

Goodness of fit indices are summarized in *Table 8*. Overall, fit indices indicate that the model fits the data well across all three age-groups. The completely standardised parameter estimates for young, middle and older age-groups are presented in Figures 3, 4, and 5 respectively (standard errors of the estimates are provided in *Table 9*). All freely estimated unstandardised parameters were statistically significant (*p*s<.001). Factor loading estimates revealed that the indicators were moderately to strongly related to their purported latent factors. Furthermore, estimates from the two-factor solution indicate a moderate to strong relationship between the dimensions of EF/PR and CCE (factor correlations range from 0.624 to 0.818).

Table 8. Fit statistics for a two-factor CFA model of EF/PR and CCE as a function of age

Statistic	**24-49 years**	**50-64 years**	**65-82 years**
χ^2	61.048	38.488	34.613
df	18	18	18
p	.000	0.003	0.011
RMSEA (90% CI)	0.055 [0.040, 0.070]	0.054 [0.030, 0.077]	0.049 [0.023, 0.073]
CFI	0.976	0.982	0.980
TLI	0.963	0.972	0.968
WRMR	0.780	0.572	0.597

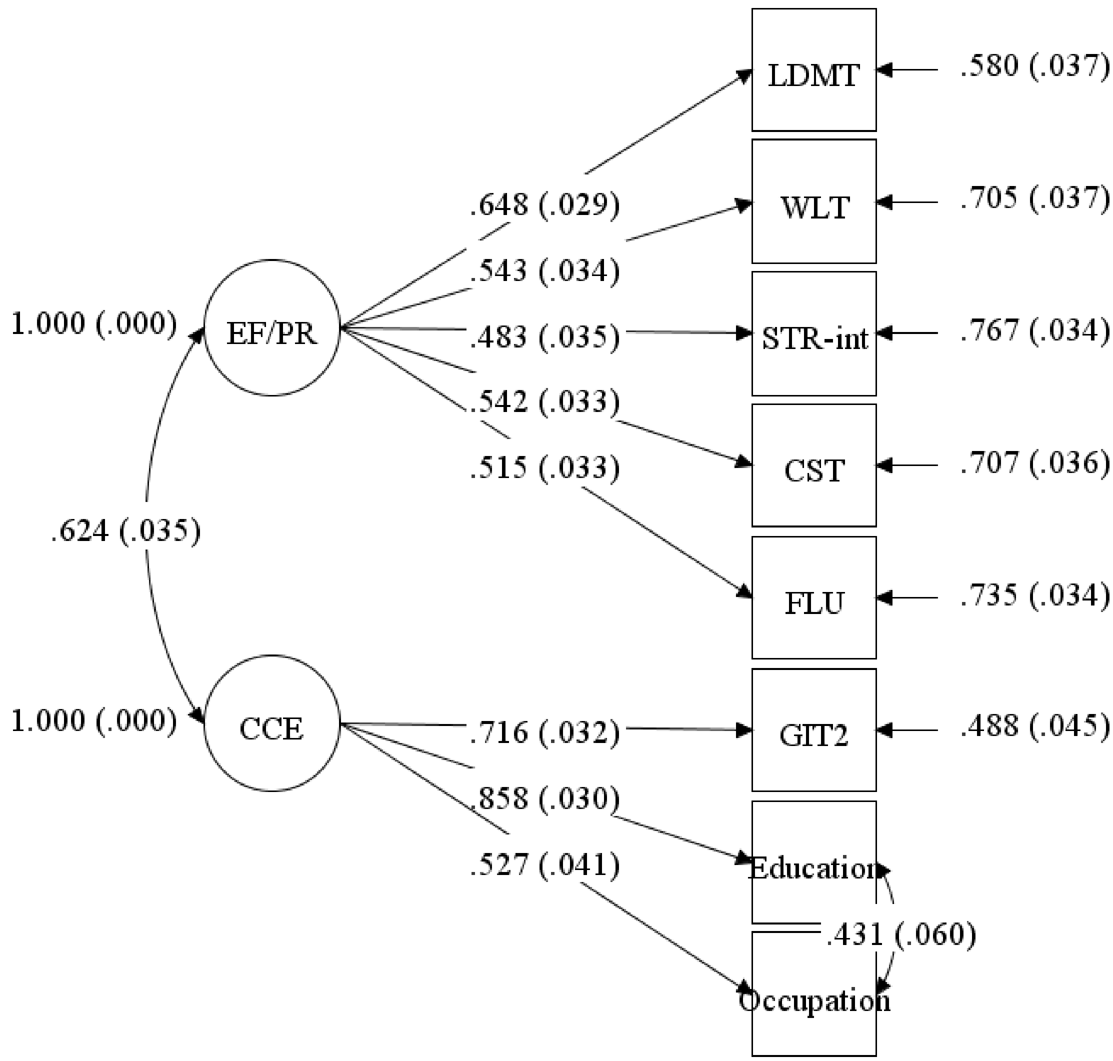


Figure 3. Two-factor model of CR capacity including standardised parameter estimates for 24-49 year olds

Note. EF/PR=Executive Function/Processing Resources; CCE=Cumulative Cognitive Enrichment; LDMT=Letter-Digit Modalities Task (Processing Speed); WLT=Verbal Learning Test (Immediate Working Memory); STR-int=Stroop Colour Word Test (Response Inhibition); CST=Concept Shifting Test (Cognitive Switching); FLU=Fluency (Verbal Fluency); GIT2=Groningen Intelligence Test 2 (Crystallised IQ); Education=Level of Education; Occupation=Level of Occupational Attainment. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

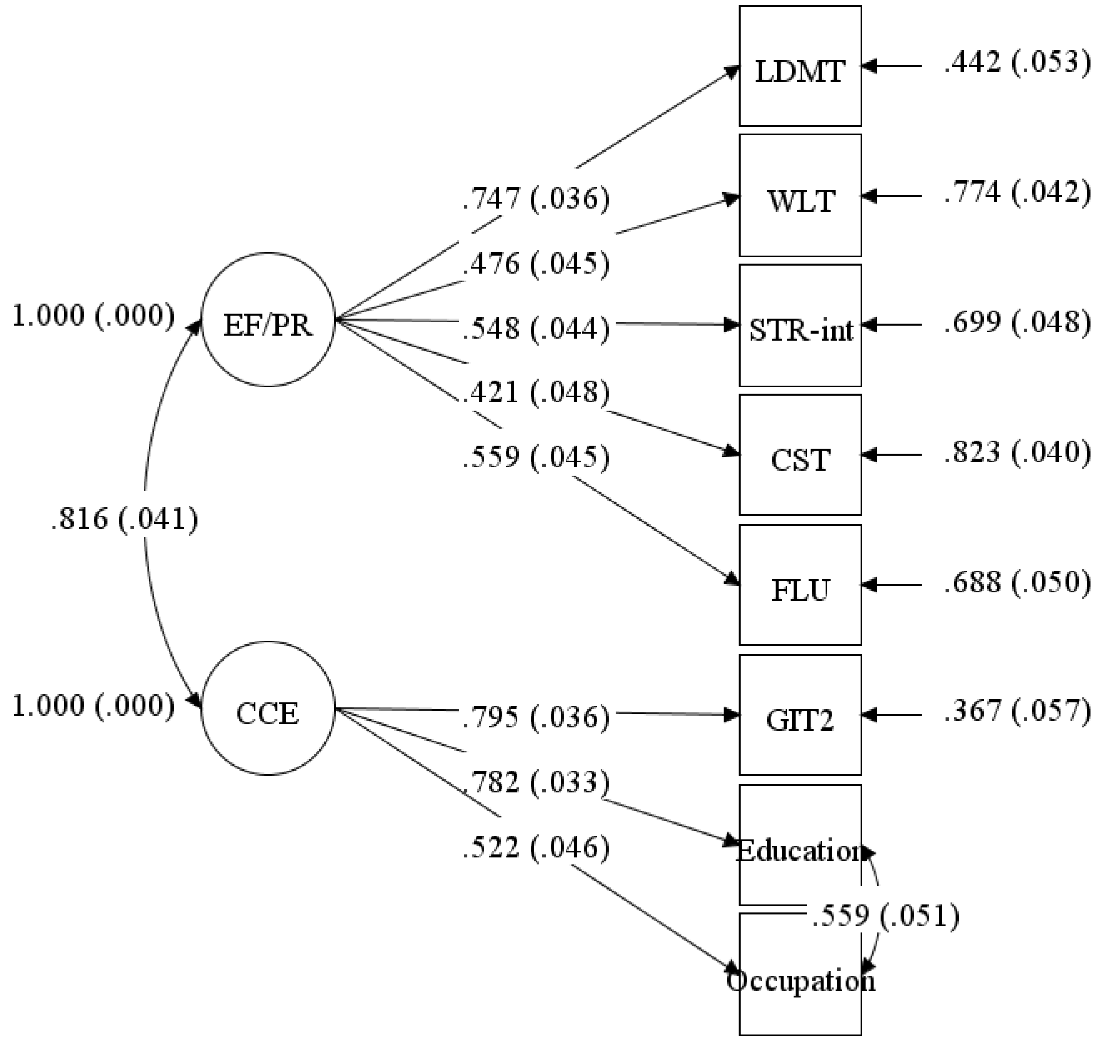


Figure 4. Two-factor model of CR capacity including standardised parameter estimates for 50-64 year olds

Note. EF/PR=Executive Function/Processing Resources; CCE=Cumulative Cognitive Enrichment; LDMT=Letter-Digit Modalities Task (Processing Speed); WLT=Verbal Learning Test (Immediate Working Memory); STR-int=Stroop Colour Word Test (Response Inhibition); CST=Concept Shifting Test (Cognitive Switching); FLU=Fluency (Verbal Fluency); GIT2=Groningen Intelligence Test 2 (Crystallised IQ); Education=Level of Education; Occupation=Level of Occupational Attainment. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

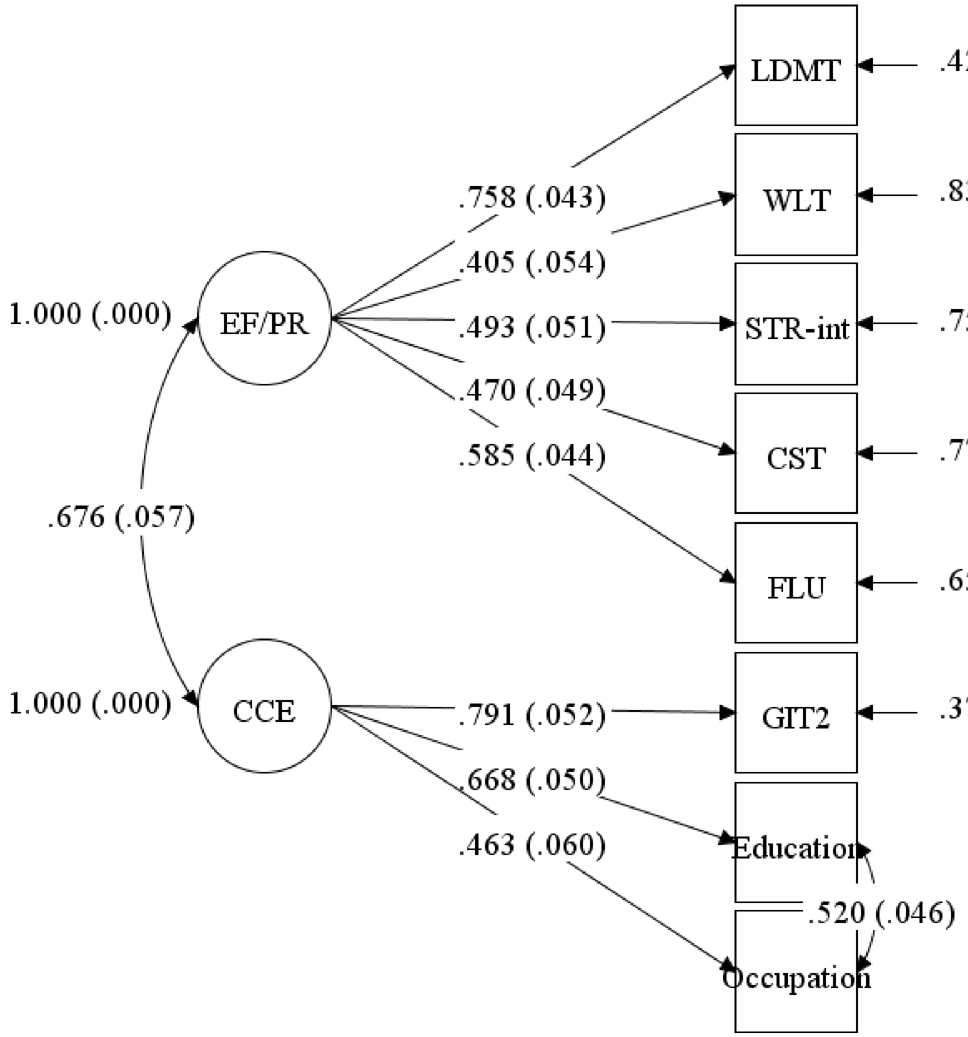


Figure 5. Two-factor model of CR capacity including standardised parameter estimates for 65-82 year olds

Note. EF/PR=Executive Function/Processing Resources; CCE=Cumulative Cognitive Enrichment; LDMT=Letter-Digit Modalities Task (Processing Speed); WLT=Verbal Learning Test (Immediate Working Memory); STR-int=Stroop Colour Word Test (Response Inhibition); CST=Concept Shifting Test (Cognitive Switching); FLU=Fluency (Verbal Fluency); GIT2=Groningen Intelligence Test 2 (Crystallised IQ); Education=Level of Education; Occupation=Level of Occupational Attainment. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

Table 9. Parameter estimates from the two-factor CFA model of EF/PR and CCE as a function of age

24-49 Year Olds	**Estimates**	**S.E.**	**Est./S.E.**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	5.92	0.65	0.42
Immediate Working Memory	0.56	0.06	11.78	4.47	0.54	0.30
Response Inhibition	1.04	0.10	10.47	6.16	0.48	0.23
Cognitive Switching	0.62	0.06	11.17	3.64	0.54	0.29
Fluency	0.53	0.05	11.51	3.11	0.52	0.27
CCE						
Crystallised IQ	1.00	0.00	999.00	1.91	0.72	0.51
Education Level	0.45	0.04	12.63	0.86	0.86	0.74
Level of Occupational Attainment	0.28	0.03	9.50	0.53	0.53	0.28
Covariance of EF/PR and CCE	7.06	0.74	9.49	0.62	0.62	-

50-64 Year Olds	**Estimates**	**S.E.**	**Est./S.E.**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	6.92	0.75	0.56
Immediate Working Memory	0.60	0.07	8.23	4.13	0.48	0.23
Response Inhibition	1.31	0.15	8.77	9.05	0.55	0.30
Cognitive Switching	0.51	0.07	7.32	3.51	0.42	0.18
Fluency	0.49	0.06	8.49	3.36	0.56	0.31
CCE						
Crystallised IQ	1.00	0.00	999.00	2.45	0.80	0.63
Education Level	0.32	0.03	11.51	0.78	0.78	0.61
Level of Occupational Attainment	0.21	0.02	8.86	0.52	0.52	0.27
Covariance of EF/PR and CCE	13.82	1.52	9.11	0.82	0.82	-

65-82 Year Olds	Estimates	S.E.	Est./S.E.	Std	StdYX	R^2
EF/PR						
Processing Speed	1.00	0.00	999.00	7.04	0.76	0.58
Immediate Working Memory	0.53	0.09	6.27	3.80	0.41	0.16
Response Inhibition	1.30	0.19	6.97	9.17	0.49	0.24
Cognitive Switching	0.65	0.10	6.77	4.54	0.47	0.22
Fluency	0.49	0.06	8.24	3.44	0.59	0.34
CCE						
Crystallised IQ	1.00	0.00	999.00	2.49	0.79	0.63
Education Level	0.27	0.04	7.66	0.67	0.67	0.45
Level of Occupational Attainment	0.19	0.03	5.96	0.46	0.46	0.21
Covariance of EF/PR and CCE	11.86	1.67	7.12	0.68	0.68	-

Note. Estimates=unstandardised parameter estimate; S.E.=standard error; Est./S.E.=test statistic (*z* value); Std=standardised parameter estimate; StdYX=completely standardised parameter estimate; R^2=square of the completely standardised parameter estimate.

3.4.5 Convergent and Discriminant Validity

CFA on Full Sample

Convergent validity can be assessed by examining the significance and the magnitude of the factor loading of each indicator on its purported latent factor (Anderson & Gerbing, 1988). As outlined above, all freely estimated unstandardised parameters were statistically significant (*p*s<.001) and factor loading estimates revealed that the indicators were moderately to strongly related to their latent factors (range of R^2s=0.264–0.890). This indicates convergent validity of the model based on the full age-range (24 to 82 years). Discriminant validity was investigated by testing to see if the confidence interval (±2 standard errors) for the standardised correlation estimate between the two latent factors included the value of 1.0 (Anderson & Gerbing, 1988). This analysis supported the discriminant validity of the factors as the confidence interval for this correlation did not contain the value of 1.0 [0.545, 0.645].

CFA on Different Age Groups

For all three age-groups, the freely estimated unstandardised parameters were statistically significant (*p*s<.001) and factor loading estimates revealed that the indicators were moderately to strongly related to their latent factors (see *Table 9*). This indicates convergent validity of the model across all age-groups. As above, discriminant validity was investigated by testing to see if the confidence interval (±2 standard errors) for the standardised correlation estimate between the two latent factors included the value of 1.0 (Anderson & Gerbing, 1988). This analysis supported the discriminant validity of the factors for all three age-groups as the 90% confidence interval for the correlations did not contain the value of 1.0: 24-49 year age group [0.554, 0.694], 50-64 year age group [0.734, 0.898], and 65-82 year age group [0.562, 0.790]. Overall, based on these analyses, the latent factors demonstrate good measurement properties.

3.5 Discussion

Exploratory factor analysis allowed for the exploration and refinement of the factor structure of Satz et al.'s (2011) proposed four-factor model and a two-factor underlying structure has been established on empirical and theoretical grounds. The finding of a two-factor structure supports hypotheses regarding the relationships between EF and PR, and experiential resources such as crystallised IQ and education. The first factor had five associated measures representing processing speed, immediate working memory, response inhibition, cognitive switching and fluency. This factor's loading items suggest it represents a latent construct of EF/PR. This factor reflects an amalgamation of the proposed indicators for Satz et al.'s hypothesised factors of EF and PR, and results are in keeping with the hypothesis that there would be some degree of overlap between these constructs. Processing speed is a core element of EF measures such as the Stroop Colour-Word Test (Stroop, 1935) and the Concept Shifting Test (van der Elst et al., 2006b), thus an overlap between these constructs was expected. The second factor had three associated measures reflecting crystallised IQ (vocabulary), education level, and level of occupational attainment. This factor is suggestive of a latent construct of CCE. There is a well-established relationship between demographic variables such as education and occupational level and crystallised abilities (Crawford et al., 1989; Potter, Helms, & Plassman, 2008), therefore it is unsurprising that the crystallised IQ measure loaded on a factor with measures such as these. These categorisations represent a distinction between two types of cognition outlined by Salthouse (2006). The EF/PR factor can be considered representative of *process* measures that reflect efficiency of information processing and cognitive function at the time of assessment, and the CCE factor can be considered representative of *product* measures that reflect the cumulative products of processing over the lifespan. A similar framework put forward by Craik and Bialystok (2006) addresses the mechanisms of cognitive change across the lifespan and can be applied to this two-factor structure. Under this framework, representational processes can be viewed as crystallised schemas reflecting knowledge of the world and are comparative to the CCE factor. Control processes can be viewed as the set of fluid operations that facilitate intentional processing and adaptive cognitive performance and are comparative to the EF/PR factor. Core to this framework is the proposition that these two systems are interactive in the sense that representations of the world are selected based on needs and desires, and in turn, these representations demonstrate control through their influence on further selection of schema-relevant information.

Confirmatory factor analysis (CFA) was used to evaluate the prespecified factor solution in terms of how well it reproduced the sample covariance matrix of the measured variables. Overall, goodness-of-fit statistics suggest that the model fits the data reasonably well when looking at the sample as whole, and very well when investigating the model structure as function of age. However, the χ^2 index of absolute model fit was consistently poor ($S \neq \Sigma$). According to Brown (2006), χ^2 is rarely used in applied research as a sole index of model fit. There are several reasons for this. For instance, if there is a small *N* or non-normal data the statistical significance tests of the model χ^2 may be compromised. This is also true of large *N* solutions which are routinely rejected on the basis of χ^2 even when there is very little difference between S and Σ. It is also based on a very demanding hypothesis that the sample variance-covariance matrix is equal to the predicted variance-covariance matrix ($S = \Sigma$). Therefore, other fit indices are usually more heavily relied upon when evaluating model fit. Although areas of ill fit were flagged by standardised residuals and modification indices, the model was not respecified. It has been argued that parameters should not be freed with the sole intention of improving the model fit. MacCallum, Roznowski and Necowitz (1992) advise against modifying a good fitting model to achieve even better fit as modification indices may be reflective of small idiosyncratic characteristics of the sample. Interpretation of the parameter estimates revealed that, as expected, estimates were positively related to the latent factor they load onto, consistent with the position that the proposed CR capacity indicators are reliable indicators of the constructs of EF/PR and CCE. For the full age range, examination of the proportion of variance of each indicator that is explained by its latent factor (i.e., communality) revealed a range of 26% to 89%, indicating a strong influence on these indicators by their underlying latent variables. Breaking out the CFA into young, middle- and older-age groups allowed for investigation into how these influences may change across the lifespan. For the young adults, the variance in education explained by CCE was the largest out of the three CCE indicators, however for the middle- and older-age groups, the variance in crystallised IQ explained by CCE was largest. This suggests that the role of education in cognitive enrichment diminishes with age and crystallised abilities become a stronger indicator of this latent factor. For all age groups, the variance in processing speed explained by EF/PR was largest out of the five indicators on this latent factor. However, age differences can be seen in relation to EF indicators, which don't load as strongly as PR indicators for the young adults, but gain in relative strength with increasing age. It may be the case that EF/PR explains more of the variance in these measures in older age due a greater reliance on EF to compensate for age-related decline, as reflected by greater prefrontal cortex recruitment (Park & Reuter-Lorenz, 2009). The factor loadings on each construct provide convergent validity for the latent variables. Additionally, across all age groups, estimates from the two-factor solutions indicate moderate to large intercorrelations of between .595 and .816 between the dimensions of EF/PR and CCE, which is of particular importance with regard to theory surrounding the relationship between these constructs.

This is the first time that CR capacity has been modelled in terms of control and representational processes and there is a strong explanatory framework within the literature of cognitive function and ageing to suggest that the relationship between these systems can be viewed as reciprocal, whereby control processes determine the construction of representations, and in turn, these representations play a role in further controlled processing (Craik & Bialystok, 2006). This framework can be applied to the two-factor CR capacity model whereby EF/PR can be viewed as a driver of CCE which in turn feeds back into EF/PR, and their evolution across the lifespan may influence cognitive ability. Additionally, Stern's (2009) theory of neural reserve underpins the protective effects of experiential resources and highlights the important role of cognitive networks in protection against the adverse effects of brain changes as a result of healthy ageing or brain pathology. As neural reserve operates by facilitating greater flexibility in network selection, an ability believed to be captured by executive processing tasks, a strong relationship between these abilities and traditional CR proxy measures was expected. Although highly related, these constructs are still seen as distinct from each other as the confidence intervals surrounding these correlations do not contain the value of 1.0. This can be considered as evidence that the discriminant validity of factors is good, thus supporting the notion that the latent factors of EF/PR and CCE, although highly related, represent distinct constructs and therefore can theoretically be viewed as each contributing uniquely to CR capacity. According to Anderson and Gerbing (1988) if convergent and discriminant validities are found to be acceptable, the next step is to test the structural model which can be viewed as a confirmatory assessment of nomological validity (consistency of structural relationships) and can help elucidate the predictive relationships between these hypothesised CR capacity factors and cognitive measures associated with MCI and dementia.

The findings of the EFA and CFA reflect previous research on the construct validity of CR and other cognitive constructs. For example, Mitchell et al. (2012), when testing a four factor model of CR and cognitive domains, also found moderate correlations between a 'CR' factor comprised of Education and NART and a 'Processing Speed/Executive Function' factor comprised of the Trail Making Test Parts A and B, and the Digit Symbol Coding subtask of the WAIS-R, in a sample of healthy elderly and a sample with aMCI. These measures are somewhat reflective of the EF/PR and CCE indicators. Results are also in keeping with the overall findings of Siedlecki et al. (2009) who concluded that a latent 'CR' construct as indicated by education, vocabulary and literacy, was a distinct construct with regard to cognitive functions. However, it must be noted that correlations ranging from 0.595 to 0.816 between the constructs are considered large and therefore a strong relationship between CCE and EF/PR can be surmised. As the traditional CR proxy indicators of education and occupation level loaded on the construct of CCE, this is suggestive of a strong relationship between these indicators and common indicators for EF and PR, thus supporting the hypothesis that all these cognitive dimensions comprise CR capacity. As the factor loadings of indicators were similar in strength across ageing models, this suggests that vulnerability factors in relation to decline outcomes may be similar across age groups.

This study has several strengths. It proposes a novel operational definition of CR capacity and assesses a theoretically driven latent-variable model of the interrelations of four purported subcomponents of CR that have, as of yet, remained untested for construct validity. It has a large sample size and employed known neuropsychological measures, which lends support to the reproducibility of the study. Mapping of the CR constructs on to the MAAS measures was based on review of the extant literature, including behavioural and imaging studies of cognitive performance in both healthy ageing and pathology. Careful consideration was given to publications based on MAAS data that documented task sensitivity (van der Elst et al., 2005, 2006a, 2006b; van der Elst, van Boxtel, van Breukelen, & Jolles, 2006c; van der Elst et al., 2006d; van Dijk et al., 2008). Furthermore, CFA is a flexible modelling approach that allows for sophisticated assessment of construct validity. In highlighting the strengths of this approach, Brown (2006) points out that CFA allows for the estimation of relationships between variables following adjustment for measurement error, unlike standard correlational and multiple regression approaches where estimates are weakened to an uncertain degree by measurement error in the variables.

However, when interpreting the EFA and CFA it must be taken into account that some of the CR capacity indicators proposed by Satz et al. (2011) could not be included in this study as the appropriate measures were not administered to the MAAS baseline participant panel selected for analysis. For instance, lifetime/current mental activity and social networks were also put forward as potential indicators of complex mental activity (CMA), however, measures for these indicators were only available in MAAS follow-up data (three years after baseline). Similarly, a measure of literacy was only administered to a small cohort. It is likely, however, that these variables would load on the CCE factor as they can be considered representational processes that contribute to crystallised abilities and are often used as traditional CR proxies in the extant literature (Lojo-Seoane, Facal, Guàrdia-Olmos, & Juncos-Rabadán, 2014; M. B. Mitchell, Shaughnessy, et al., 2012; Siedlecki et al., 2009). Additionally, measures for divided attention and reasoning were administered to a small cohort of the MAAS dataset and were therefore not suitable for EFA/CFA analyses. There were also a number of measures that had to be removed from analysis during the iterative processes of EFA. Selective attention (STR3) was removed from the analysis as the measure for response inhibition (STR-int) was derived from an equation that used the measure for selective attention, creating a dependency that was inappropriate for factor analysis. Also, problematic indicators for error monitoring (Stroop Spontaneous Corrections) and fluid IQ (Groningen Intelligence Test-Mental Rotation) were removed due to small loadings on all factors. Previous research suggests that it is likely that indicators such as divided and selective attention, reasoning and error monitoring would load on the EF/PR factor as they have been found to be related to control processes (Kyllonen & Christal, 1990; Salthouse & Davis, 2006; Süß et al., 2002). The fluid IQ measure was found to cross-load on both factors, but was removed from the analysis due to weak loadings on both. However, previous research supports this cross-loading as fluid IQ has been shown to be related to both control and representational processes such as executive abilities, crystallised IQ, education, and occupation (Schooler et al., 1999; Sternberg et al., 2001) so it is likely this indicator would cross-load on both constructs. Finally, as the CFA was conducted on the same sample as the EFA, findings may be the result of sample idiosyncrasies. Henson and Roberts (2006) argue that it can potentially be misleading to follow an EFA with a CFA on the same dataset, therefore, as part of the research programme, a secondary CFA will be conducted on a different longitudinal dataset, the Irish longitudinal Study on Ageing (TILDA). In summary, the model goes some way toward supporting the construct validity of a two-factor CR capacity model and lays the groundwork to explore relationships between these constructs and global cognition/memory outcomes.

Chapter 4: Study 2 - Validating a Measurement Model of Cognitive Reserve Capacity

4.1 Introduction

Exploration of Satz et al.'s (2011) theoretically driven CR capacity model in study 1 goes some way toward supporting the construct validity of a two-factor CR capacity model. This two-factor model can be viewed under the framework of representation and control across the lifespan put forward by Craik and Bialystok (2006). In this sense, the EF/PR factor characterises control processes, or the fluid operations that facilitate intentional processing and adaptive cognitive performance, while the CCE factor characterises representational processes, or crystallised schemas reflecting knowledge of the world. The MAAS CFA in study 1 establishes a strong correlation between the EF/PR and CCE factors when looking at the sample as a whole and as a function of age. This dual framework finds support in theory positing a reciprocal relationship between representational and control processes (Craik & Bialystok, 2006). As already discussed in study 1, EF/PR may be a driver of CCE, which may in turn influence EF/PR, and this relationship may evolve differentially across the lifespan. The finding of a strong relationship between EF/PR and CCE is also supported by Stern's (2009) theory of neural reserve which underpins the protective effects of experiential resources in pathology and/or age-related cognitive decline. As neural reserve is believed to draw on executive processing abilities, a strong relationship between representational processes (CCE) and underlying control processes (EF/PR) would be expected.

Although the results of study 1 support the convergent and discriminant validity of the two-factor CR capacity model, the EFA and CFA were performed on the same sample and therefore findings may be the result of sample idiosyncrasies. Henson and Roberts (2006) argue that a secondary CFA should be conducted on a new sample where possible in order to avoid potentially misleading results. Furthermore, the initial models were tested using data from a Dutch ageing study (MAAS) so it is of interest to see if the relationships hold in an Irish sample. The MAAS study began in 1991, which could mean the data reflect societal differences in relation to educational and occupational opportunities compared to more recent data, particularly for the older cohort and women recruited for the study. Testing the model using data from the more recent TILDA study, which began in 2011, may help to redress these potential confounds.

The aim of this study was to validate the models explored in study 1 in a secondary sample using TILDA data. This validation study sought to answer the following question:

1. Does the two-factor measurement model, derived from EFA/CFA in study 1, hold in a secondary dataset (TILDA) from an Irish population?

4.2 Method

4.2.1 Participants

The Irish Longitudinal Study on Ageing (TILDA) (Kearney et al., 2011) is a population-representative prospective cohort study of community-dwelling adults in Ireland. Participants were recruited from a clustered random sample of all households in Ireland. Only participants with the ability to personally consent were included in the study. Wave 1 of the study was completed in 2011 and wave 2 was completed in 2013. The baseline (wave 1) sample consisted of 8,504 participants, of which 8,163 were aged 50 and older. The remaining 341 participants were the younger partners of respondents who also agreed to take part in the study. For the purposes of this analysis, those aged under 50 years at baseline were excluded. Those aged 80 years or older were also excluded as these participants had been group coded as 80+ and precise age was unclear. These participants were excluded in order to keep the TILDA sample as similar as possible to the MAAS sample. A further number of participants were also excluded from the sample: 3,293 participants whose education level and/or occupation level were unknown, or who never held a formal occupation, and 1,257 participants with a score of less than 24 on the Mini-Mental State Examination (MMSE) or had an unknown MMSE score. In keeping with the MAAS analyses, the sample was divided into middle aged (50-64 years) and older aged (65-79 years) participants. Analysis was based on 3,351 participants, of which 1,947 were aged between 50 and 64 (880 Male; 1,067 female) and 1,404 were aged between 65 and 79 years (823 male; 581 female) at baseline.

4.2.2 Measures of Cognitive Reserve Capacity

TILDA data were accessed via application to the Irish Social Science Data Archive (ISSDA), which holds a range of Irish and international quantitative datasets for secondary analysis. The TILDA data were originally obtained through interviews in participants' homes using computer-assisted personal interviewing (CAPI), a self-completion questionnaire to complete in their own time, and through a comprehensive health assessment in either a health centre or their own home. For the purposes of this study, measures were selected from TILDA that were as similar as possible to the CR capacity measures used in the MAAS data analyses.

CCE Indicators

Level of education was determined by asking participants to indicate their highest level of education completed. The levels of education were defined as follows: 1 (*some primary – not complete*), 2 (*primary or equivalent*), 3 (*intermediate/junior/group certificate or equivalent*), 4 (*leaving certificate or equivalent*), 5 (*diploma/certificate*), 6 (*primary degree*) and 7 (*postgraduate/higher degree*).

Occupation level was based on a six-point scale that estimates the highest level of professional activity. Occupation level was determined as follows: 1 (*professional workers*), 2 (*managerial and technical*), 3 (*non-manual*), 4 (*skilled manual*), 5 (*semi-skilled*), and 6 (*unskilled*).

EF/PR Indicators

The *Sustained Attention to Response Task* (SART) (I. H. Robertson, Manly, Andrade, Baddeley, & Yiend, 1997) was used as a measure of response inhibition. This task tests a participant's ability to sustain attention and inhibit prepotent responses. Although originally developed as a measure of sustained attention, recent research suggests that the SART places high response inhibition demands on participants (Carter, Russell, & Helton, 2013). During this computer-based task the numbers 1-9 were presented one at a time in a fixed order. Participants were instructed to respond to every number except the number '3' by pressing a key. The number of errors of commission (pressing in response to the number '3') was used as a measure of response inhibition.

The *Fluency* test is a measure of self-initiated activity, categorisation and mental flexibility (A. Barrett et al., 2011). Participants were asked to produce as many animal names as possible in 1 minute. The number of correct responses was taken as a measure of verbal fluency.

The *Colour Trails Tasks 1 and 2* (CTT1 and CTT2) (D'Elia, 1996) were used to derive a measure of cognitive switching. Colour Trail 1 mainly reflects visual scanning and sustained attention, and Colour Trail 2 requires mental flexibility. A measure of cognitive switching was calculated by taking the time required to complete Colour Trail 1 from the time require to complete Colour Trail 2 (CTT2 – CTT1).

Choice Reaction Time (CRT), or speed of processing, was measured using a computer-based CRT test that was developed in-house for TILDA using E-Prime software (Cronin, O'Regan, Finucane, Kearney, & Kenny, 2013; Schneider, Eschman, & Zuccolotto, 2002). During the CRT task participants are required to press a keyboard button until a stimulus (yes/no) appears on the screen. Participants must respond to the stimuli by pressing the corresponding yes/no button on the keyboard. Mean intra-individual reaction time in milliseconds was used as a measure of processing speed.

The *Word List Learning Test* (WLLT) required participants to recall 10 aurally presented words both immediately after presentation and again after a delay, over two trials. Immediate recall is believed to tap short term memory. As discussed in Chapter 3, traditionally, "span" tasks, and other tasks that tap short term memory, have been used as measures of working memory. As this immediate recall task was the closest to a measure of working memory in the TILDA dataset, the total number of correctly recalled words over both trials was used as a measure of immediate working memory.

It was not possible to include a measure for one of the CR capacity indicators from the model developed using MAAS data. A measure of crystallised IQ was unavailable in TILDA. A comparison of the selected MAAS and TILDA variables is outlined in *Table 10*.

Table 10. CR model indicators in MAAS and TILDA

CR Model Indicator	MAAS Measure	TILDA Measure
EF/PR		
Response Inhibition	Stroop Colour-Word Test (STR-Int)	Sustained Attention to Response Task (SART)
Fluency	Verbal Fluency Test – animals (FLU)	Verbal Fluency Test – animals (FLU)
Cognitive Switching	Concept Shifting Test (CST-Int)	Colour Trails Tasks 1 and 2 (CTT)
Processing Speed	Letter-Digit Modalities Task (LDMT)	Choice Reaction Time Test (CRT)
Immediate Working Memory	Verbal Learning Test (WLT)	Word List Learning Test (WLLT)
CCE		
Occupation	Level of Occupational Attainment (LOA) – 7-point scale	Occupation level – 6-point scale
Education	Level of Education – 8-point scale	Level of Education – 7-point scale
Crystallised IQ	Groningen Intelligence Test (GIT2 - Vocabulary)	No available measures in TILDA

4.3 Analysis

In order to validate the model of CR capacity outlined in study 1, CFA was conducted using robust weighted least squares estimation (WLSMV). The software package used for the analyses was Mplus version 7.3 (L. K. Muthén & Muthén, 2011). Data cleaning procedures followed the same protocol as MAAS data cleaning and scores more than three standard deviations beyond the mean were removed from the dataset prior to analysis. Kolmogorov-Smirnov (K-S) tests of normality were conducted on all measures. From these tests, it appeared that most measures deviated from the normal distribution (*p*s<.001) (see Appendix D for TILDA K-S test statistics). Therefore, an estimator robust to the effects of non-normality was used (WLSMV). As per the procedure outlined in study 1, the acceptability of the model was evaluated by overall goodness of fit, examination of specific points of ill fit using standardised residuals and modification indices, and the interpretability and statistical significance of the resulting parameter estimates. A two-factor model was specified in which processing speed (Choice Reaction Time Test), immediate working memory (Word List Learning Test – Immediate Recall), response inhibition (Sustained Attention to Response Task), cognitive switching (Colour Trails Test), and fluency (Fluency - animals) loaded onto the latent variable of EF/PR. Education (Education Level), and Occupation (Level of Occupational Attainment) loaded onto the latent variable of CCE. The Mplus default of selecting the first indicator on each latent variable (Processing Speed and Education Level) as marker indicators was implemented. In the MAAS model, the error terms for education level and level of occupational attainment were allowed to correlate due to the relatively strong relationship between these variables. In TILDA there is also evidence for a strong relationship between these variables (r=.559, p<.001), however as education and occupation are the only two indicators for the CCE latent variable, allowing them to correlate may be problematic with regard to model identification. According to Kenny (2011) in order for the measurement model to be identified, at least two indicators are required per latent variable and those indicator's errors must be uncorrelated. Therefore, all measurement error was presumed to be uncorrelated for the CFA. Scores on the SART, the Colour Trails Test and the Choice Reaction Time test were reflected in order for high scores to represent better performance.

This reflection was conducted for ease of interpretation of results, with high scores equating to better performance across all measures. The latent factors were allowed to be correlated based on prior evidence of a relationship between these dimensions. Accordingly, the model was overidentified with 13 *df*.

4.4 Results

4.4.1 Descriptive Statistics

Table 11 contains details of the descriptive statistics for the sample participants on demographics and CR capacity measures. Participants were aged between 50 and 79 years (*n*=3,351). CFA was conducted on the full sample as well two separate age groupings: 50-64 year olds (*n*=1947) and 65-79 year olds (*n*=1,404). The mean education level for both age groups was 'Leaving Certificate or Equivalent'. The mean occupation level for both age groups was 'Non-manual'. Mean scores on the cognitive tasks indicate consistently higher scores in the 50-64 year age group compared to those aged over 65 years.

Table 11. TILDA descriptive statistics of demographic and CR measures at baseline

	Full Age Range (50-79 years)				50 – 64 Years				65 – 79 Years			
	N	Mean	Range	*SD*	*N*	Mean	Range	*SD*	*N*	Mean	Range	*SD*
Age	3351	62.60	50.00-79.00	8.13	1947	56.72	50.00-64.00	4.28	1404	70.75	65.00-79.00	4.24
EF/PR												
Sustained Attention to Response Task	3153	3.53	0.00-16.00	3.26	1896	2.87	0.00-16.00	2.73	1257	4.53	0.00-16.00	3.72
Sustained Attention to Response Task (Reflected)	3153	13.47	1.00-17.00	3.26	1896	14.13	1.00-17.00	2.73	1257	12.47	1.00-17.00	3.72
Fluency (animals)	3321	21.54	0.00-41.00	6.61	1929	22.62	1.00-41.00	6.58	1392	20.05	0.00-41.00	6.36
Colour Trails Test	3276	52.96	-24.50-137.78	24.45	1931	48.69	-24.50-131.47	21.82	1345	59.08	-23.38-137.78	26.62
Colour Trails Test (Reflected)	3276	85.82	1.00-163.28	24.45	1931	90.09	7.31-163.28	21.82	1345	79.70	1.00-162.16	26.62
Choice Reaction Time Test	3239	495.63	258.97-959.45	96.82	1918	478.32	258.97-959.45	88.81	1321	520.77	282.11-959.03	102.34
Choice Reaction Time Test (Reflected)	3239	464.82	1.00-701.48	96.82	1918	482.13	1.00-701.48	88.81	1321	439.68	1.42-678.34	102.34
Word List Learning	3337	13.82	4.00-20.00	2.90	1941	14.53	5.00-20.00	2.67	1396	12.82	4.00-20.00	2.91
CCE												
Education Level	3351	4.00	1.00-7.00	1.61	1947	4.26	1.00-7.00	1.54	1404	3.64	1.00-7.00	1.64
Level of Occupational Attainment (LOA)	3351	3.84	1.00-6.00	1.30	1947	3.87	1.00-6.00	1.27	1404	3.78	1.00-6.00	1.33
Global Cognition/Memory												
Word List Learning – Delayed Recall	3321	6.28	1.00-10.00	2.23	1942	6.79	1.00-10.00	2.10	1379	5.56	1.00-10.00	2.22
Subjective Memory	3349	3.47	1.00-5.00	0.94	1945	3.61	1.00-5.00	0.93	1404	3.28	1.00-5.00	0.92
Mini-Mental State Examination	3351	28.73	24.00-30.00	1.43	1947	29.01	24.00-30.00	1.26	1404	28.35	24.00-30.00	1.55

Note. Mean and SD values represent scores prior to transformation of Subjective Memory and MMSE variables.

4.4.2 Confirmatory Factor Analysis

Analysis was conducted on the sample variance-covariance matrix for the full sample (*n*=3,351) using Robust Weighted Least Squares estimation (WLSMV). The software package used for the analyses was Mplus version 7.3 (L. K. Muthén & Muthén, 2011). Goodness of fit was evaluated using the χ^2 index of absolute model fit, the weighted root mean square residual (WRMR), root mean square error of approximation (RMSEA) and its 90% confidence interval (90% CI), comparative fit index (CFI) and the Tucker-Lewis index (TLI). Results are summarised in *Table 12*. The χ^2 index of absolute model fit indicates that the model does not fit the data well as the sample variance-covariance matrix does not equal the predicted variance-covariance matrix ($S \neq \sum$) ($\chi^2(13)=100.526$, $p<.001$). The WRMR value of 1.159 supports this finding. However, all other goodness-of-fit indices examined suggest that the two-factor model fits the data very well: RMSEA=0.045, 90% CI [0.037, 0.053], TLI=0.973, CFI=0.983. The completely standardised parameter estimates from this solution are presented in *Figure 6* (standard errors of the estimates are provided in *Table 13*). All freely estimated unstandardised parameters were statistically significant (*ps*<.001). Factor loading estimates revealed that the indicators were moderately to strongly related to their purported latent factors (range of R^2s=0.172–0.899). Furthermore, estimates from the two-factor solution indicate a moderate to strong relationship between the dimensions of EF/PR and CCE (.592).

Table 12. TILDA fit statistics for a two-factor CFA model of EF/PR and CCE

Statistic	Result
χ^2	100.526
df	13
p	.0000
RMSEA (90% CI)	0.045 [0.037, 0.053]
CFI	0.983
TLI	0.973
WRMR	1.159

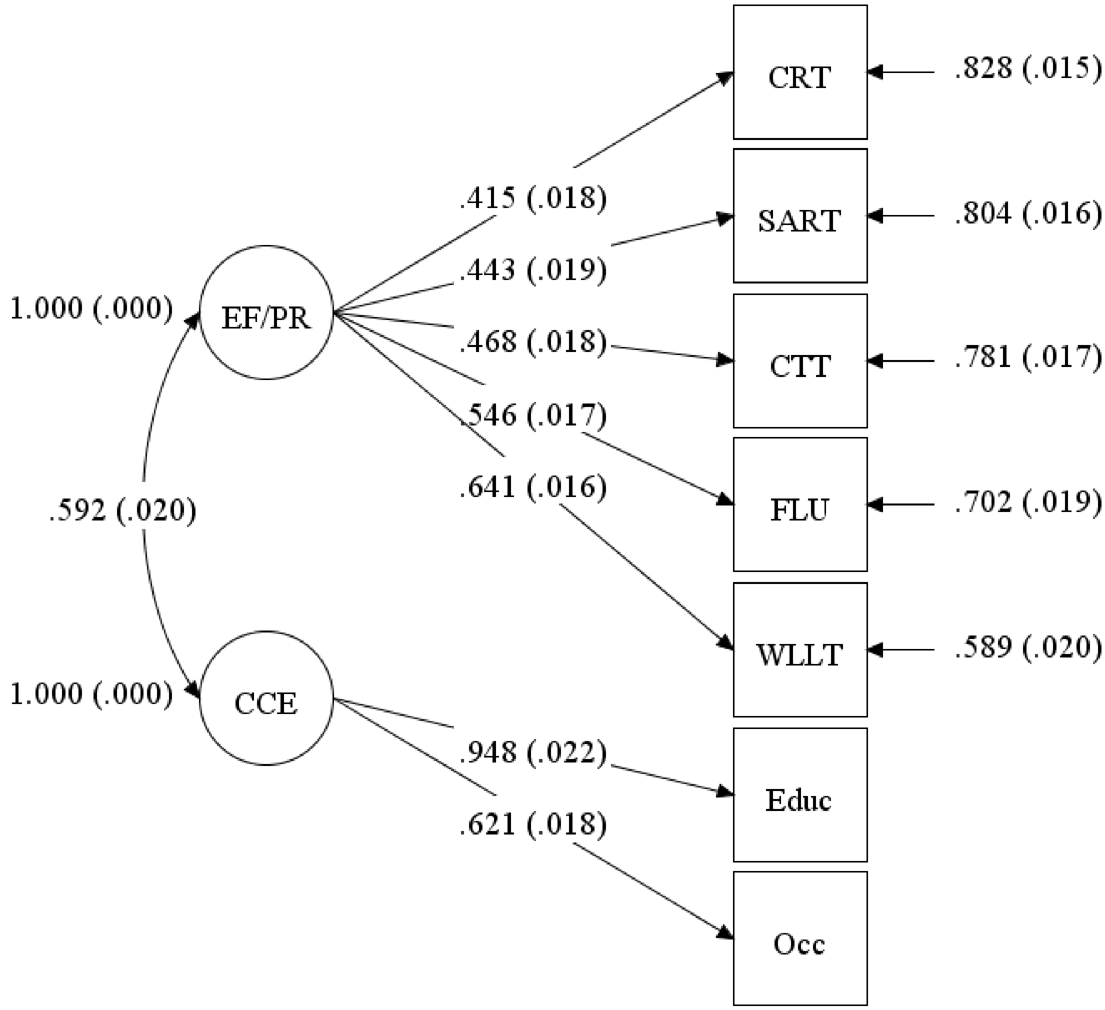


Figure 6. TILDA two-factor model of CR capacity including standardised parameter estimates

Note: EF/PR=Executive Function/Processing Resources; CCE=Cumulative Cognitive Enrichment; CRT=Choice Reaction Time (Processing Speed); SART=Sustained Attention to Response Task (Response Inhibition); CTT=Colour Trails Test (Cognitive Switching); FLU=Fluency (Verbal Fluency); WLLT=Word List Learning Test (Immediate Recall); Educ=Education Level; Occ=Level of Occupational Attainment. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

Table 13. TILDA parameter estimates from the two-factor CFA Model of EF/PR and CCE

	Estimates	**S.E.**	**Est./S.E.**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	4.02	0.42	0.17
Immediate Working Memory	0.46	0.03	17.78	1.86	0.64	0.41
Response Inhibition	0.36	0.02	15.92	1.44	0.44	0.20
Cognitive Switching	0.57	0.04	16.41	2.29	0.47	0.22
Fluency	0.18	0.01	17.38	0.72	0.55	0.30
CCE						
Education Level	1.00	0.00	999.00	0.95	0.95	0.90
Level of Occupational Attainment	0.66	0.03	20.70	0.62	0.62	0.39
Covariance of EF/PR and CCE	2.25	0.12	18.33	0.59	0.59	-

Note. Estimates=unstandardised parameter estimate; S.E.=standard error; Est./S.E.=test statistic (*z* value); Std=standardised parameter estimate; StdYX=completely standardised parameter estimate; R^2=square of the completely standardised parameter estimate.

Cognitive Reserve Capacity as a Function of Age

As with MAAS data, the two-factor structure of the CR capacity model was further investigated as a function of age. As TILDA did not contain sufficient data for those aged under 50, the model was only investigated in middle and old age. The full sample was divided into two age groups: 50-64 years (*n*=1,947) and 65-79 years (*n*=1,404). Following the same procedure as above, analyses were conducted on the sample variance-covariance matrices (WLSMV estimation; Mplus version 7.3). The acceptability of the model for both age groups was evaluated by overall goodness of fit, examination of specific points of ill fit, and evaluation of parameter estimates. Goodness of fit indices are summarized in *Table 14*. Overall, fit indices indicate that the model has excellent fit across both age groups. The completely standardised parameter estimates for both age groups are presented in *Figure 7* and *Figure 8* (standard errors of the estimates are provided in *Table 15*). All freely estimated unstandardised parameters were statistically significant (*ps*<.001). Factor loading estimates revealed that the indicators were moderately to strongly related to their purported latent factors. Furthermore, estimates from the two-factor solution indicate a moderate to strong relationship between the dimensions of EF/PR and Cognitive Activity for both age groups (factor correlations of 0.617 to 0.581 respectively).

Table 14. TILDA fit statistics for a two-factor CFA model of EF/PR and CCE as a function of age

Statistic	50-64 years	65-79 years
χ^2	65.889	36.215
df	13	13
p	0.0000	0.0005
RMSEA (90% CI)	0.046 [0.035, 0.057]	0.036 [0.022, 0.050]
CFI	0.980	0.988
TLI	0.968	0.981
WRMR	0.964	0.722

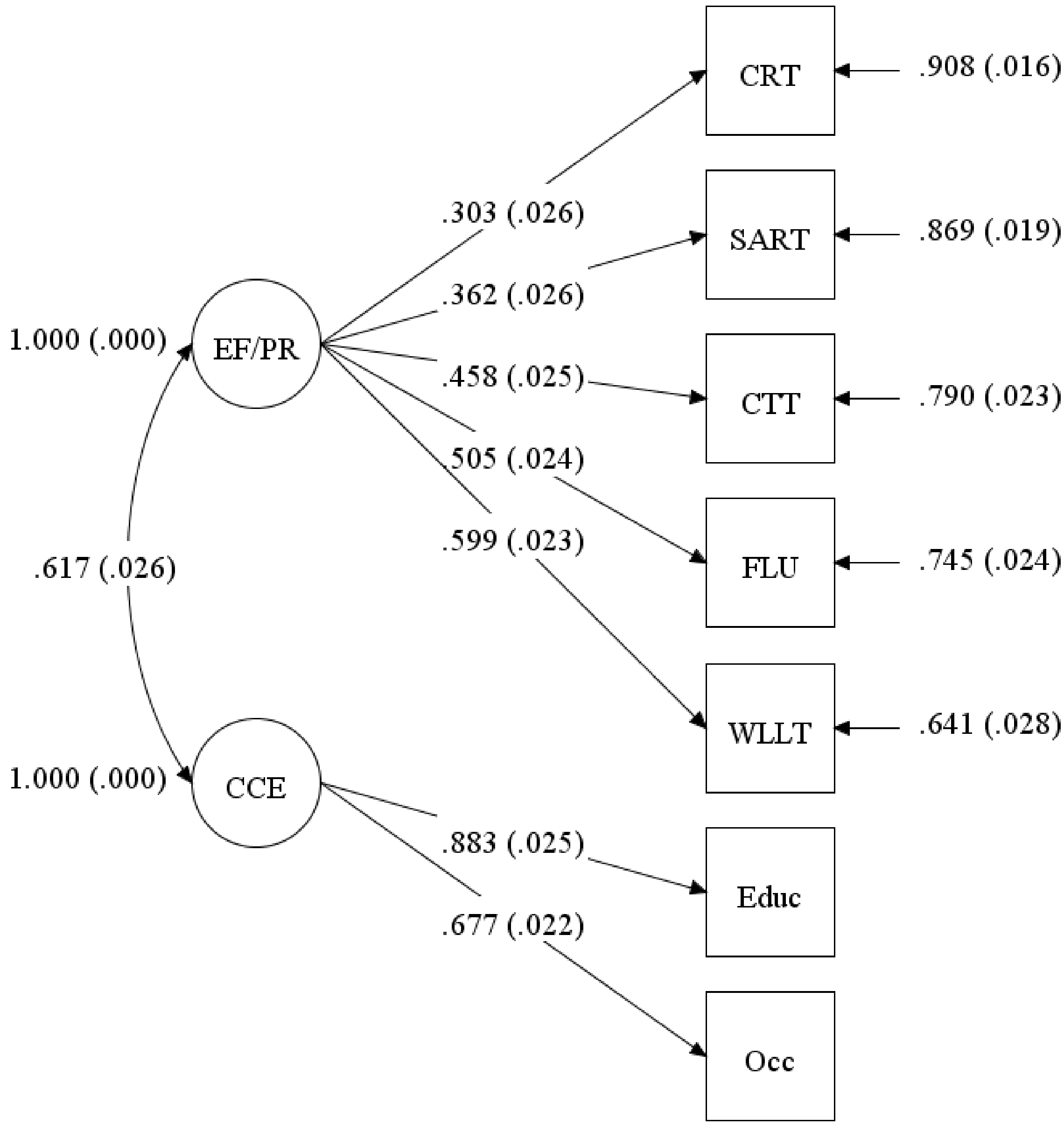


Figure 7. TILDA two-factor model of CR capacity including standardised parameter estimates for 50-64 year olds

Note. EF/PR=Executive Function/Processing Resources; CCE=Cumulative Cognitive Enrichment; CRT=Choice Reaction Time (Processing Speed); SART=Sustained Attention to Response Task (Response Inhibition); CTT=Colour Trails Test (Cognitive Switching); FLU=Fluency (Verbal Fluency); WLLT=Word List Learning Test (Immediate Recall); Educ=Education Level; Occ=Level of Occupational Attainment. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

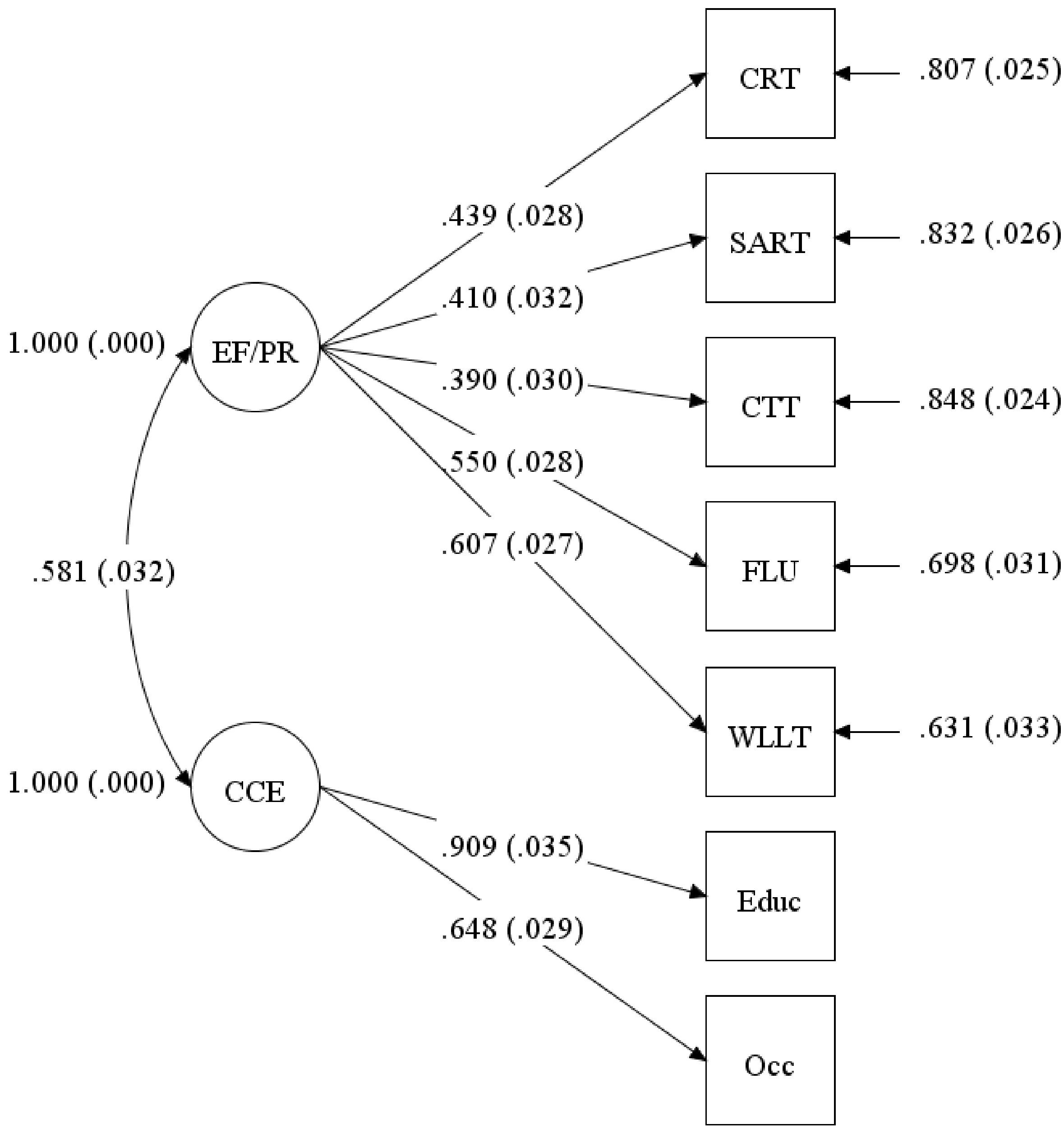


Figure 8. TILDA two-factor model of CR capacity including standardised parameter estimates for 65-79 year olds

Note. EF/PR=Executive Function/Processing Resources; CCE=Cumulative Cognitive Enrichment; CRT=Choice Reaction Time (Processing Speed); SART=Sustained Attention to Response Task (Response Inhibition); CTT=Colour Trails Test (Cognitive Switching); FLU=Fluency (Verbal Fluency); WLLT=Word List Learning Test (Immediate Recall); Educ=Education Level; Occ=Level of Occupational Attainment. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

Table 15. TILDA parameter estimates from the two-factor CFA model of EF/PR and CCE as a function of age

50-64 Year Olds	**Estimates**	**S.E.**	**Est./S.E.**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	2.69	0.30	0.09
Working Memory Verbal	0.59	0.06	10.00	1.60	0.60	0.36
Response Inhibition	0.37	0.04	8.91	0.99	0.36	0.13
Cognitive Switching	0.74	0.08	9.69	2.00	0.46	0.21
Fluency	0.25	0.03	9.65	0.67	0.51	0.26
CCE						
Education Level	1.00	0.00	999.00	0.88	0.88	0.78
Level of Occupational Attainment	0.77	0.04	17.74	0.68	0.68	0.46
Covariance of EF/PR and CCE	1.47	0.14	10.28	0.62	0.62	-

65-79 Year Olds	**Estimates**	**S.E.**	**Est./S.E.**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	4.49	0.44	0.19
Immediate Working Memory	0.39	0.04	11.12	1.77	0.61	0.37
Response Inhibition	0.34	0.04	9.38	1.52	0.41	0.17
Cognitive Switching	0.46	0.05	9.29	2.08	0.39	0.15
Fluency	0.16	0.01	11.33	0.70	0.55	0.30
CCE						
Education Level	1.00	0.00	999.00	0.91	0.91	0.83
Level of Occupational Attainment	0.71	0.06	12.81	0.65	0.65	0.42
Covariance of EF/PR and CCE	2.37	0.21	11.25	0.58	0.58	-

Note. Estimates=unstandardised parameter estimate; S.E.=standard error; Est./S.E.=test statistic (*z* value); Std=standardised parameter estimate; StdYX=completely standardised parameter estimate; R^2=square of the completely standardised parameter estimate.

Convergent and Discriminant Validity

CFA on Full Sample

Convergent validity can be examined by examining the significance and the magnitude of the factor loading of each indicator on its purported latent factor (Anderson & Gerbing, 1988). For the TILDA CFA on the full age range, all freely estimated unstandardised parameters were statistically significant (*p*s<.001) and factor loading estimates revealed that the indicators were moderately to strongly related to their latent factors (range of R^2s=0.172–0.899). This indicates convergent validity of the model based on the full age-range (50 to 79 years). Discriminant validity was investigated by testing to see if the confidence interval (±2 standard errors) for the standardised correlation estimate between the two latent factors included the value of 1.0 (Anderson & Gerbing, 1988). This analysis supported the discriminant validity of the factors as the confidence interval for this correlation did not contain the value of 1.0 [0.559, 0.624].

CFA on Different Age Groups

For both age-groups, the freely estimated unstandardised parameters were statistically significant (*ps*<.001) and factor loading estimates revealed that the indicators were moderately to strongly related to their latent factors (see *Table 15* for range of R^2s for both age groups). This indicates convergent validity of the model across both age groups. As above, discriminant validity was investigated by testing to see if the confidence interval (±2 standard errors) for the standardised correlation estimate between the two latent factors included the value of 1.0 (Anderson & Gerbing, 1988). This analysis supported the discriminant validity of the factors for both age groups as the 90% confidence interval for the correlations did not contain the value of 1.0 (50-64 year age group [0.574, 0.660], 65-79 year age group [0.529, 0.634]). Therefore, the TILDA CFAs provide further evidence for the discriminant validity of the EF/PR and CCE latent factors.

4.5 Discussion

This validation study sought to replicate the CR capacity measurement model in a secondary, Irish longitudinal ageing dataset, TILDA. CFA was used to validate the factor solution derived from the EFA in study 1 in terms of how well it reproduced the sample covariance matrix of the measured variables. Goodness-of-fit indices suggest that for both the full sample, and the sample broken into middle and older age groups, the TILDA CFA models fit the data very well. Similar to the MAAS models, the χ^2 index of absolute model fit was consistently poor ($S \neq \Sigma$). However, as outlined by Brown (2006), χ^2 is rarely used in applied research as a sole index of model fit and other fit indices such as RMSEA may be more appropriate when sample size is large. Parameter estimates were all positively related to their latent factors across all age groups. Convergent validity is evidenced by the proportion of variance of each indicator that is explained by its latent factor, which ranged from 17% to 89% for the full sample model. This signals a moderate to strong influence on these indicators by their underlying latent factors. This pattern was closely replicated when the sample was broken into age groups and is consistent with findings of convergent validity in the MAAS CFAs. As there was no available measure of crystallised IQ in TILDA, it was not possible to compare the change in strength of this indicator as a function of age. However, the variance in education explained by CCE was seen to increase somewhat in the older age group, perhaps reflecting the diminishing role of occupation in older age. While, like MAAS, the EF/PR factor loadings supported the convergent validity of this factor, the relative weighting of indicators differed slightly from MAAS. While processing speed was consistently the strongest indicator in MAAS across age groups, this indicator was the weakest indicator for the middle-aged group in TILDA, but increased in strength in the older age group. This may be due to differences in the measurement of processing speed (Letter Digit Task vs. Choice Reaction Time). Although both of these tasks are considered to reflect choice reaction time (Salthouse, 2000), their administration differed (pen and pencil vs. computerised).

Regardless of slight differences in the indicator weightings, the TILDA CFA supports the convergent validity of both the CCE and EF/PR latent factors. In addition to these findings, estimates from the two-factor solutions for all CFAs indicate moderate intercorrelations of between 0.581 and 0.617 between the dimensions of EF/PR and CCE which can be viewed as further evidence of the discriminant validity of the factors. These findings support the results of the MAAS CFAs, as well as previous research on the construct validity of CR and other cognitive constructs (M. B. Mitchell, Shaughnessy, et al., 2012; Siedlecki et al., 2009). The TILDA CFAs also support the segregation of the CR capacity indicators into two factors that embody control and representational processes (Craik & Bialystok, 2006). Like MAAS, the EF/PR factor can be seen to represent control processes that facilitate intentional processing and flexible cognitive performance whereas, the CCE factor can be viewed as representing crystallised schemas that reflect knowledge of the world. The consistent strong relationship between these factors across MAAS and TILDA support the theory that these processes have a reciprocal relationship, whereby control processes influence the construction of representations, and in turn, these crystallised representations influence further controlled processing.

Overall, the TILDA CFAs validate the two-factor solution that arose from the MAAS EFA, although it must be noted that the TILDA CFA was limited by the lack of a measure of crystallised IQ in the TILDA dataset. Consequently, only two indicators loaded on the CCE factor. From a theoretical point of view, literature has suggested that education level may be a good proxy of crystallised IQ (Kaufman, Kaufman, Liu, & Johnson, 2009; Kaufman & Lichtenberger, 2006), and therefore its absence should not change the representational processes interpretation of the CCE factor. From a statistical point of view, according to Mitchell et al. (2012) having only two indicators for a factor can place a burden on the data-model covariance fit structure. However, in this case, the fit of the models was very good. Also, having only two indicators for the CCE factor in the CFA meant that, unlike MAAS, the error terms for Education Level and Level of Occupational Attainment could not be correlated due to identification issues (Kenny, 2011). Nevertheless, the fit of the CFA models was good. In sum, the TILDA CFA validation study provides strong support for a two-factor CR capacity model comprised of EF/PR and CCE. The next step is to examine the structural model of CR capacity using the confirmed two-factor measurement model, and predict cognitive function based on these latent CR capacities. This necessarily involves two primary aims: (1) To develop a structural CR capacity model in the MAAS data set (Study 3) and (2) To validate the structural CR capacity model in the TILDA data set (Study 4).

Chapter 5: Study 3 - A Structural Model of Cognitive Reserve Capacity

5.1 Introduction

The EFA and CFA in study 1 and the CFA validation in study 2 have helped to refine the measurement of CR capacity by establishing the construct validity of a two-factor CR capacity model. However, the structural relationships between a CR capacity construct driven by EF/PR and CCE, and cognitive outcomes sensitive to age-related decline, remains unclear. Traditionally, CR is modelled using proxy indicators reflecting environmental variables (Jones et al., 2011). However, it has been established that other cognitive dimensions are involved in CR capacity, such as EF, PR, and IQ, due to their strong relationship with traditional CR enrichment proxies (Satz et al., 2011). For instance, in a CFA conducted by Mitchell et al. (2012) a latent variable comprised of traditional CR proxies was found to be moderately correlated with a latent variable comprised of EF and PR measures in both healthy older adults and aMCI individuals. Furthermore, traditional CR proxy indicators such as education have been found to have a strong relationship with measures of general and crystallised IQ (Sternberg et al., 2001). Such is the degree of overlap between these dimensions and the traditional CR proxy construct that it is necessary to redefine CR in such a way that accounts for this overlap. Previous research has operationally defined CR as a complex structure of latent variables (Lojo-Seoane et al., 2014). Expanding on this definition, based on the findings of studies 1 and 2, CR capacity can be viewed as the reciprocal relationship between control and representational processes and their combined role in sustaining cognitive abilities across the lifespan. Latent variable analysis can be used to clarify the nature of the relationships between these CR capacity variables and their predictive relationships with global cognition/memory outcomes that have been shown to be indicative of cognitive decline due to normal ageing or pathology. The measurement model explored and validated in studies 1 and 2 supports the construct validity of a two-factor CR capacity model, and provides evidence for a strong relationship between these two CR components. The structural relationships between a CR capacity construct, comprised of EF/PR and CCE, and global cognition/memory abilities over time, however, remains unclear. The next step, therefore, is to test the CR capacity model for consistency of the hypothesised structural relationships (nomological validity) (Anderson & Gerbing, 1988).

5.1.1 Relationships between Control and Representational Processes and Global Cognition/Memory

As shown in studies 1 and 2, the EF/PR and CCE latent variables are highly correlated and can theoretically be viewed as contributing to CR capacity. Across the lifespan, these constructs undergo varying growth and decrement patterns which may have implications for their relationship with each other and measures of cognitive performance over time. The CCE construct is comprised of traditional enrichment proxies of CR (education level, level of occupational attainment, crystallised IQ), and the protective effects of these indicators are well established and have been outlined in Chapter 2 (Bosma et al., 2002; Crowe et al., 2003; Scarmeas et al., 2001; Valenzuela & Sachdev, 2009; Wilson et al., 2013). These indicators reflect crystallised abilities that increase during childhood and into middle age, and remain relatively stable into old age (Cattell, 1971). Conversely, research has shown that EF/PR indicators are vulnerable to the effects of normal ageing. De Luca et al. (De Luca et al., 2003) investigated the development of EFs over the lifespan. The study used the computer-based Cambridge Neuropsychological Test Automated Battery (CANTAB) to pinpoint periods of developmental change in executive abilities in a normative sample of 194 participants aged 8 to 64 years. It was found that these abilities develop in childhood, plateau in early adulthood and remain stable until mid-life, with performance decrements observed in the 50 to 64 year age group. Similarly, a study by Zelazo, Craik and Booth (2004) investigated age-related changes in EF using sorting tasks. It was found that both children (aged 8-9) and older adults (aged 65-74) made more perseverative errors than young adults (aged 19-26). This U-shaped developmental trend in EF is also observable in studies investigating age-related changes in processing speed (Kail & Salthouse, 1994; Li et al., 2004). Therefore, while it is likely that representational processes like CCE either increase or remain relatively stable across the lifespan, the control processes like EF/PR are more likely to peak and then decline from mid-life onwards. While many studies have investigated the effect of traditional CR measures on cognitive functioning, as measured by tasks that tap EF and PR, it may be the case that these control processes also affect traditional CR measures, and therefore both can be viewed as contributing to CR capacity. In order to establish the nomological validity of the CR capacity model, it is necessary to investigate how EF/PR and CCE jointly contribute to CR capacity by sustaining cognitive abilities like global cognition and memory over time.

Theoretical models of CR differ with regard to their predictions. For instance, models that predict rates of decline in cognitive performance often regard traditional CR proxies as moderators of rates of decline. Alternative models regard traditional CR proxies as predictive of cognitive status over time, rather than rates of decline. In models that predict rates of decline, individuals deemed to have high CR are able to maintain performance levels better than low CR individuals who experience a more rapid decline. Several studies have found that CR levels are predictive of rates of cognitive decline. For instance, participation in cognitively stimulating activities has been associated with reduced levels of late-life cognitive decline as measured by variables such as recall, vocabulary knowledge, processing speed, working memory and fluency (Bosma et al., 2002; Hultsch, Hertzog, Small, & Dixon, 1999). These predictions are similar to what Salthouse (1991) referred to as “differential preservation”, or the prediction that individuals higher in CR show less negative change in cognitive functioning over time.

An alternative viewpoint put forward by Salthouse is that of “preserved differentiation”, where models predict that baseline performance differences remain stable over time. In other words, high- and low-CR individuals differ in their initial levels of cognitive ability, but their rates of decline over time are similar. A study by Bielak et al. (2012) supports the idea of preserved differentiation as results suggest that participation in cognitively stimulating activities is related to cognitive ability (as measured by processing speed, short-term memory, working memory, episodic memory, and vocabulary) but not rates of change in these cognitive abilities over time. Similar results were found in a study where CR was indicated by years of education and vocabulary knowledge, and cognitive ability (measured by processing speed and reasoning) was assessed at both baseline and five-year follow-up (Tucker-Drob et al., 2009). It was found that CR was related to levels of cognitive functioning at both baseline and five-year follow-up, but CR was not related to rates of cognitive change.

This supports the idea of preserved differentiation in that CR characterises the persistence of baseline differences in cognitive functioning rather than differential rates of decline associated with healthy ageing. The authors also argue that results of studies where CR is treated as a moderator of rates of decline may be confounded by correlations between levels of cognitive functioning and rates of decline in functioning (level-slope relations). Therefore, it may be the case that rather than experiential resources having a direct protective role in cognitive decline, these resources influence levels of cognitive functioning in early adulthood that are predictive of cognitive functioning in later life. This idea can be applied to a CR capacity model comprised of both control and representational processes, whereby the reciprocal relationship between these processes reflects baseline differences in CR capacity, which in turn is predictive of cognitive status over time. Glymour (2005) supports this idea by arguing that if experiential resources/representational processes such as education influence cognitive function or CR in middle-age, then they will also impact in the incidence of cognitive impairment in later life, even if it has no effect on rates of decline in healthy ageing.

Given the strong positive relationship between EF/PR and CCE observed in studies 1 and 2, an investigation into their individual contributions to CR capacity and in turn the structural relationship between CR capacity and cognitive decline outcomes over time is of interest. These relationships are unclear given the differential growth and decrement patterns of EF/PR and CCE over the lifespan. Given the vulnerability to decline in EF/PR in those aged 50 and over, modelling CR capacity and its relationship with cognitive outcomes in this age group is of particular importance. Also of interest is whether CR capacity predicts differential associations with cognitive decline outcomes in mid-life and later life. Based on the findings from the previous chapter, the indicators that constitute the CR capacity factors and their loading values are similar for both 50-64 year olds and 65-82 year olds, suggesting that vulnerability factors may be similar for both of these age groups.

5.1.2 A Structural Model of CR Capacity and Global Cognition/Memory

The next step in testing the CR model initially proposed by Satz et al. (2011) is to explore the predictive relationship between CR capacity and cognitive decline outcomes in both mid- and late-life over time. Therefore, the main objective of the present study is to develop a structural model that includes the CR capacity factors from the measurement model developed in Chapter 3, and to use this model to establish the relationships between, and the impact of, CR capacity on cognitive measures shown to be predictive of clinically significant decline, such as the Mini Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975), measures of long-term memory and measures of subjective memory (Jacobs et al., 1995; Jessen et al., 2010; A. J. Mitchell, Beaumont, Ferguson, Yadegarfar, & Stubbs, 2014; Tombaugh & McIntyre, 1992). More specifically, this study investigates whether EF/PR and CCE contribute to the formation of a hierarchical CR capacity construct and if this CR capacity construct is predictive of baseline levels of global cognition/memory outcomes and their status over time. In doing so, the following questions will be addressed:

1. Do EF/PR and CCE contribute to a hierarchical CR capacity construct?
2. Is CR capacity predictive of cognitive performance at baseline?
3. Is baseline CR capacity predictive of cognitive performance at 6-year and 12-year follow-up (FU)?
4. Do these relationships differ from mid- to late-life?

5.2 Method

5.2.1 Participants

The sample was selected from the Maastricht Ageing Study (MAAS), a 12-year longitudinal study on the determinants of cognitive ageing (Jolles et al., 1995). The baseline sample consisted of 1,823 participants, aged 24 to 82 years (see Chapter 3 for detailed information on the MAAS sample frame). A number of individuals were excluded from the sample, including 236 whose education and occupation were unknown and nine participants who converted to dementia during the course of the 12-year study. Outlying values greater than three standard deviations beyond the mean were removed for each variable. For the purposes of this analysis, those aged under 50 years at baseline were also excluded and the sample was divided into middle aged (50-64 years) and older aged (65-82 years) participants. Analysis was based on 777 individuals, of which 393 were aged between 50 and 64 (224 male; 169 female) and 384 were aged between 65 and 82 years (233 male; 151 female) at baseline.

5.2.2 Measures of Cognitive Reserve Capacity

The CCE and EF/PR measures used in this study are the same as those used in the MAAS CFA analysis. Please see Chapter 3 and *Table 2* for a more detailed description of the CR capacity measures.

Briefly, the CCE indicators used in this study were as follows: Level of education, level of occupational attainment and crystallised IQ as measured by the *Groningen Intelligence Test* (GIT). The GIT is a test of general intelligence used as frequently as the Wechsler Adult Intelligence Scale (WAIS) in the Netherlands (Luteijn & Van der Ploeg, 1983). The total score on the GIT2 was used as a measure of crystallised IQ (vocabulary).

Briefly, the EF/PR indicators used in this study were as follows: The *Stroop Colour-Word Test* (Stroop, 1935; van der Elst et al., 2006d) was used as a measure of response inhibition. The *Fluency* test measures strategy-driven retrieval of information from semantic memory (Lezak et al., 2004; van der Elst et al., 2006a). The number of correct responses was taken as a measure of semantic fluency. The *Concept Shifting Test* (CST) (van der Elst et al., 2006b; Vink

& Jolles, 1985) is a modified version of the Trail Making Test (Reitan, 1958). A measure of set shifting was calculated by subtracting the average time needed to complete CST A and CST B from the time needed to complete CST C. The *Letter-Digit Modalities Test* (LDMT) is an adapted version of the Digit-Symbol Substitution Test (A. Smith, 1968). The number of correctly completed letters in 90 seconds served as a measure of processing speed. The *Verbal Learning Test* (Brand & Jolles, 1985; van der Elst et al., 2005) is a modified version of the word-list learning test by Rey (1958). The total number of correctly recalled words after the five trials was used as a measure of working memory.

5.2.3 Measures of Cognitive Outcome

The *Mini Mental State Examination* (MMSE) is an internationally accepted dementia screening instrument (Folstein et al., 1975). It consists of the following subscales: Orientation, registration, recall, attention, language, and construction. The total score on the MMSE was used as a measure of global cognitive performance.

Delayed Recall was measured as part of the *Verbal Learning Test* (WLT) (Brand & Jolles, 1985; van der Elst et al., 2005). Twenty minutes after presentation and immediate recall of a series of words, participants were asked to again recall these words. This test of delayed recall was used as a measure of long term memory, which has been shown to be predictive of cognitive decline (Chodosh, Reuben, Albert, & Seeman, 2002).

Subjective memory was assessed by asking participants the following question: ‘Do you consider yourself to be forgetful?’ Participants were asked to respond with either ‘yes’ or ‘no’.

5.3 Analysis

5.3.1 Structural Equation Modelling

Structural equation modelling (SEM) in the form of structural regression (SR) was used to investigate the structural relationships between a measurement model of CR capacity and global cognition/memory performance over time. SR is a combination of a structural model and a measurement model (Kline, 2011). While there are a number of SEM approaches that could be used in multivariate modelling studies, such as latent growth modelling or multilevel modelling, the SR approach was most appropriate for the research questions at hand as it is capable of testing hypotheses about both structural and measurement relations within a single model. The main goal is to test a theory by specifying a model representative of predictions of that theory (Hayduk, Cummings, Boadu, Pazderka-Robinson, & Boulianne, 2007). According to Kline (2011), SR allows tests of hypotheses about direct and indirect effects which involve latent variables or formative constructs. Another major strength of SR is its ability to address the issue of measurement error (unreliability) within a model (Little, Card, Bovaird, Preacher, & Crandall, 2007). While a path analysis containing only observed variables assumes that all variables are measured without error, SR has the ability to account for measurement error using latent variables. In a SR the common variance of multiple indicators of a latent variable are estimated taking into account their associated measurement error. As latent variables are not directly measured they do not have measurement error associated with them, therefore the structural relations among latent constructs can be modelled without measurement error. A model is a fully latent model if every variable in its structural model is latent. However, it is also possible to represent in a SR an observed (manifest) variable that is a single indicator of a construct. Such models can be referred to as partially latent models (Kline, 2011). Therefore, this study employed partially latent SEM, in the form of SR, where scores for the outcome measures (MMSE, delayed recall and subjective memory) were included as single indicators of global cognition and memory performance.

5.3.2 A Higher-Order Formative Conceptualisation of CR

Higher-order formative constructs have multiple dimensions that each represent important aspects of the construct (Bollen & Lennox, 1991). Following the EFA and CFA models in studies 1 and 2, it was established that EF/PR and CCE are empirically related but also distinct dimensions and could theoretically represent facets of a hierarchical CR capacity construct. According to Jones et al. (2011) modelling CR as a latent variable with reflective indicators (EF/PR and CCE) may be problematic as it assumes that its indicators are *caused* by an unobserved variable. (i.e., CR capacity causes EF/PR and CCE levels). Jones et al. argue that factors believed to be involved in CR capacity are formative indicators in that they *create* CR, therefore theoretically, a causal ordering is appropriate (i.e., CR capacity is created by EF/PR and CCE levels). MacKenzie, Podsakoff and Jarvis (2005) argue that in order for a construct to be modelled as formative rather than reflective, certain conditions need to be met. For instance, formative indicators need to be viewed as defining characteristics of the construct in question. In this case, the EF/PR and CCE latent variables encompass a large number of the indicators previously implicated in CR capacity. For instance, each of the four constructs that Satz et al. (2011) suggest contribute to CR capacity (EF, PR, CMA, and IQ) are represented by the EF/PR and CCE indicators. Another condition states that changes in any of the formative indicators will result in changes in the formative construct, lending support to the idea that modifying a formative indicator of CR capacity such as EF/PR could impact on CR capacity.

5.3.3 Model Specification

This study specifies CR as a first-order reflective, second-order formative model. The EF/PR and CCE latent variables, each of which are reflected by multiple indicators, act as formative indicators of CR capacity. Structure and fit of three versions of the model were investigated using partially latent SEM (see *Figure 9* for a diagram of the proposed structural model). A baseline model (Model 1) used raw baseline data for both the predictor variables (exogenous variables) (EF/PR and CCE constructs) and the outcome variables (endogenous variables) (baseline MMSE, delayed recall and subjective memory). A longitudinal model (Model 2) used raw baseline data for exogenous variables (EF/PR and CCE constructs) and raw follow-up data at six years for the endogenous variables (MMSE, delayed recall and subjective memory at six-year follow-up). A further longitudinal model (Model 3) used raw baseline data for exogenous variables (EF/PR and CCE constructs) and raw follow-up data at 12-years for the endogenous variables (MMSE, delayed recall and subjective memory at 12-year follow-up). The parameter estimates for the longitudinal models, however, may not adequately reflect scores on the endogenous variables at 6- and 12-year follow-up as they have not taken into account baseline values of the outcome measures. Methods used to predict outcomes in longitudinal models include the act of controlling for baseline levels of the outcomes (regressor variable method), or alternatively, the use of change scores (change score method) from baseline to follow-up. Allison (1990) argues that while in certain instances the use of change scores is preferable to the regressor variable method (e.g., experimental designs with control groups) the change score method has also received much criticism due to unreliability and regression toward the mean effects. Vickers and Altman (2001) note that change scores do not control for baseline imbalance in values of the outcome measures and due to regression toward the mean, participants with low scores at baseline may have higher scores at follow-up, whereas participants with high scores at baseline may have lower scores at follow-up. In order to avoid this occurrence, additional analyses using the regressor variable method were conducted on Models 2 and 3 in order to investigate if controlling for baseline scores for the endogenous variables impacted on parameter estimates. Parameter estimates both before and after controlling for these variables are reported.

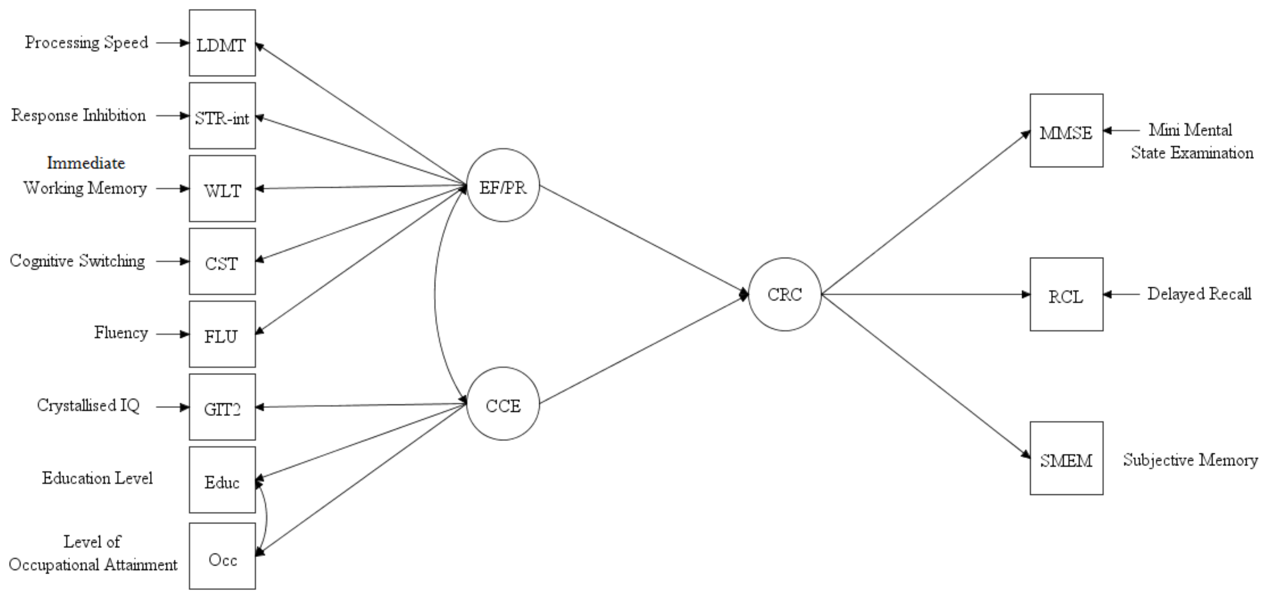


Figure 9. Diagram of the proposed structural model

Note. EF/PR=Executive Function/Processing Resources; CCE=Cumulative Cognitive Enrichment; CRC=Cognitive Reserve Capacity. Three models were tested using this structure: Model 1 - raw baseline data for both exogenous variables (EF/PR and CCE) and endogenous variables (baseline MMSE, delayed recall and subjective memory). Model 2 - raw baseline data for exogenous variables (baseline EF/PR and CCE) and raw follow-up data at six years for the endogenous variables (MMSE, delayed recall and subjective memory at six-year follow-up). Model 3 - raw baseline data for exogenous variables (baseline EF/PR and CCE) and raw follow-up data at 12 years for endogenous variables (MMSE, delayed recall and subjective memory at 12-year follow-up).

5.3.4 Statistical Analysis

Structural regression was conducted using robust weighted least squares estimation (WLSMV). The software package used for the analyses was Mplus version 7.3 (L. K. Muthén & Muthén, 2011). Scores more than three standard deviations beyond the mean were removed from the dataset prior to analysis. Kolmogorov-Smirnov and Shapiro-Wilk tests of normality were conducted on the residuals of all measures. From these tests, it appeared that most measures deviated from the normal distribution (*ps*<.001). Therefore, an estimator robust to the effects of non-normality in exogenous indicators was used (WLSMV). As the endogenous delayed recall variable violated assumptions of normality it was necessary to perform a square transformation on this variable. Two measures were reflected in order for high scores to represent better performance (Stroop Colour Word Test and Concept Shifting Test). This reflection was conducted for ease of interpretation of results, with high scores equating to better performance across all measures. Multicollinearity was assessed using SPSS version 21

(IBM Corp, 2012) through examination of the correlation matrix and collinearity diagnostics (the Variance Inflation Factor and the Tolerance Statistic). There was no indication of multicollinearity among the factor indicators. As subjective memory is a binary outcome variable, the paths from predictors to this variable are probit regression coefficients and are interpreted based on significance, sign and magnitude. For instance, if the subjective memory variable is coded with values of '0' for Yes and '1' for No, a positive sign means that the probability of the category coded '1' is increased when the predictor value increases. The larger the magnitude, the faster this probability increases (B. O. Muthén, 1999).

A potential methodological issue in serial cognitive assessment is that of practice/retest effects, which refers to improvements in performance over time due to repeated exposure (Abner et al., 2012). Repeated testing effects are common in longitudinal ageing datasets and variability in performance is influenced by age and the type of neurocognitive ability being measured (Salthouse, 2010). For instance, previous research has shown that MMSE scores are not likely to decline in healthy ageing populations. A study by Jacqmin-Gadda et al. (1997) found that MMSE scores in healthy older adults improved from baseline to one-year follow-up, before declining slightly at five-year follow-up, with a slightly steeper decline for the oldest age group (85 years and over). This improvement could be due to test-retest effects, or alternatively it may be the result of increased stress experienced by the participants at baseline testing. Overall, the authors suggest that decline in MMSE scores is very slow in healthy ageing. As very little decline was observed over a five-year period it may be the case that the different cognitive processes measured by the MMSE are not strongly affected by the ageing process. With regard to memory measures such as delayed recall, previous research has suggested that practice effects tend to be larger for memory-related measures than for tests of processing speed (Ferrer, Salthouse, Stewart, & Schwartz, 2004). However, it has also been suggested that practice effects are generally not as pronounced in older adults, possibly reflecting a failure in this group to use controlled processing strategies to facilitate performance (Reuter-Lorenz & Lustig, 2005). Another potential explanation for improvements over time may be due to selective dropout of poor performers, and therefore examination of scores on the outcome measures over time should focus on complete cases only in order to avoid this confound. Although controlling for practice effects is beyond the scope of this research, the participants in this study were exposed to similar experimental conditions (i.e., the same tests were administered and participants were subject to the same number of assessments), and this allowed for comparison between age groups, with cognitive change over time being defined as the cumulative effect of retest and ageing (van Dijk et al., 2008).

5.4 Results

5.4.1 Descriptive Statistics

Table 16 contains details of the descriptive statistics for the sample participants on demographic, CR measures and outcome measures at baseline. Participants were aged between 50 and 82 years and were divided into two age groupings for analysis: 50-64 year olds (*n*=393) and 65-82 year olds (*n*=384). The mean education level for both age groups was 'intermediate secondary education'. The mean occupation level for both age groups was 'work requiring considerable experience'. Mean scores on the measure of crystallised IQ (Groningen Intelligence Test – Vocabulary) were very similar for both age categories. Mean scores on the remaining cognitive tasks indicate consistently higher scores in the 50-64 year age group compared to those aged over 65. *Table 17* contains details of descriptive statistics for the sample participants on outcome measures at 6- and 12-year follow-up. *Table 18* and *Figure 10* summarise descriptive statistics for sample participants on outcome measures at baseline, six- and 12-year follow-up for complete cases only.

Table 16. Descriptive statistics for demographic, CR capacity, and Global Cognition/Memory measures at baseline

	50 – 64 Years				65 – 82 Years			
	N	Mean	Range	SD	N	Mean	Range	SD
Age (years)	393	56.68	50.00-64.00	4.36	384	71.77	65.00-82.00	4.72
EF/PR								
Stroop Colour Word Test (time in seconds)	378	46.14	15.20-104.25	16.53	338	57.55	21.20-107.30	18.64
Stroop Colour Word Test (Reflected) (time in seconds)	378	63.41	5.30-94.35	16.53	338	52.00	2.25-88.35	18.64
Fluency (animals) (No. correct)	391	23.22	9.00-41.00	6.02	381	21.66	6.00-41.00	5.89
Concept Shifting Test (time in seconds)	380	11.94	-2.05-46.10	8.34	360	15.29	-9.80-46.30	9.66
Concept Shifting Test (Reflected) (time in seconds)	380	35.36	1.20-49.35	8.34	360	32.01	1.00-57.10	9.66
Letter Digit Modalities Test (No. correct)	391	46.47	20.00-73.00	9.27	377	38.73	16.00-66.00	9.30
Verbal Learning Test (No. correct)	388	44.91	24.00-68.00	8.69	377	38.76	18.00-68.00	9.30
CCE								
Education Level	393	3.38	1.00-8.00	1.83	384	3.06	1.00-8.00	1.87
Level of Occupational Attainment (LOA)	393	3.86	1.00-7.00	1.70	384	3.79	1.00-7.00	1.67
Groningen Intelligence Test (Vocabulary) (No. correct)	388	13.63	5.00-20.00	3.08	378	13.82	5.00-19.00	3.15
Global Cognition/Memory								
Verbal Learning Test – Delayed Recall (No. correct)	391	9.50	1.00-15.00	2.77	381	7.65	1.00-15.00	3.05
Subjective Memory (binary scale)	390	0.64	0.00-1.00	0.48	375	0.61	0.00-1.00	0.49
Mini-Mental State Examination (No. correct)	392	28.43	23.00-30.00	1.49	381	27.54	23.00-30.00	1.70

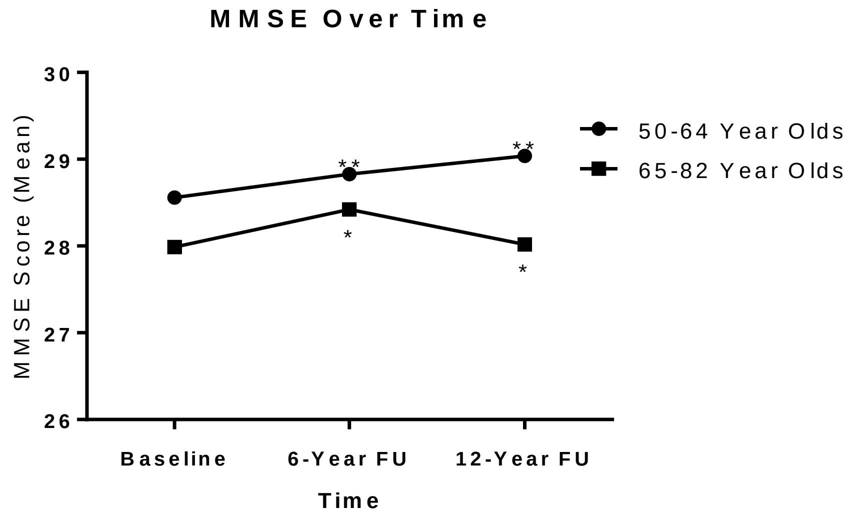
Note. Mean and SD values represent scores following reflection of the Stroop Colour Word Test and Concept Shifting Test and prior to transformation of the delayed recall variable

Table 17. Descriptive statistics for Global Cognition/Memory measures at 6- and 12-year follow-up

	50 – 64 Years				65 – 82 Years			
6-Year Follow-Up	N	Mean	Range	SD	N	Mean	Range	SD
Verbal Learning Test – Delayed Recall	323	10.31	2.00-15.00	2.89	233	8.70	2.00-15.00	3.20
Subjective Memory	320	0.64	0.00-1.00	0.48	220	0.57	0.00-1.00	0.50
Mini-Mental State Examination	325	28.78	24.00-30.00	1.21	231	28.03	24.00-30.00	1.54
12-Year Follow-Up								
Verbal Learning Test – Delayed Recall	280	10.11	2.00-15.00	2.93	117	8.13	2.00-15.00	3.21
Subjective Memory	269	0.59	0.00-1.00	0.49	126	0.48	0.00-1.00	0.50
Mini-Mental State Examination	285	29.03	24.00-30.00	1.13	135	27.99	24.00-30.00	1.75

Table 18. Descriptive Statistics for Global Cognition/Memory measures over time for complete cases only

	50 – 64 Years				65 – 82 Years			
Baseline	N	Mean	Range	SD	N	Mean	Range	SD
Verbal Learning Test – Delayed Recall	263	9.52	2.00-15.00	2.68	113	9.08	2.00-15.00	2.86
Subjective Memory	256	0.65	0.00-1.00	0.48	114	0.69	0.00-1.00	0.46
Mini-Mental State Examination	272	28.56	24.00-30.00	1.41	130	27.99	24.00-30.00	1.59
6-Year Follow-Up								
Verbal Learning Test – Delayed Recall	263	10.52	4.00-15.00	2.78	113	9.83	3.00-15.00	2.73
Subjective Memory	256	0.66	0.00-1.00	0.47	114	0.57	0.00-1.00	0.50
Mini-Mental State Examination	272	28.83	24.00-30.00	1.16	130	28.42	24.00-30.00	1.35
12-Year Follow-Up								
Verbal Learning Test – Delayed Recall	263	10.07	2.00-15.00	2.92	113	8.18	2.00-15.00	3.23
Subjective Memory	256	0.58	0.00-1.00	0.49	114	0.47	0.00-1.00	0.50
Mini-Mental State Examination	272	29.04	24.00-30.00	1.13	130	28.02	24.00-30.00	1.77



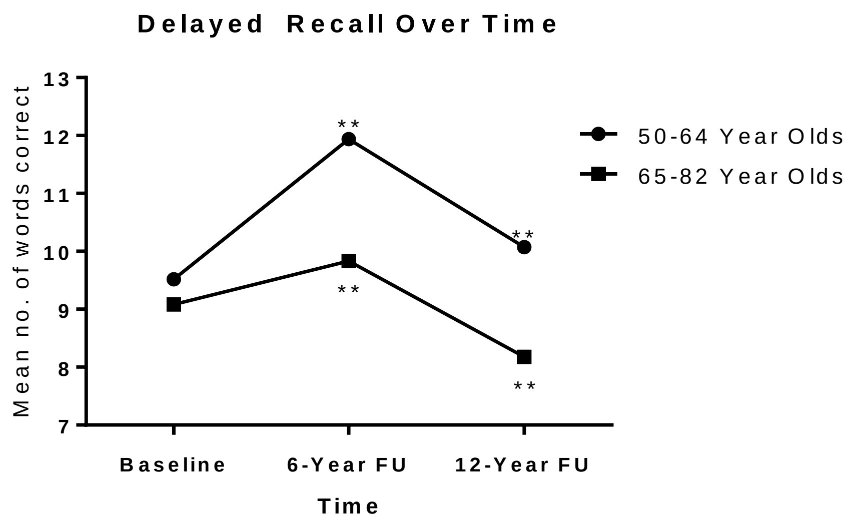


Figure 10. Mean Scores on MMSE and Delayed Recall for age groups over time (complete cases)

Note. *p<.05, **p<.001; Significance of differences across time points is based on a repeated measures ANOVA with time as a within factor. Significance indicated at six-year FU refers to a difference from baseline. Significance indicated at 12-year FU refers to the difference between scores at 12-year FU and baseline, and between 12-year FU and six-year FU.

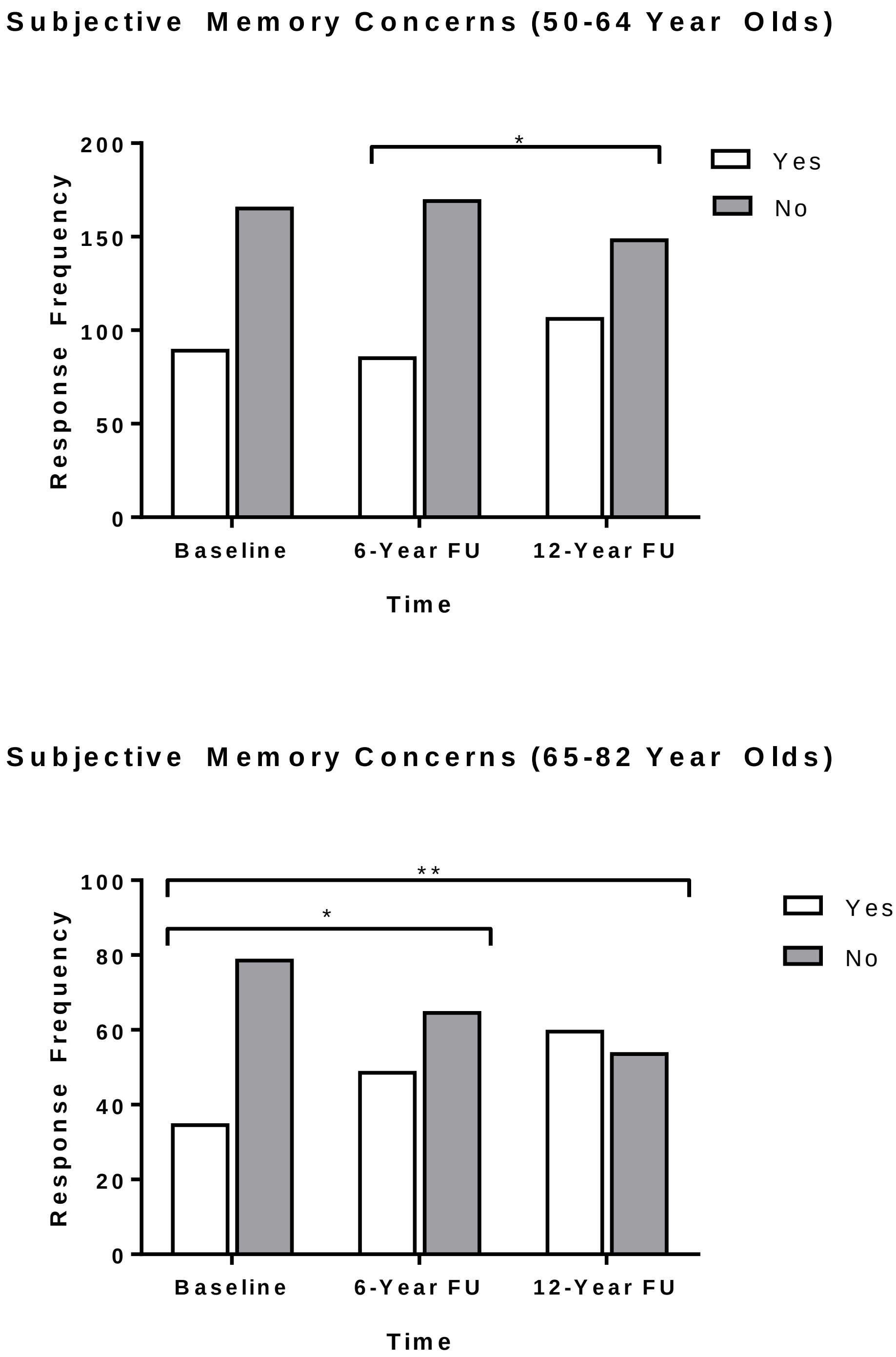


Figure 11. Frequency of yes/no responses to the question 'Do you consider yourself to be forgetful?' over time and across age groups (complete cases)

Note. **p*<.05, ***p*<.001; Significance of differences across time points is based on McNemar test for binary matched pairs data.

5.4.2 Model 1 – Baseline Model

Structural Equation Modelling

Goodness of fit was evaluated using the χ^2 index of absolute model fit, weighted root mean square residual (WRMR), root mean square error of approximation (RMSEA) and its 90% confidence interval (90% CI), comparative fit index (CFI) and the Tucker-Lewis index (TLI). Model fit was determined by the following criteria: RMSEA (.05 - .08) WRMR (≤ 1.0), CFI (≥ .90), and TLI (≥ .90). Fit statistics for Model 1 are summarised in *Table 19*. Overall, goodness-of-fit indices suggest that the structural model fits the data reasonably well in the 50-64 age-group but does not fit well for the 65-82 year age group.

Table 19. Fit statistics for Model 1 across age-groups

Statistic	**50-64 years**	**65-82 years**
χ^2	157.443	188.705
df	42	42
p	.0000	.0000
RMSEA (90% CI)	0.084 [0.070-0.098]	0.095 [0.082-0.109]
CFI	0.911	0.851
TLI	0.883	0.805
WRMR	1.026	1.252

The completely standardised parameter estimates for 50-64 year olds are presented in *Figure 12* (standard errors of the estimates are provided in *Table 20*). All freely estimated unstandardised parameters for the measurement model were statistically significant (*p*s<.001). The significant component weights for EF/PR (1.442) and CCE (-.540) suggest that each component is an important determinant of CR capacity. The relationship between EF/PR and CCE is high at 0.881. Discriminant validity was investigated by testing to see if the confidence interval (±2 standard errors) for the standardised correlation estimate between the two latent factors included the value of 1.0 (Anderson & Gerbing, 1988). This analysis supported the discriminant validity of the factors as the confidence interval for this correlation did not contain the value of 1.0 [0.819, 0.943]. Baseline CR capacity was predictive of baseline scores on both MMSE and the delayed recall task (standardised coefficients = 0.614 and 0.516 respectively). However, baseline CR was not a significant predictor of subjective memory at baseline.

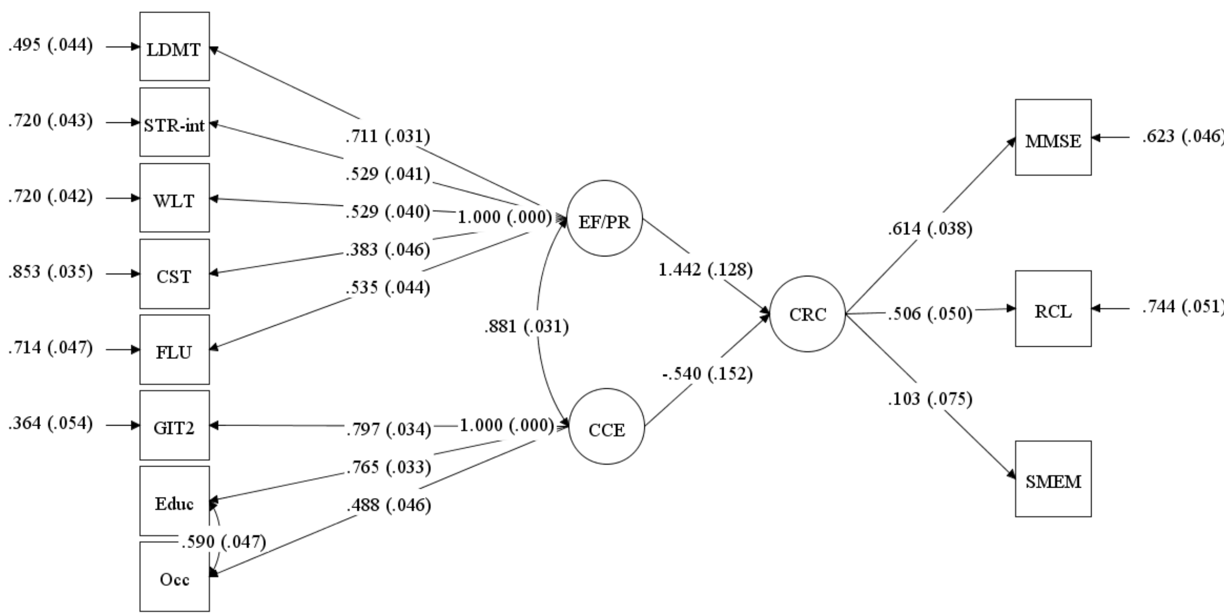


Figure 12. Model 1: Completely standardised estimates of free parameters in the structural model for healthy adults aged 50-64 years

Note. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

The completely standardised parameter estimates for 65-82 year olds are presented in *Figure 13* (standard errors of the estimates are provided in *Table 20*). All freely estimated unstandardised parameters for the measurement model were statistically significant (*p*s<.001). The significant component weights for EF/PR (1.250) and CCE (-.417) suggest that each component is an important determinant of CR capacity. There was a high correlation between EF/PR and CCE (0.706). Analysis supported the discriminant validity of the factors with a CI ranging from 0.604 – 0.808. Baseline CR capacity was predictive of baseline scores on MMSE, the delayed recall task and subjective memory (standardised coefficients = 0.619, 0.547 and 0.195 respectively).

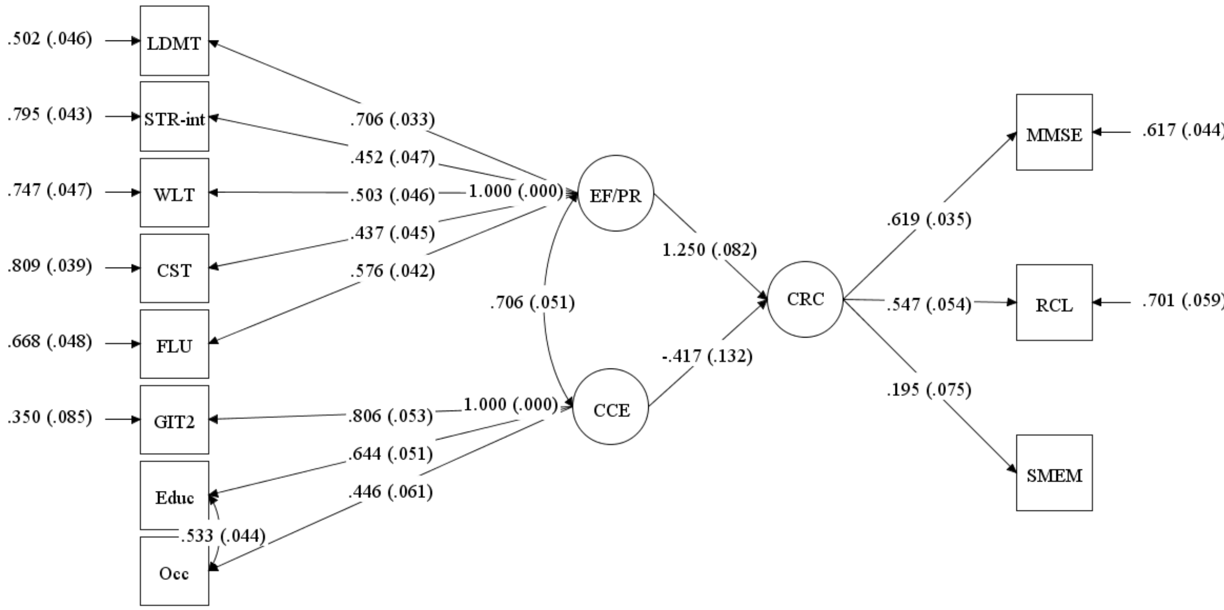


Figure 13. Model 1: Completely standardised estimates of free parameters in the structural model for healthy adults aged 65-82 years

Note. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

Table 20. Parameter estimates for Model 1

50- 64 Year Olds	**Estimates**	**S.E.**	**Est./S.E.**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	1.32	0.71	0.51
Immediate Working Memory	0.70	0.08	9.03	0.92	0.53	0.28
Response Inhibition	0.66	0.07	9.47	0.87	0.53	0.28
Cognitive Switching	0.49	0.07	7.37	0.64	0.38	0.15
Fluency	0.49	0.06	8.77	0.64	0.54	0.29
CCE						
Crystallised IQ	1.00	0.00	999.00	2.45	0.80	0.64
Education Level	0.31	0.03	12.34	0.77	0.77	0.59
Level of Occupational Attainment	0.20	0.02	8.87	0.49	0.49	0.24
Global Cognition/Memory						
MMSE	1.00	0.00	999.00	0.91	0.61	0.38
Delayed Recall	28.74	4.45	6.47	26.22	0.51	0.26
Subjective Memory	0.11	0.08	1.36	0.10	0.10	0.01
EF/PR → CR Capacity	1.00	0.00	999.00	1.44	1.44	-
CCE → CR Capacity	-0.20	0.05	-3.90	-0.54	-0.54	-
Covariance of EF/PR and CCE	2.84	0.30	9.44	0.88	0.88	-

65-82 Year Olds	**Estimates**	**S.E.**	**Est./S.E.**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	1.31	0.71	0.50
Immediate Working Memory	0.71	0.09	7.89	0.94	0.50	0.25
Response Inhibition	0.64	0.09	7.34	0.84	0.45	0.21
Cognitive Switching	0.64	0.09	7.33	0.84	0.44	0.19
Fluency	0.52	0.05	9.50	0.68	0.58	0.33
CCE						
Crystallised IQ	1.00	0.00	999.00	2.54	0.81	0.65
Education Level	0.25	0.03	7.58	0.64	0.64	0.42
Level of Occupational Attainment	0.18	0.03	5.69	0.45	0.45	0.20
Global Cognition/Memory						
MMSE	1.00	0.00	999.00	1.05	0.62	0.38
Delayed Recall	25.63	3.55	7.22	26.86	0.55	0.30
Subjective Memory	0.19	0.07	2.58	0.20	0.20	0.04
EF/PR → CR Capacity	1.00	0.00	999.00	1.25	1.25	-
CCE → CR Capacity	-0.17	0.05	-3.18	-0.42	-0.42	-
Covariance of EF/PR and CCE	2.35	0.33	7.19	0.71	0.71	-

Note. Estimates=unstandardised parameter estimate; S.E.=standard error; Est./S.E.=test statistic (*z* value); Std=standardised parameter estimate; StdYX=completely standardised parameter estimate; R^2=square of the completely standardised parameter estimate.

5.4.3 Model 2 – Longitudinal Model (6-Year Follow-Up)

Structural Equation modelling

Goodness of fit was evaluated using the same indices as Model 1 and fit statistics for Model 2 are summarised in *Table 21*. Overall, goodness-of-fit indices suggest that the structural model fits the data well for both age groups.

Table 21. Fit statistics for Model 2 across age-groups

Statistic	**50-64 years**	**65-82 years**
χ^2	98.173	100.047
df	42	42
p	0.000	0.000
RMSEA (90% CI)	0.058 [0.043, 0.073]	0.060 [0.045, 0.075]
CFI	0.957	0.938
TLI	0.944	0.919
WRMR	0.808	0.874

The completely standardised parameter estimates for the 50-64 year old group are presented in *Figure 14*. All freely estimated unstandardised parameters for the measurement model were statistically significant (*p*s<.001). The significant component weights for EF/PR (1.736) and CCE (-0.899) suggest that each component is an important determinant of CR capacity. There was a high correlation between EF/PR and CCE (0.904). Analysis supported the discriminant validity of the factors as the confidence interval for this correlation ranged from 0.852 – 0.956. Baseline CR capacity was predictive of scores on MMSE and the delayed recall task at six-year follow-up (standardised coefficients = 0.609 and 0.574 respectively). However, baseline CR capacity was not a significant predictor of subjective memory at six-year follow-up.

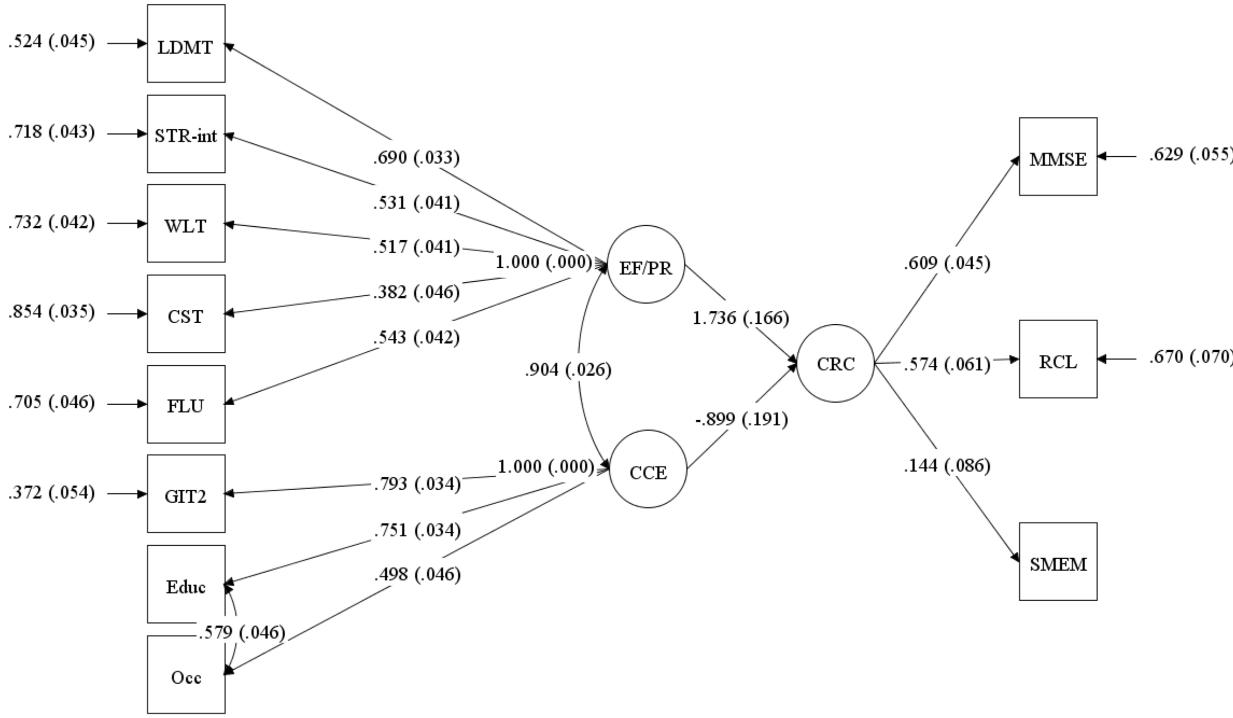


Figure 14. Model 2: Completely standardised estimates of free parameters in the proposed structural model for healthy adults aged 50-64 years

Note. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

The completely standardised parameter estimates for 65-82 year olds are presented in *Figure 15*. All freely estimated unstandardised parameters for the measurement model were statistically significant (*p*s<.001). The significant component weights for EF/PR (1.325) and CCE (-0.510) suggest that each component is an important determinant of CR capacity. There was a high correlation between EF/PR and CCE (0.752). Discriminant validity was supported as the confidence interval for this correlation ranged from 0.644 – 0.860. Baseline CR capacity was predictive of scores on MMSE, the delayed recall task and subjective memory at six-year follow-up (standardised coefficients = 0.609 and 0.567 and 0.343 respectively).

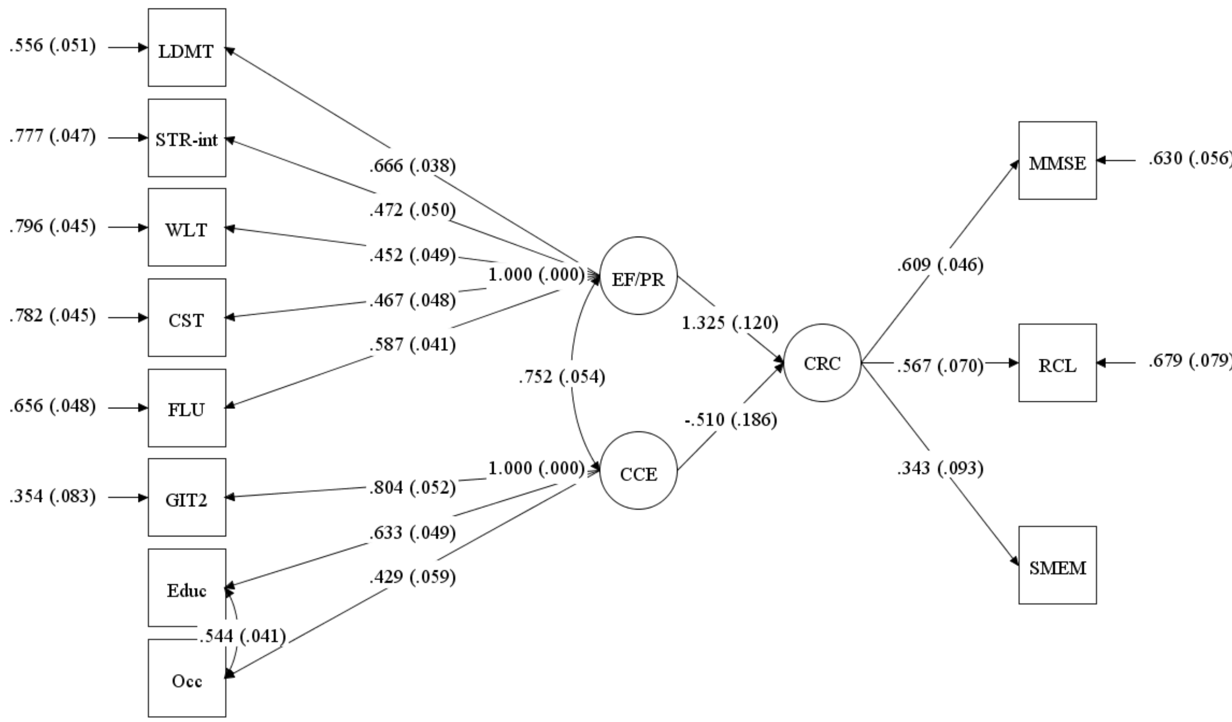


Figure 15. Model 2: Completely standardised estimates of free parameters in the proposed structural model for healthy adults aged 65-82 years

Note. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

Parameter Estimates when Adjusting for Covariates

Controlling for baseline levels of the outcomes by including them as covariates was necessary in order to adequately reflect scores at six-year follow-up. In Mplus v.7.3, missing data is not permitted for observed covariates because they are not part of the model (L. K. Muthén, 2005). Therefore, any observations with missing data on observed exogenous variables were excluded from the analysis. For the 50-64 year age group, six participants with missing data on the observed covariates were excluded from analysis (remaining *n*=387) and for the 65-82 year age-group 15 participants with missing data on the observed covariates were excluded (remaining *n*=369).

The adjusted parameter estimates including standard errors of the estimates for Model 2 are presented in *Table 22* and a comparison of the completely standardised parameter estimates for the model, before and after adjusting for covariates, are presented in *Table 23*. When the covariates were included in Model 2 for the 50-64 year age group, all freely estimated unstandardised parameters for the measurement model remained statistically significant (*p*s<.001). The significant component weights for EF/PR (1.267) and CCE (-0.887) suggest that each component is an important determinant of CR capacity. The correlation between EF/PR and CCE remained high at 0.924 (*SE*=0.026), however, examination of the confidence interval surrounding this correlation supported the discriminant validity of the factors [0.872, 0.976]. Baseline CR capacity was predictive of scores on MMSE and the delayed recall task at six-year follow-up (standardised coefficients = 0.589 and 0.710 respectively). Baseline CR was not a significant predictor of subjective memory at six-year follow-up. When the covariates were included in Model 2 for the 65-82 year age group, all freely estimated unstandardised parameters for the measurement model remained statistically significant (*p*s<.001). The significant component weights for EF/PR (1.048) and CCE (-0.696) suggest that each component is an important determinant of CR capacity. The correlation between EF/PR and CCE was still high at 0.880 (*SE*=0.041). Discriminant validity was investigated and supported as the confidence interval surrounding the correlation ranged from 0.798 – 0.962. Baseline CR capacity was predictive of scores on MMSE, delayed recall, and subjective memory at six-year follow-up (standardised coefficients = 0.560, 0.710, and 0.530 respectively).

Table 22. Parameter estimates for Model 2 (adjusting for baseline)

50-64 Year Olds	**Estimates**	**S.E.**	**Est./S.E.**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	0.96	0.58	0.34
Immediate Working Memory	0.22	0.06	3.50	0.21	0.20	0.04
Response Inhibition	0.62	0.10	6.17	0.59	0.39	0.15
Cognitive Switching	0.62	0.11	5.83	0.59	0.36	0.13
Fluency	0.55	0.08	6.70	0.52	0.46	0.21
CCE						
Crystallised IQ	1.00	0.00	999.00	1.94	0.71	0.51
Education Level	0.35	0.04	8.72	0.68	0.68	0.46
Level of Occupational Attainment	0.26	0.04	7.52	0.51	0.51	0.26
Global Cognition/Memory						
MMSE	1.00	0.00	999.00	0.76	0.59	0.35
Delayed Recall	51.44	8.41	6.11	38.85	0.71	0.51
Subjective Memory	0.21	0.15	1.36	0.16	0.16	0.02
EF/PR → CR Capacity	1.00	0.00	999.00	1.27	1.27	-
CCE → CR Capacity	-0.35	0.06	-5.74	-0.89	-0.89	-
Covariance of EF/PR and CCE	1.72	0.23	7.50	0.92	0.92	-

65-82 Year Olds	**Estimates**	**S.E.**	**Est./S.E.**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	0.94	0.57	0.33
Immediate Working Memory	0.26	0.07	3.95	0.25	0.23	0.05
Response Inhibition	0.75	0.13	5.91	0.71	0.40	0.16
Cognitive Switching	0.77	0.14	5.32	0.72	0.39	0.15
Fluency	0.54	0.08	6.75	0.51	0.47	0.22
CCE						
Crystallised IQ	1.00	0.00	999.00	1.95	0.67	0.45
Education Level	0.33	0.05	7.23	0.64	0.64	0.41
Level of Occupational Attainment	0.21	0.04	5.52	0.41	0.41	0.17
Global Cognition/Memory						
MMSE	1.00	0.00	999.00	0.90	0.56	0.31
Delayed Recall	41.56	7.37	5.64	37.36	0.71	0.50
Subjective Memory	0.66	0.15	4.43	0.59	0.53	0.28
EF/PR → CR Capacity	1.00	0.00	999.00	1.05	1.05	-
CCE → CR Capacity	-0.32	0.08	-4.18	-0.70	-0.70	-
Covariance of EF/PR and CCE	1.62	0.24	6.67	0.88	0.88	-

Note. Estimates=unstandardised parameter estimate; S.E.=standard error; Est./S.E.=test statistic (*z* value); Std=standardised parameter estimate; StdYX=completely standardised parameter estimate; R^2=square of the completely standardised parameter estimate.

Table 23. Completely standardised parameter estimates for Model 2: Before and after adjusting for baseline

	50-54 Year Olds		65-82 Year Olds	
	Model 2	**Model 2 Adjusted**	**Model 2**	**Model 2 Adjusted**
Path				
EF/PR → CR Capacity	1.736**	1.267**	1.325**	1.048**
CCE → CR Capacity	-0.899**	-0.887**	-0.510**	-0.696
CR Capacity → MMSE	0.609**	0.589**	0.609**	0.560**
CR Capacity → Delayed Recall	0.574**	0.710**	0.567**	0.710**
CR Capacity → Subjective Memory	0.144	0.156	0.343**	0.530**
Covariance of EF/PR and CCE	0.904**	0.924**	0.752**	0.880**

Note. ***p*<.01; **p*<.05

5.4.4 Model 3 – Longitudinal Model (12-Year Follow-Up)

Structural Equation modelling

Goodness of fit was evaluated using the same fit indices as Models 1 and 2. Fit statistics for Model 3 are summarised in *Table 24*. Overall, goodness-of-fit indices suggest that the structural model fits the data well for both age groups.

Table 24. Fit statistics for Model 3 across age-groups

Statistic	**50-64 years**	**65-82 years**
χ^2	102.180	67.500
df	42	42
p	.0000	.0075
RMSEA (90% CI)	0.060 [0.046, 0.075]	0.040 [0.021, 0.057]
CFI	0.954	0.971
TLI	0.940	0.962
WRMR	0.832	0.710

The completely standardised parameter estimates for 50-64 year olds are presented in *Figure 16*. All freely estimated unstandardised parameters for the measurement model were statistically significant (*p*s<.001). The significant component weights for EF/PR (1.867) and

CCE (-1.008) suggest that each component is an important determinant of CR capacity. There was a high correlation between EF/PR and CCE (0.931), but the confidence interval for this correlation did not contain the value of 1.0 [0.883, 0.979], thus supporting discriminant validity. Baseline CR capacity was predictive of scores on MMSE and the delayed recall task at 12-year follow-up (standardised coefficients = 0.617 and 0.507 respectively). However, baseline CR capacity was not a significant predictor of subjective memory at 12-year follow-up.

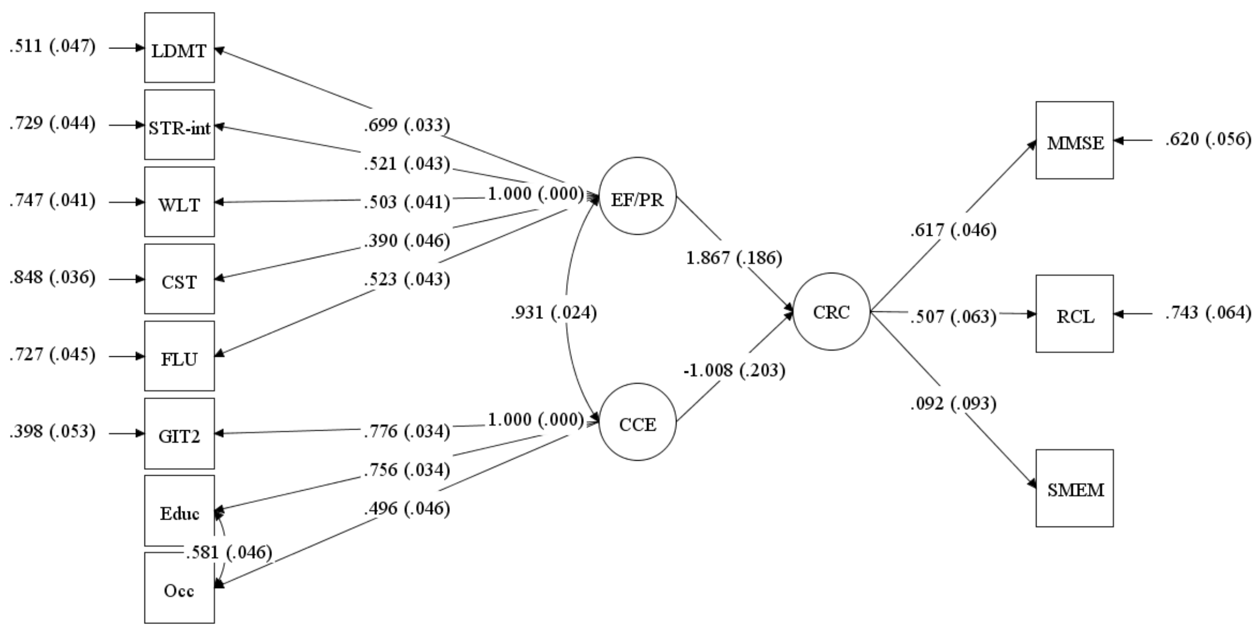


Figure 16. Model 3: Completely standardised estimates of free parameters in the proposed structural model for healthy adults aged 50-64 years

Note. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

The completely standardised parameter estimates for 65-82 year olds are presented in *Figure 17*. All freely estimated unstandardised parameters for the measurement model were statistically significant (*p*s<.001). The significant component weights for EF/PR (1.374) and CCE (-0.616) suggest that each component is an important contributor to CR capacity. There was a high correlation between EF/PR and CCE (0.749). It's confidence interval however, did not contain the value of 1.0 [0.637, 0.861]. Baseline CR capacity was predictive of scores on MMSE, the delayed recall task and subjective memory at 12-year follow-up (standardised coefficients = 0.535, 0.761, and 0.310 respectively).

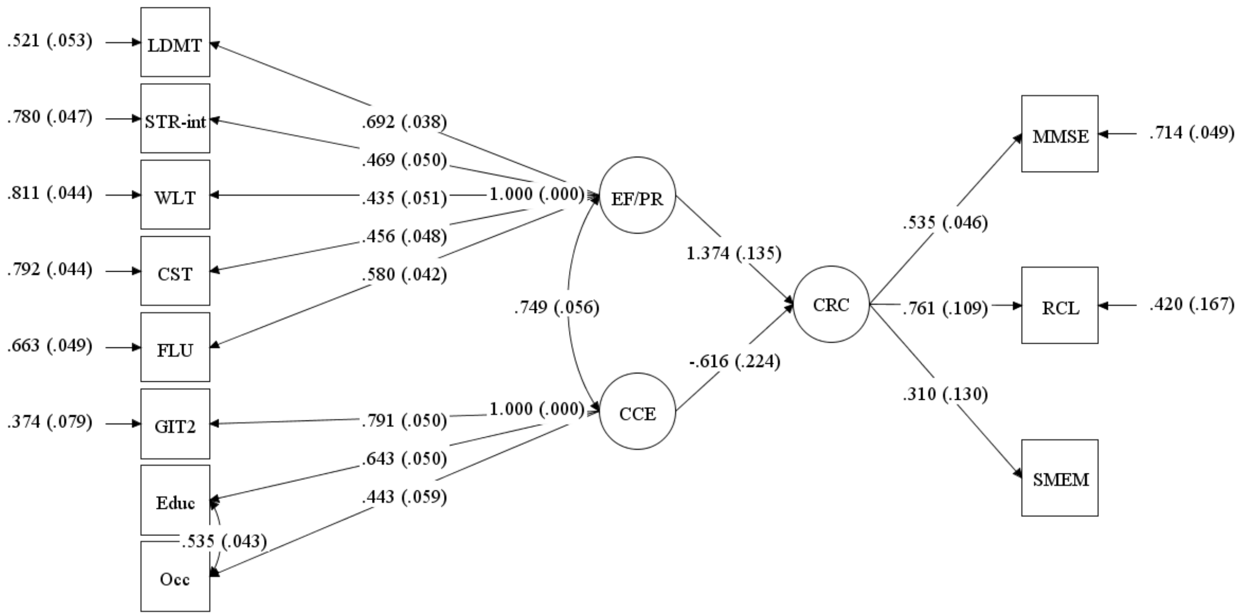


Figure 17. Model 3: Completely standardised estimates of free parameters in the proposed structural model for healthy adults aged 65-82 years

Note. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

Parameter Estimates When Adjusting for Covariates

The model parameter estimates were further investigated when controlling for baseline levels of the outcomes by including them as covariates. Following the same procedure as the six-year follow-up, observations with missing data on observed exogenous variables were excluded from the analysis.

The adjusted parameter estimates, including standard errors of the estimates for Model 3, are presented in *Table 25* and the completely standardised parameter estimates for Model 3, before and after adjusting for covariates, are presented in *Table 26*. When the covariates were included in Model 3 for the 50-64 year age group, all freely estimated unstandardised parameters for the measurement model remained statistically significant (*p*s<.001). As with the previous models, the significant component weights for EF/PR (1.320) and CCE (-0.860) suggest that each component contributes significantly to CR capacity. The significant correlation between EF/PR and CCE remained high at 0.959 (*SE*=0.029). Assessment of discriminant validity called into question the separability of the factors as the upper-bound confidence interval for this correlation contained the value of 1.0 [0.901, 1.017]. Baseline CR was predictive of scores on MMSE and the delayed recall task at 12-year follow-up (standardised coefficients = 0.605 and 0.531 respectively). Baseline CR was not a significant predictor of subjective memory at 12-year follow-up. When the covariates were included in Model 3 for the 65-82 year age group, all freely estimated unstandardised parameters for the measurement model remained statistically significant (*p*s<.001). The significant component weights for EF/PR (1.034) and CCE (-0.631) suggest that each component is an important determinant of CR capacity. The correlation between EF/PR and CCE remained high at 0.836 (*SE*=0.050). In this case, discriminant validity was supported as the confidence interval ranged from 0.736 – 0.936. Baseline CR was predictive of scores on MMSE and the delayed recall task at 12-year follow-up (standardised coefficients = 0.540 and 0.809 respectively). However, baseline CR was no longer a significant predictor of subjective memory at 12-year follow-up.

Table 25. Parameter estimates for Model 3 (adjusted)

50- 64 Year Olds	**Estimates**	**S.E.**	**Est./S.E.**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	0.95	0.58	0.34
Working Memory Verbal	0.23	0.06	3.62	0.22	0.21	0.04
Response Inhibition	0.62	0.10	5.93	0.59	0.38	0.15
Cognitive Switching	0.63	0.11	5.88	0.60	0.37	0.13
Fluency	0.52	0.08	6.42	0.50	0.44	0.19
CCE						
Crystallised IQ	1.00	0.00	999.00	1.90	0.70	0.48
Education Level	0.36	0.04	8.83	0.68	0.68	0.46
Level of Occupational Attainment	0.27	0.04	7.65	0.50	0.50	0.25
Global Cognition/Memory						
MMSE	1.00	0.00	999.00	0.72	0.61	0.37
Delayed Recall	38.22	6.75	5.67	27.64	0.53	0.28
Subjective Memory	0.05	0.15	0.34	0.04	0.04	0.00
EF/PR → CR Capacity	1.00	0.00	999.00	1.32	1.32	-
CCE → CR Capacity	-0.33	0.06	-5.29	-0.86	-0.86	-
Covariance of EF/PR and CCE	1.74	0.23	7.50	0.96	0.96	-

65-82 Year Olds	**Estimates**	**S.E.**	**Est./S.E.**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	0.99	0.60	0.36
Working Memory Verbal	0.25	0.07	3.79	0.25	0.23	0.05
Response Inhibition	0.70	0.12	5.68	0.70	0.39	0.15
Cognitive Switching	0.72	0.14	5.25	0.71	0.38	0.15
Fluency	0.51	0.08	6.62	0.51	0.47	0.22
CCE						
Crystallised IQ	1.00	0.00	999.00	1.95	0.67	0.45
Education Level	0.34	0.05	7.16	0.66	0.66	0.44
Level of Occupational Attainment	0.22	0.04	5.49	0.43	0.43	0.18
Global Cognition/Memory						
MMSE	1.00	0.00	999.00	0.95	0.54	0.29
Delayed Recall	4.71	1.10	4.28	4.49	0.81	0.66
Subjective Memory	0.32	0.18	1.80	0.30	0.30	0.09
EF/PR → CR Capacity	1.00	0.00	999.00	1.03	1.03	-
CCE → CR Capacity	-0.31	0.08	-3.96	-0.63	-0.63	-
Covariance of EF/PR and CCE	1.61	0.25	6.48	0.84	0.84	-

Note. Estimates=unstandardised parameter estimate; S.E.=standard error; Est./S.E.=test statistic (*z* value); Std=standardised parameter estimate; StdYX=completely standardised parameter estimate; R^2=square of the completely standardised parameter estimate.

Table 26. Completely standardised parameter estimates for Model 3: Before and after adjusting for covariates

	50-54 Year Olds		**65-82 Year Olds**	
	Model 3	***Model 3 Adjusted***	***Model 3***	***Model 3 Adjusted***
Path				
EF/PR → CR Capacity	1.867**	1.320**	1.374**	1.034**
CCE → CR Capacity	-1.008**	-0.860**	-0.616**	-0.631**
CR Capacity → MMSE	0.617**	0.605**	0.535**	0.540**
CR Capacity → Delayed Recall	0.507**	0.531**	0.761**	0.809**
CR Capacity → Subjective Memory	0.092	0.037	0.310*	0.295
Covariance of EF/PR and CCE	0.931**	0.959**	0.749**	0.836**

Note. ***p*<.01; **p*<.05

5.4.5 Structural Integrity of the CR Capacity Model

Due to the unexpected negative component weighting of CCE on the CR construct, as well as the questionable discriminant validity of the EF/PR and CCE factors for 50-64 year olds at 12-year follow-up, post-hoc analyses were conducted to assess the integrity of the proposed model. The unexpected negative component weighting of CCE may have been the result of a statistical anomaly such as multicollinearity or suppression, or model misspecification. For instance, a mediation or moderation model might have been a more appropriate specification than the two-factor model. Furthermore, questionable discriminant validity of the EF/PR and CCE factors may have implied that a one-factor CR capacity model was more suitable than the two-factor model. Therefore, post-hoc model integrity tests were conducted to explore the following: (1) The dependability of the weightings of both arms of the CR capacity model through investigation of multicollinearity and suppression effects that may impact on parameter estimates; and (2) The suitability of a one-factor model, a mediation model (EF/PR as mediator), and a moderation model (CCE as moderator) in terms of model fit and theoretical credibility (see *Figure 18* for flow chart of model integrity testing). Based on these analyses, suppression effects could not be concluded. None of the respecified models were superior to the original two-factor CR capacity model based on both assessment criteria (model fit and theoretical credibility). The integrity tests are outlined in detail below.

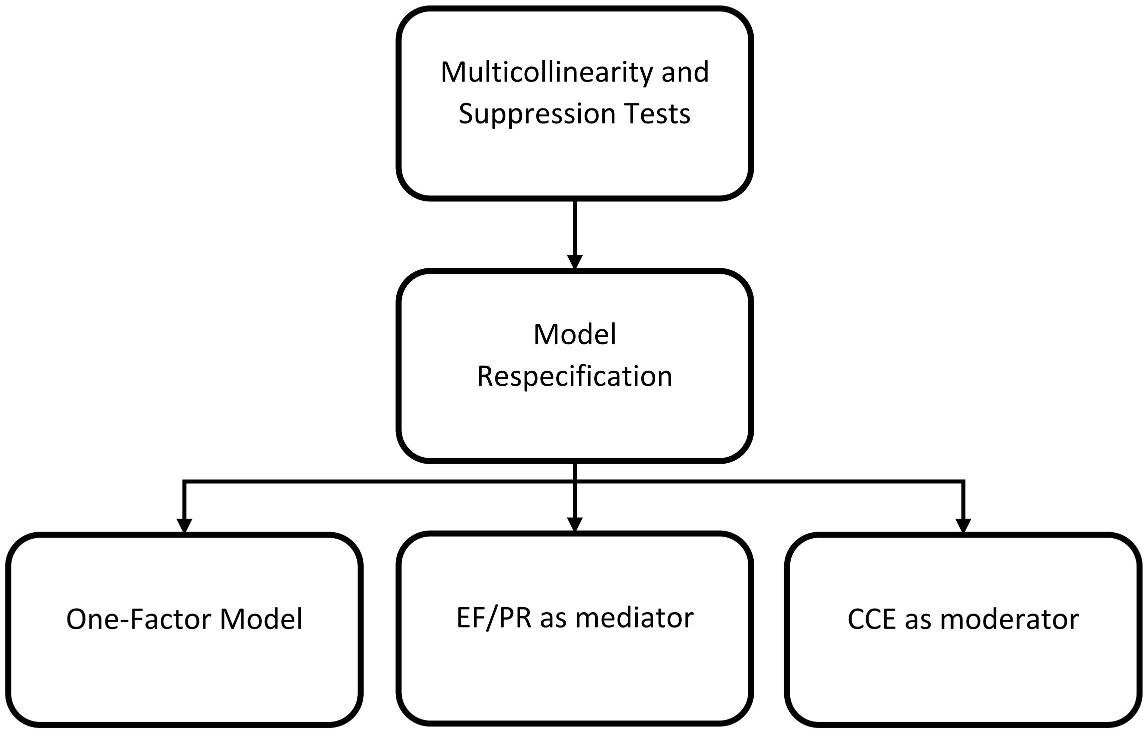


Figure 18. Flow chart of steps in model integrity testing

Multicollinearity and Suppression Effects

The negative weighting of the CCE factor on CR capacity may be the result of multicollinearity between the predictor variables. Multicollinearity refers to the non-independence of predictor variables and is a common feature of observational studies. It is considered problematic in relation to parameter estimation as it can inflate the variance of regression parameters (Dormann et al., 2013). However, as multicollinearity tests prior to analyses ruled out collinearity issues among the predictors, the unexpected negative weighting of the CCE factor on CR capacity may indicate a suppression effect. A suppressant is defined as a variable that correlates with one or more of the predictors in a model but has no relationship with the outcome. When the predictor and suppressant are positively correlated in a model, then the suppressant will have a negative regression weight after inclusion in the regression equation (Maassen & Bakker, 2001). The possibility that CCE is acting as a suppressant in the model was interrogated using a three-pronged approach (see *Table 27* for a summary of findings):

(1) The relationships between EF/PR, CCE and the outcome variables were investigated at the indicator level in order to ascertain whether CCE met the definition of a suppressant as outlined above. It was found that the CCE indicators all correlated with one or more of the EF/PR indicators, with significant low to moderate positive correlations with the EF/PR indicators observed in both age groups. However, none of the CCE indicators had a relationship with subjective memory at either baseline or 6- and 12-year follow-up. The same trend was observed in the older age group in relation to the EF/PR indicators. In the middle-aged group, occupation did not significantly correlate with delayed recall at baseline. For the older age group, occupation did not significantly correlate with delayed recall at baseline or 6- and 12-year follow-up, and education did not correlate with delayed recall at baseline and six-year follow-up. While some of the CCE indicators met the criteria of a suppressor in relation to the subjective memory and delayed recall outcomes, the effect was not consistent across age-groups and time-points and therefore firm conclusions could not be drawn.

(2) The semi-partial correlations (correlations between predictors and outcomes with the effects of other predictors partialed out) between predictors and outcomes were examined to see if their values were larger than the zero-order correlations ($spc > r$) as this is considered to be consistent with the definition of a suppression effect (Ludlow & Klein, 2014). While there were a few instances where the *spc* was greater than *r*, all of these correlations were non-significant (*p*s>.05) and therefore cannot be interpreted further.

(3) A latent variable approach to testing suppression was employed (Cheung & Lau, 2007). Similar to the examination of a mediation effect, suppression was operationalised as the indirect effect of the predictor on the outcome going through a potential suppressor (mediator) variable (in this case CCE). Suppression is indicated if the indirect effect has a value less than zero. Significance of the indirect effect was determined using the Delta method (the Mplus equivalent to the Sobel test) (MacKinnon, 2008). CCE appears to be acting as a suppressor in relation to delayed recall and subjective memory in the baseline

model and in relation to delayed recall in the six-year follow-up model. However, suppression tests for the 12-year follow-up model were non-significant. As the negative weighting of CCE was also found in the 12-year follow-up models, suppression effects cannot conclusively explain this negative weighting. However, as suppression effects have been suggested in relation to delayed recall and subjective memory outcomes in tests (1) and (3) above, a further precautionary test was conducted whereby these two outcomes were excluded from the model to investigate whether or not this had an effect on the negative CCE weighting. The significant negative weighting of CCE on CR capacity remained for all models, with the exception of the baseline model in the older age group where CCE had a non-significant, but still negative, weighting. Therefore, suppression, as indicated by a lack of a relationship between the predictors and outcomes and the Delta method approach, cannot be concluded.

Table 27. Summary of three-pronged approach to suppression testing

	Model 1	Model 2	Model 3
1. Relationships between IVs and DVs	*IV's*: - Significant correlations between all IV's for the middle-aged group. - For older age group, immediate working memory does not correlate with Education and Occupation *DV's*: - CCE indicators (Education, Occupation and Crystallised IQ) have non-significant correlations with subjective memory - Occupation has no relationship with delayed recall - For older group only, Education has no relationship with delayed recall	*IV's:* As per Model 1 *DV's:* - CCE indicators (Education, Occupation and Crystallised IQ) have non-significant correlations with subjective memory - For older group only, Education and Occupation have no relationship with delayed recall	*IV's*: As per Model 1 *DV's*: - For both age groups, CCE indicators (Education, Occupation and Crystallised IQ) have non-significant correlations with subjective memory - For older group only, none of the IV's have a relationship with subjective memory - For older group only, Occupation has no relationship with delayed recall
2. *spc > r*	Non-significant (*p*s>.05)	Non-significant (*p*s>.05)	Non-significant (*p*s>.05)
3. Delta Method (CCE as mediator)	- Indirect effect of EF/PR on delayed recall < 0 - For older group only, indirect effect of EF/PR on subjective memory < 0	- Indirect effect of EF/PR on delayed recall < 0	- No indication of suppression effects

Mediation and Moderation Models

The model was respecified in three ways in order to investigate if alternative models demonstrated similar parameter estimates with regard to both arms of the CR capacity model and whether an alternative specification demonstrated superior model fit and theoretical credibility. The following models were tested: (a) A one factor model of CR capacity where all indicators load onto a latent CR capacity factor; (b) EF/PR as mediator between CCE and outcomes; and (c) CCE as moderator of the relationship between EF/PR and outcomes. Firstly, the model was respecified as a one-factor model, so that all EF/PR and CCE indicators loaded on the same CR capacity factor (see *Figure 19*). The model was then assessed in terms of goodness of fit and whether or not the model was theoretically sound. Fit statistics for the model at baseline (Model 1), six-year (Model 2), and 12-year follow-up (Model 3) for both age-groups are summarised in *Table 28*. While the one-factor model fits the data well for models at six-year and 12-year follow-up, the fit of the two-factor model is superior. Also, theory does not support the unity of the EF/PR and CCE factors as previous research has found their indicators to be related but separable (M. B. Mitchell, Shaughnessy, et al., 2012; Siedlecki et al., 2009).

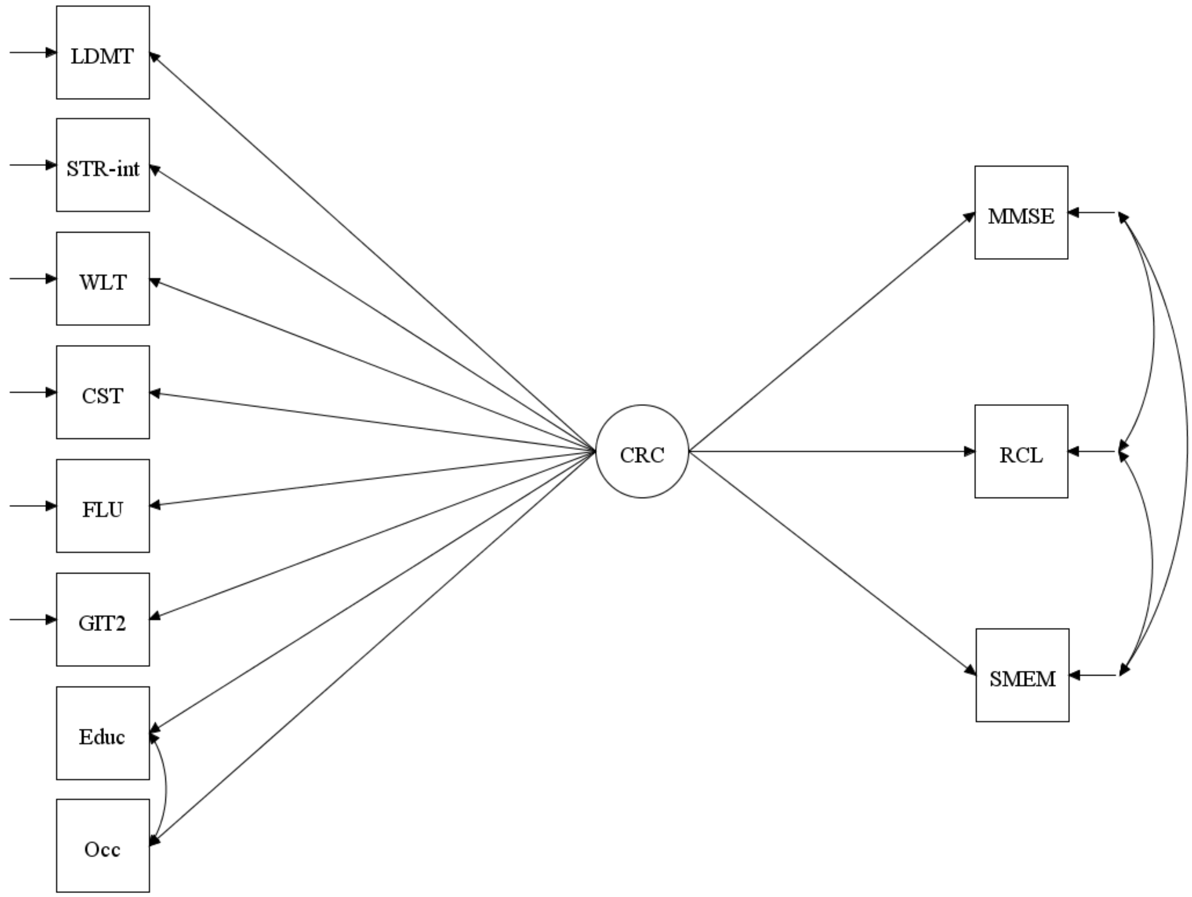


Figure 19. A one-factor model of CR capacity

Secondly, the model was respecified so that EF/PR acted as a mediator between CCE and the outcome variables (see *Figure 20*). A variable can be described a mediator if it can be shown to account, or partially account, for the relation between the predictor and the criterion (Baron & Kenny, 1986). The model was assessed in terms of goodness of fit, the direction of the relationship between CCE and the outcomes, and whether or not the model was theoretically sound. Fit was very similar to that of the two-factor models at both baseline and follow-up, with marginally better fit for the mediation model in the older age group at baseline and six-year follow-up, but not at 12-year follow-up. There was marginally better fit for the two-factor model in the middle-aged group at baseline and both 6- and 12-year follow-up (see *Table 28* for summary of fit statistics). The strong positive relationships between EF/PR and the criterion variables, and the negative relationships between CCE and the criterion variables persisted in the mediation model with CCE being a significant negative predictor of delayed recall and subjective memory in the older age group at baseline. CCE was also a significant negative predictor of delayed recall at six-year follow-up in the older age group. There is some theoretical support for the idea that EF/PR may be a mediator of CCE. For instance, Sandry et al. (2015; 2014) have found that working memory, a cognitive function closely related to EF, mediated the relationship between CR (measured by WAIS-vocabulary) and long-term memory in separate samples of TBI and MS participants. However, the relationship between CR and long-term memory in this case was positive, and thus does not support the finding of significant negative relationships in the MAAS mediation models.

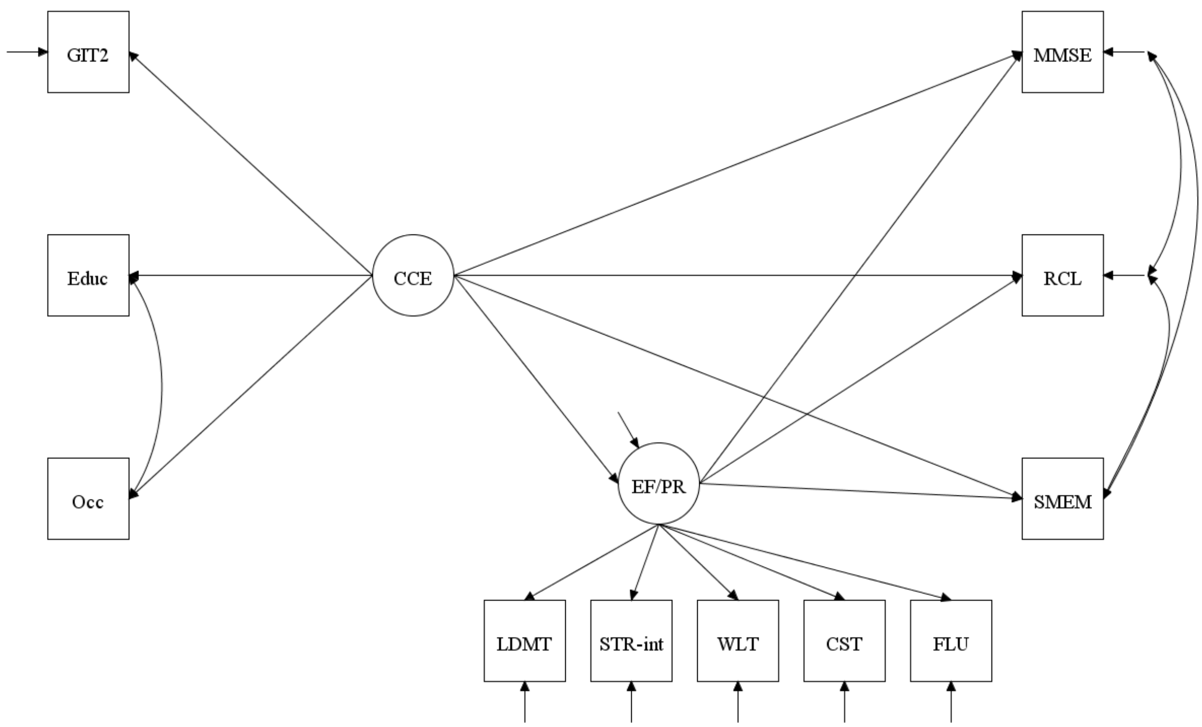


Figure 20. EF/PR as mediator of the relationship between CCE and the outcome variables

Finally, the model was respecified so that the relationship between EF/PR and the outcomes was moderated by CCE (see *Figure 21*). A moderator variable affects the direction and/or strength of the relationship between an predictor and outcome and can be represented as an interaction between the predictor and the moderator (Baron & Kenny, 1986). In previous research, CR, as measured by traditional proxies such as education level, has been viewed as a moderator of the relationship between brain pathology and symptom expression (Richards & Deary, 2005; Satz, 1993; Y. Stern, 2002). It is possible that the relationship between EF/PR and global cognition/memory outcomes also differs as a function of CCE. In order to run a moderation analysis using Mplus an interaction between EF/PR and CCE was specified and used as a predictor in the model along with the individual latent variables. As Mplus can only run this type of analysis with continuous predictors, it is acceptable to use MLR estimation instead of WLSMV when there are categorical predictors in the model (B. O. Muthén & Muthén, 2012). Moderation analysis is incapable of generating fit statistics, but it does generate the Akaike Information Criterion (AIC), which is an information theory approach to data analysis that can be used as a fit index (Kline, 2011). When comparing models based on AIC, the lower value is generally considered to indicate a better fitting model. In order to compare the moderation models and the two-factor models in terms of fit, it was necessary to re-run the two-factor model SEMs using MLR estimator to generate the AIC fit index. The relationship trends observed in the two-factor MAAS models run using MLR estimator were very similar to the parameter estimates using WLSMV estimator. The moderation models fit the data slightly better at baseline, however at 6- and 12-year follow-up the two-factor models were generally a better fit, although differences were small (see *Table 29* for comparison of AIC fit statistics). The negative relationships with CCE persist in this model with CCE having a significant negative relationship with delayed recall, and the interaction term (CCExEFPR) having a significant negative relationship with MMSE score for some of the models at both baseline and 6- and 12-year follow-up. It is also notable that for both mediation and moderation models the significant relationship between EF/PR and the outcome measures at all time-points were consistently in a positive direction, which was expected with regard to previous literature.

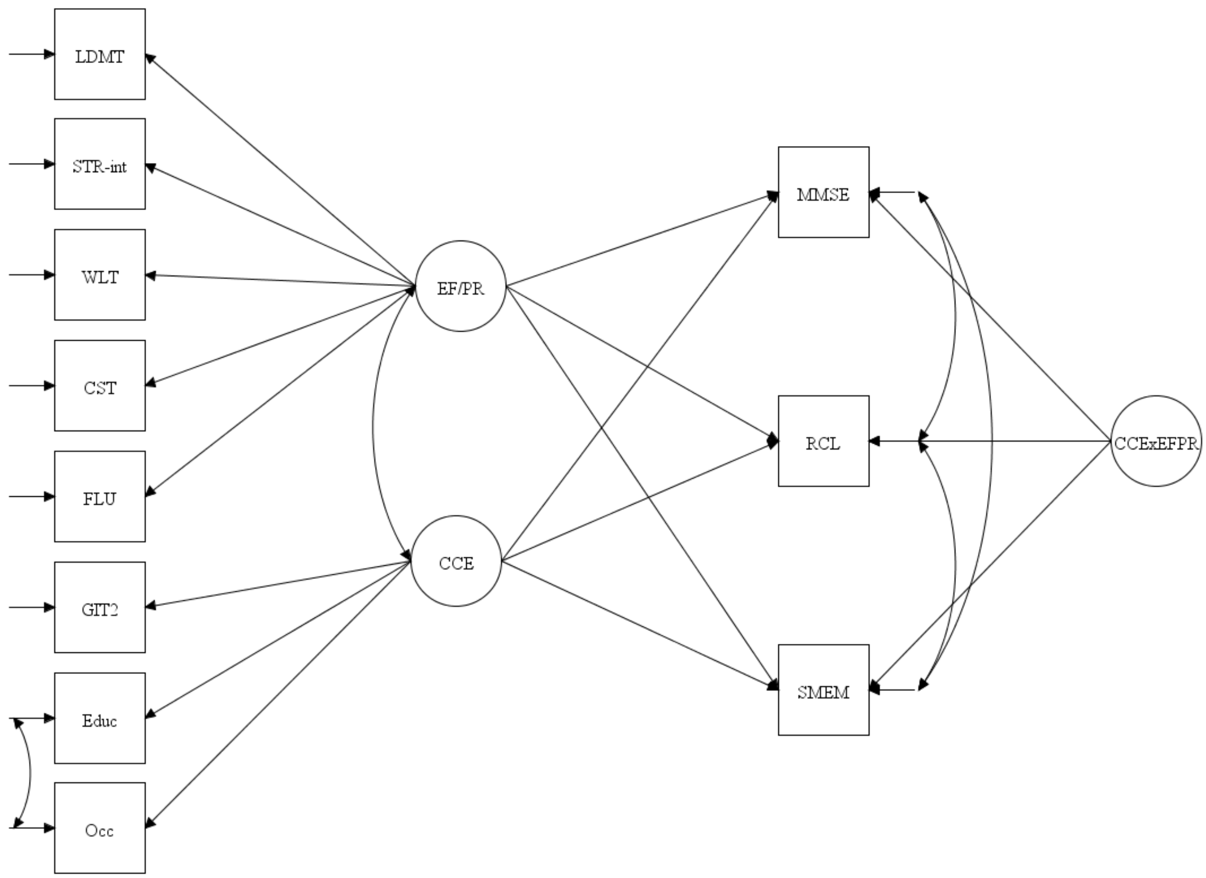


Figure 21. CCE as moderator of the relationship between EF/PR and the outcome variables

To conclude, as none of the respecified models were superior to the two-factor model based on the assessment criteria (model fit and theoretical credibility) the model was not respecified. Based on these model integrity tests it can be tentatively reasoned that the EF/PR and CCE weightings on the CR capacity construct are not due to statistical anomalies. However, in order to draw firmer conclusions in this regard, it is necessary to replicate the two-factor model in a secondary dataset: TILDA.

Table 28. Fit statistics for the respecified one-factor and mediator models across age-groups

	One-Factor Model		**EF/PR as Mediator**		**Original Two-Factor Model**	
Model 1	50-64 years	65-82 years	50-64 years	65-82 years	50-64 years	65-82 years
χ^2	180.031	245.670	143.113	154.199	157.443	188.705
df	40	40	36	36	42	42
p	0.000	0.000	0.000	0.000	.0000	.0000
RMSEA	0.094	0.116	0.087	0.092	0.084	0.095
(90% CI)	[0.081, 0.109]	[0.102, 0.130]	[0.072, 0.102]	[0.078, 0.108]	[0.070, 0.098]	[0.082, 0.109]
CFI	0.892	0.791	0.917	0.880	0.911	0.851
TLI	0.851	0.713	0.873	0.817	0.883	0.805
WRMR	1.081	1.412	0.940	1.079	1.026	1.252
Model 2						
χ^2	115.794	134.500	91.990	83.306	98.173	100.047
df	40	40	36	36	42	42
p	0.000	0.000	0.000	0.000	0.000	0.000
RMSEA	0.069	0.078	0.063	0.058	0.058	0.060
(90% CI)	[0.055, 0.084]	[0.064, 0.093]	[0.047, 0.079]	[0.042, 0.075]	[0.043, 0.073]	[0.045, 0.075]
CFI	0.943	0.899	0.958	0.949	0.957	0.938
TLI	0.921	0.861	0.935	0.923	0.944	0.919
WRMR	0.869	1.013	0.759	0.764	0.808	0.874
Model 3						
χ^2	111.174	99.001	91.033	61.314	102.180	67.500
df	40	40	36	36	42	42
p	0.000	0.000	0.000	0.005	.0000	.0075
RMSEA	0.067	0.062	0.062	0.043	0.060	0.040
(90% CI)	[0.053, 0.082]	[0.047, 0.077]	[0.047, 0.078]	[0.023, 0.061]	[0.046, 0.075]	[0.021, 0.057]
CFI	0.946	0.933	0.958	0.971	0.954	0.971
TLI	0.925	0.907	0.936	0.956	0.940	0.962
WRMR	0.858	0.866	0.759	0.653	0.832	0.710

Table 29. AIC fit statistics for moderation model and two-factor model (re-run using MLR estimator)

	CCE as moderator		**Two-Factor model**	
Model 1	*50-64 years*	*65-82 years*	*50-64 years*	*65-82 years*
AIC	15659.24	15911.32	17493.73	17632.81
Model 2				
AIC	14960.67	14082.11	14713.04	14588.14
Model 3				
AIC	14206.44	12716.78	15552.34	12458.43

5.5 Discussion

The structural relationships between the CR capacity components, CR capacity, and cognitive outcomes were examined in a sample of healthy adults aged 50-64 and 65-82 years at baseline. The relationships between baseline CR capacity and global cognition/memory outcomes were assessed at baseline, six-year, and 12-year follow-up. As hypothesised, baseline CR capacity was predictive of global cognition/memory outcomes at baseline and follow-up, suggesting that higher baseline levels of CR capacity are associated with higher global cognition/memory scores at baseline, six years, and 12 years later. While the EF/PR component had a positive weighting on the CR capacity construct, CCE had a negative weighting across models. These findings are discussed below with regard to age-related differences.

5.5.1 CR Capacity as a Predicitor of Cognitive Status Over Time

With regard to prediction, overall, CR capacity appears to be a strong predictor of MMSE scores and scores on the delayed recall task at both baseline and longitudinally. CR capacity is a strong predictor of delayed recall at baseline and is also predictive of delayed recall scores at six-year and 12-year follow-up, when controlling for baseline, in both age groups. The standardised beta weights increase over time for the older age group, with the strongest relationship evident for scores at 12 year follow-up. This suggests that with increased engagement of baseline CR capacity, scores in delayed recall increase, and the magnitude of the increase is larger over time. CR capacity is also a strong predictor of MMSE scores at baseline, six-year and 12-year follow-up, when controlling for baseline, for both age groups. The strongest relationship is again evident in the older age group. Similar to delayed recall, this suggests that when CR capacity is engaged, MMSE scores increase, however, unlike with delayed recall scores, the magnitude of the increase reduces over time. These patterns were similar for the middle-aged group, with the relationship between CR capacity and delayed recall being weakest at baseline and strongest at six-year follow-up, and the relationship between CR capacity and MMSE scores being strongest at baseline and weakest at six-year follow-up. The strong positive relationships between CR capacity and global cognition/delayed recall outcomes over time are in line with research highlighting the influence of control processes on memory. CR capacity may be driven by EF/PR and previous research has shown that memory in older adults relies on controlled processing such as strategic elaboration during memorisation and facilitating search at retrieval (Buckner, 2004). The fact that these relationships exist not just cross-sectionally, but hold longitudinally, supports the idea that CR capacity, specified as the reciprocal relationship between control and representational processes, plays a role in sustaining cognitive abilities in healthy ageing.

CR capacity was also predictive of subjective memory at baseline and six-year follow-up for the 65-82 year age group, however it was not found to be predictive of subjective memory at either baseline or follow-up for the 50-64 year age group. Also, as model fit for the baseline model was poor, this significant finding must be interpreted with caution. The relationship between CR capacity and subjective memory was of interest as research has shown that individuals with subjective memory complaints, but no objective complaints, were twice as likely to develop dementia than those without complaints about their memory (A. J. Mitchell et al., 2014). Support for a relationship between CR capacity and subjective memory is strongest in the older age group at six-year follow-up. As subjective memory was measured on a binary scale in response to the question “Do you consider yourself to be forgetful?”, results suggest that the probability of participants responding “No” at six-year follow-up increases when baseline CR capacity is engaged. However, this finding did not hold at 12-year follow-up. It may be the case that CR capacity predicts subjective memory in older adults, but not middle-aged adults, as the older group may also be experiencing objective cognitive complaints reflected by EF/PR performance. However, as this finding was not observed at 12-year follow-up, firm conclusions cannot be drawn. The lack of a significant relationship between CR capacity and subjective memory in the middle-aged group may also be the result of a weak binary measure of subjective complaints and further research could benefit from the inclusion of a more comprehensive measure of subjective memory. Overall, the results of the study are in keeping with the hypothesis that CR capacity is predictive of cognitive outcomes in healthy ageing over time.

5.5.2 The CR Capacity Construct

The significant negative relationship between CCE and CR Capacity was unexpected due to previous research suggesting a protective effect of CCE with regard to decline outcomes (Crowe et al., 2003; Valenzuela & Sachdev, 2009; Wilson et al., 2013). Based on much of the extant literature, a positive relationship was hypothesised between CCE and CR capacity. As there is a significant negative relationship between CCE and CR capacity across all models this may be indicative of a statistical problem such as collinearity. It was established in studies 1 and 2, and further validated in this study, that there is a strong relationship between the EF/PR and CCE latent factors across both age groups, although this relationship is always slightly weaker for the older age group, as opposed to the middle-aged group. The discriminant validity of EF/PR and CCE also came into question in the adjusted model at 12-year follow-up for the middle-aged group. As a result of these findings, model integrity was investigated with regard to both multicollinearity and suppression effects and model respecification. Multicollinearity and suppression do not appear to be problematic in the data and the respecified models were not superior to the two-factor model with regard to fit and theoretical credibility.

There was no indication of multicollinearity among the factor indicators. Multicollinearity was assessed through examination of the correlation matrix and collinearity diagnostics (the Variance Inflation Factor and the Tolerance Statistic) and there was no indication of multicollinearity among the factor indicators. Myers (1990) suggests that a VIF value greater than 10 is a cause for concern and the colleariety diagnostics showed that all VIF values were less than 2.5. Suppression was investigated using a three-pronged approach and no suppression effects could be determined (see Table 27). According to Cenfetelli and Bassellier (2009), if negatively weighted items in a formative model are found to be neither collinear nor suppressors, and otherwise have a positive bivariate correlation with the formative construct, they should be interpreted as having a negative effect on the construct when controlling for the effects of other indicators. The CCE factor correlates positively with CR capacity across models (see Appendix E for correlations between latent variables); so in this sense, the negative loading can be interpreted as CCE negatively contributing to CR capacity when the effects of EF/PR on CR capacity are controlled for. As collinearity and suppression effects do not appear to be problematic in the data, and re-specification is not appropriate, theoretical explanations for this finding may be put forward concerning the differential involvement of control and representational processes in CR capacity. However, prior to this, it is necessary to investigate if this negative relationship is replicated in an Irish sample using data from TILDA. If so, this would suggest that the finding is generalisable and therefore theoretical explanations for the structural relationships are required.

5.5.3 Nomological Validity of the CR Capacity Model

With regard to the formation of the CR construct and its predictive ability, this study makes two contributions. Firstly, CR capacity has been specified by two related but distinct latent variables whose indicators have been separately shown to be predictive of decline outcomes. This operationalisation of CR was derived both theoretically and empirically using EFA/CFA and provides a more comprehensive, multiple indicator approach to measuring CR than the traditional use of single lifestyle/enrichment proxy indicators. Secondly, CR capacity operationalised in this way has been shown to predict decline outcomes both cross-sectionally and longitudinally in both mid- and late-life healthy adults. The study assessed the nomological validity of a theoretically driven, partially-latent model of the interrelations between a two-factor CR capacity model and cognitive outcomes at baseline, six-year, and 12-year follow-up. The study's strengths lie in its novel approach to modelling CR capacity, the assessment of relationships longitudinally, and the use of established neuropsychological measures that lend support to the reproducibility of the study.

A potential issue with regard to testing a predictive model of longitudinal decline in healthy ageing relates to the observation of improvements over time in the outcome measures. There was a significant improvement in performance on MMSE scores at six-year and 12-year follow-up compared to baseline for the middle-aged group. For the older age group, MMSE scores also significantly improved at six-year follow-up but significantly declined at 12-year follow-up. Similarly, scores on delayed recall significantly improved from baseline to six-year follow-up, and significantly declined from six- to 12-year follow-up for both age groups. It is notable that the improvement at six-year follow-up was steeper for the middle-aged group and the decline at 12-year follow-up was steeper for the older age group. The increased scores at six-year follow-up are likely due to retest effects. Similar to previous research using data from MAAS (van Dijk et al., 2008), non-linear effects of time were observed for the outcome measures, indicating that practice effects levelled off after the six-year follow-up assessment. The apparent presence of retest effects in this study suggests that results may underestimate the degree of age-related decline. However, the significant performance decrement from six-year to 12-year follow-up in MMSE scores for the older age group and delayed recall scores for both age groups (see *Figure 10*) shows that, for the older age group in particular, the effects of cognitive ageing are greater than the retest effects. No such retest effects were observed in relation to the binary subjective memory variable, with both age groups displaying trends toward greater frequency of memory concerns over time.

A limitation to the study is the omission of measures relevant to CR capacity such as measures of social and mental engagement. These measures were proposed by Satz et al. (2011) as potential indicators of CMA, however, measures for these indicators were only available in MAAS follow-up data and not at baseline. Reed et al. (2011) suggest that once education ends, alternative cognitive activities provide mental exercise which develops and maintains CR. The role of mental and social engagement in the CR capacity model was beyond the scope of this study and is a potential avenue for future research. It may be the case that indicators of mental and social engagement load on the CCE factor as they have been found to be related to cognitively enriching activities (Lojo-Seoane et al., 2014). Despite this limitation, there is sufficient evidence for the retention of the current model and it has helped to advance understanding of how EF/PR and CCE relate to CR capacity, and in turn cognitive decline outcomes.

The next steps will involve validation of the structural model through replication in a secondary dataset in order to further assess the nomological validity of the CR capacity model. This will help to clarify if the relationships found in the MAAS dataset are generalisable or are the result of idiosyncrasies in the data.

Chapter 6: Study 4 – Replication of a Structural Model of Cognitive Reserve Capacity

6.1 Introduction

The EFA, CFA, and SEM analyses in Studies 1, 2, and 3 provide support for a two-factor CR capacity measurement model as well as support for the predictive relationship between CR capacity and global cognition/memory outcomes at baseline, six-year, and 12-year follow-up. Of particular importance is the consistent positive relationship between EF/PR and CR capacity, which in turn positively predicts MMSE scores and performance on the delayed recall task at baseline, six-year, and 12-year follow-up, with prediction of subjective memory complaints limited to the older age group at baseline and six-year follow-up. Also of importance is the unexpected negative weighting of CCE on the CR capacity construct. Although this finding was interrogated through a number of model integrity tests, it is still necessary to further investigate its validity through model replication in a secondary dataset. Before firm conclusions can be drawn regarding any of the structural relationships between CR capacity and global cognition/memory, SEM replication in a secondary dataset is necessary (Kline, 2011). Furthermore, as the initial models were tested using data from a Dutch ageing study (MAAS), it is of interest to see if the relationships hold in an Irish sample.

The aim of this study was to validate the models investigated in study 3 in a secondary sample using data from the Irish longitudinal ageing study (TILDA). This study sought to answer the following questions:

1. What are the contributions of EF/PR and CCE to a hierarchical CR capacity construct?
2. Do the predictive relationships between CR capacity and cognitive outcomes hold in a secondary sample of Irish participants (TILDA), both at baseline and two-year follow-up?

6.2 Method

6.2.1 Participants

The sample was selected from the Irish Longitudinal Study on Ageing (TILDA) (Kearney et al., 2011), a population-representative prospective cohort study of community-dwelling adults in Ireland. The baseline (wave 1) sample consisted of 8,504 participants, of which 8,163 were aged 50 and older (see Chapter 4 for more detailed information on the TILDA sample frame). Those aged under 50 years at baseline were excluded. Those aged 80 years or older were also excluded as these participants had been group coded as 80+ and precise age was unclear. In addition, 3,293 participants whose education level and/or occupation level were unknown, or who never held a formal occupation were removed from the sample, as well as participants with a score that was unknown or less than 24 on the Mini-Mental State Examination (MMSE). The sample was divided into middle aged (50-64 years) and older aged (65-79 years) participants. Analysis was based on 3,351 participants, of which 1,947 were aged between 50 and 64 (880 male; 1,067 female) and 1,404 were aged between 65 and 79 years (823 male; 581 female) at baseline.

6.2.2 Measures of Cognitive Reserve Capacity

The CCE and EF/PR measures used in this study are the same as those used in the TILDA CFA validation study. Please see Chapter 4 for a more detailed description of the measures.

Briefly, the CCE measures used in this study are as follows: *Level of education* was determined by asking participants to indicate their highest level of education completed and was measured on a seven-point scale. *Occupation level* was based on a six-point scale that estimates the highest level of professional activity.

Briefly, the EF/PR measures used in this study are as follows: The *Sustained Attention to Response Task* (SART) (I. H. Robertson et al., 1997) was used as a measure of response inhibition. The *Fluency* test is a measure of self-initiated activity, categorisation and mental flexibility (A. Barrett et al., 2011). The number of correct responses was taken as a measure of verbal fluency. The *Colour Trails Tasks 1 and 2* (CTT1 and CTT2) (D’Elia, 1996) were used to derive a measure of cognitive switching by taking the time required to complete Colour Trail

1 from the time require to complete Colour Trail 2 (CTT2 – CTT1). *Choice Reaction Time* (CRT), or speed of processing, was measured using a computer-based CRT test that was developed in-house for TILDA using E-Prime software (Cronin et al., 2013; Schneider et al., 2002). The *Word List Learning Test* (WLLT) required participants to recall 10 aurally presented words both immediately after presentation and again after a delay, over two trials. The total number of correctly recalled words over both trials was used as a measure of working memory.

It was not possible to include a measure for one of the CCE indicators from the model developed using MAAS data as a measure of crystallised IQ was unavailable in TILDA.

6.2.3 Measures of Cognitive Outcome

The *Mini Mental State Examination* (MMSE) is an internationally accepted dementia screening instrument (Folstein et al., 1975). Total score on the MMSE was used as a measure of global cognitive performance.

Delayed Recall was measured as part of the *Word List Learning Test*. After a delay following presentation and immediate recall of a series of words, participants were again asked to recall the words This test of delayed recall was used as a measure of long term memory which has been shown to be predictive of cognitive decline (Chodosh et al., 2002).

Subjective memory at baseline was assessed by asking participants the following question: 'How would you rate your day-to-day memory at the present time?' Participants responded on a five-point scale, ranging from 'excellent' to 'poor'. At two-year follow-up, any change in subjective memory was assessed by asking participants the following question: 'Compared to the last time we interviewed you in [insert month and year of last interview], would you say your memory is better now, about the same, or worse now than it was then?'

A comparison of selected MAAS and TILDA variables is outlined in *Table 30*.

Table 30. CR model indicators and global cognition/memory measures in MAAS and TILDA

CR Model Indicator	MAAS Measure	TILDA Measure
EF/PR		
Response Inhibition	Stroop Colour-Word Test (STR-Int)	Sustained Attention to Response Task (SART)
Fluency	Verbal Fluency Test – animals (FLU)	Verbal Fluency Test – animals (FLU)
Cognitive Switching	Concept Shifting Test (CST-Int)	Color Trails Tasks 1 and 2 (CTT)
Processing Speed	Letter-Digit Modalities Task (LDMT)	Choice Reaction Time Test (CRT)
Immediate Working Memory	Verbal Learning Test (WLT)	Word List Learning Test (WLLT)
CCE		
Occupation	Level of Occupational Attainment (LOA) – 7-point scale	Occupation level – 6-point scale
Education	Level of Education – 8-point scale	Level of Education – 7-point scale
Crystallised IQ	Groningen Intelligence Test (GIT2 - Vocabulary)	No available measures in TILDA
Global Cognition/Memory		
Global Cognition	Mini Mental State Examination (MMSE)	Mini Mental State Examination (MMSE)
Delayed Recall	Verbal Learning Test (WLT)	Word List Learning Test (WLLT)
Subjective Memory	Do you consider yourself to be forgetful? (yes/no)	Baseline: How would you rate your day-to-day memory at the present time? (5-point scale) 2-Year Follow-Up: Compared to the last time we interviewed you in [insert month and year of last interview], would you say your memory is better now, about the same, or worse now than it was then? (3-point scale)

6.3 Analysis

6.3.1 Structural Equation Modelling - Model Specification

Structural equation modelling was performed in order to investigate if the relationships between the CR capacity model and global cognition/memory outcomes observed in MAAS persist in a secondary ageing dataset from an Irish population. In keeping with the model developed using MAAS data, this study specifies CR as a second-order formative, first-order reflective model. The EF/PR and CCE latent variables, each of which are reflected by multiple indicators, act as formative indicators of CR. The structure and fit of two versions of the model were investigated using partially latent SEM (see *Figure 22* for a diagram of the proposed structural model). Model specification is identical to that of the MAAS model with the exception of the CCE indicators. As there was no available measure of crystallised IQ in TILDA, CCE is represented by two indicators: education level and level of occupational attainment. Education and occupation were unable to be correlated in the TILDA CFA due to problems with model identification (see Chapter 4 for details). However, according to Kenny (2011) it is possible for some underidentified measurement models to be identified when the structural model is overidentified. In order to keep the specification of the validation models as similar as possible to the MAAS models, the error terms for education level and occupation level were allowed to correlate in the structural equation models.

A baseline model (Model 1) used raw baseline data for both exogenous (EF/PR and CCE constructs) and the endogenous variables (baseline MMSE, delayed recall, and subjective memory). A longitudinal model (Model 2) used raw baseline data for exogenous variables (EF/PR and CCE constructs) and raw follow-up data at two years for the endogenous variables (MMSE, delayed recall, and subjective memory at two-year follow-up). As with the MAAS models, additional analysis using the regressor variable method was conducted on Model 2 in order to investigate if controlling for baseline scores for the endogenous variables impacted on parameter estimates.

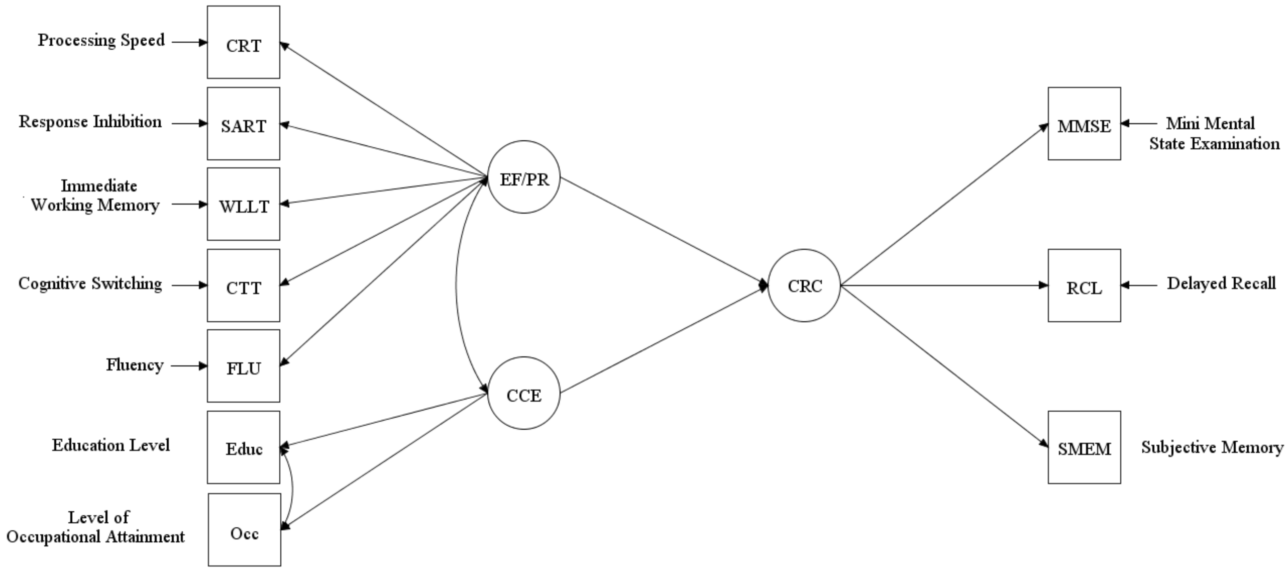


Figure 22. TILDA diagram of the proposed structural model

Note: EF/PR=Executive Function/Processing Speed; CCE=Cumulative Cognitive Enrichment; CRC=Cognitive Reserve Capacity. Two models were tested using this structure: Model 1 - raw baseline data for both exogenous (EF/PR and CCE constructs) and endogenous variables (baseline MMSE, delayed recall and subjective memory). Model 2 - raw baseline data for exogenous variables (EF/PR and CCE constructs) and raw follow-up data at two years for endogenous variables (MMSE, delayed recall and subjective memory at two-year follow-up).

6.3.2 Statistical Analysis

Structural Equation Modelling was conducted using robust weighted least squares estimation (WLSMV). The software package used for the analyses was Mplus version 7.3 (L. K. Muthén & Muthén, 2011). Data cleaning procedures followed the same protocol as MAAS data cleaning and scores more than three standard deviations beyond the mean were removed from the dataset prior to analysis. Kolmogorov-Smirnov and Shapiro-Wilk tests of normality were conducted on the residuals of all measures. From these tests, it appeared that most measures deviated from the normal distribution (*p*s<.001), and therefore an estimator robust to the effects of non-normality in exogenous indicators was used (WLSMV). As the endogenous subjective memory and MMSE variables violated assumptions of normality at both baseline and follow up it was necessary to perform a square root transformation on these variables. Scores on the SART, the Colour Trails Test and the Choice Reaction Time test were reflected in order for high scores to represent better performance. Multicollinearity was assessed using SPSS version 21 (IBM Corp, 2012) through examination of the correlation matrix and collinearity diagnostics (the Variance Inflation Factor and the Tolerance Statistic). With all correlations between the IVs less than 0.8, VIF statistics less than four and Tolerance statistics greater than .1 (guidelines as per Leahy, 2000), there was no indication of multicollinearity among the factor indicators.

6.4 Results

6.4.1 Descriptive Statistics

Table 31 contains details of the descriptive statistics for the sample participants on demographics, CR measures, and outcome measures at baseline. Participants were aged between 50 and 79 years and were divided into two age groupings for SEM analysis: 50-64 year olds (*n*=1,947) and 65-79 year olds (*n*=1,404). The mean education level for both age groups was 'Leaving Certificate or Equivalent'. The mean occupation level for both age groups was 'Non-manual'. Mean scores on the cognitive tasks indicate consistently higher scores in the 50-64 year age group compared to those aged over 65. *Table 32* contains details of descriptive statistics for the sample participants on outcome measures at two-year follow-up.

Table 31. TILDA descriptive statistics of demographic, CR capacity, and global cognition/memory measures at baseline

	50 – 64 Years				65 – 79 Years			
	N	Mean	Range	*SD*	*N*	Mean	Range	*SD*
Age	1947	56.72	50.00-64.00	4.28	1404	70.75	65.00-79.00	4.24
EF/PR								
Sustained Attention to Response Task	1896	2.87	0.00-16.00	2.73	1257	4.53	0.00-16.00	3.72
Sustained Attention to Response Task (Reflected)	1896	14.13	1.00-17.00	2.73	1257	12.47	1.00-17.00	3.72
Fluency (animals)	1929	22.62	1.00-41.00	6.58	1392	20.05	0.00-41.00	6.36
Colour Trails Test	1931	48.69	-24.50-131.47	21.82	1345	59.08	-23.38-137.78	26.62
Colour Trails Test (Reflected)	1931	90.09	7.31-163.28	21.82	1345	79.70	1.00-162.16	26.62
Choice Reaction Time Test	1918	478.32	258.97-959.45	88.81	1321	520.77	282.11-959.03	102.34
Choice Reaction Time Test (Reflected)	1918	482.13	1.00-701.48	88.81	1321	439.68	1.42-678.34	102.34
Word List Learning	1941	14.53	5.00-20.00	2.67	1396	12.82	4.00-20.00	2.91
CCE								
Education Level	1947	4.26	1.00-7.00	1.54	1404	3.64	1.00-7.00	1.64
Level of Occupational Attainment (LOA)	1947	3.87	1.00-6.00	1.27	1404	3.78	1.00-6.00	1.33
Global Cognition/Memory								
Word List Learning - Delayed Recall	1942	6.79	1.00-10.00	2.10	1379	5.56	1.00-10.00	2.22
Subjective Memory	1945	3.61	1.00-5.00	0.93	1404	3.28	1.00-5.00	0.92
Mini-Mental State Examination	1947	29.01	24.00-30.00	1.26	1404	28.35	24.00-30.00	1.55

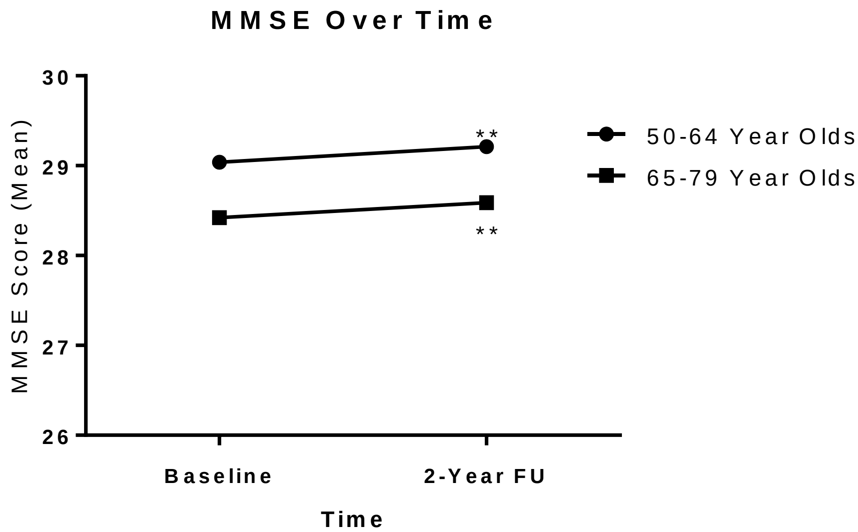
Note. Mean and SD values represent scores following reflection of the Sustained Attention to Response Task, Colour Trails Task and Choice Reaction Time Test and prior to transformation of Subjective Memory and MMSE variables.

Table 32. TILDA descriptive statistics of global cognition/memory measures at two-year follow-up

	50 – 64 Years				65 – 79 Years			
	N	Mean	*Range*	*SD*	*N*	Mean	*Range*	*SD*
Word List Learning – Delayed Recall	1841	6.93	0.00-10.00	2.16	1271	5.53	0.00-10.00	2.45
Subjective Memory	1840	1.86	1.00-3.00	0.38	1277	1.76	1.00-3.00	0.45
Mini-Mental State Examination	1838	29.21	23.00-30.00	1.16	1267	28.59	23.00-30.00	1.50

Table 33. TILDA descriptive statistics of global cognition/memory measures at over time for complete cases only

	50 – 64 Years				65 – 79 Years			
Baseline	*N*	Mean	*Range*	*SD*	*N*	Mean	*Range*	*SD*
Word List Learning – Delayed Recall	1836	6.84	1.00-10.00	2.09	1249	5.62	1.00-10.00	2.21
Subjective Memory	1840	3.61	1.00-5.00	0.93	1277	3.29	1.00-5.00	0.92
Mini-Mental State Examination	1838	29.04	24.00-30.00	1.22	1267	28.42	24.00-30.00	1.50
2-Year Follow-Up								
Word List Learning – Delayed Recall	1836	6.93	0.00-10.00	2.16	1249	5.55	0.00-10.00	2.44
Subjective Memory	1840	1.86	1.00-3.00	0.38	1277	1.76	1.00-3.00	0.45
Mini-Mental State Examination	1838	29.21	23.00-30.00	1.16	1267	28.59	23.00-30.00	1.50



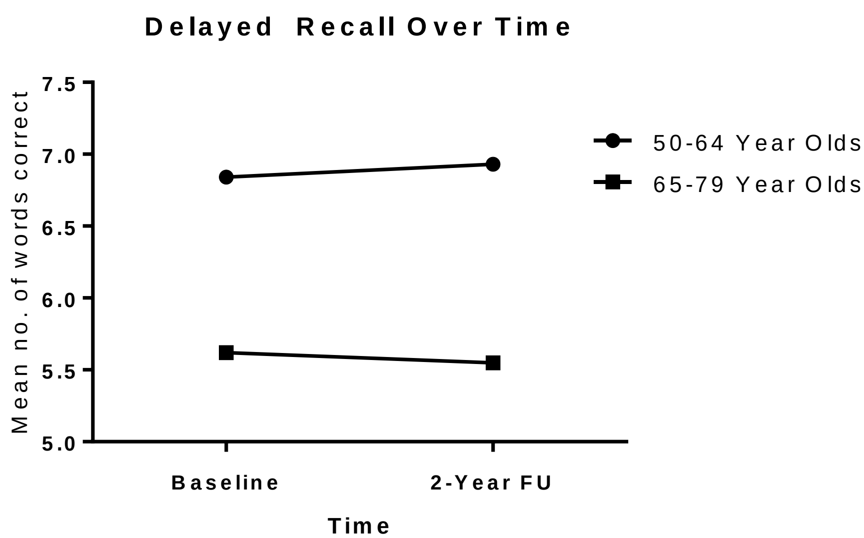


Figure 23. TILDA mean scores on MMSE and Delayed Recall for age groups over time (complete cases)

Note. **p<.001; Significance of differences across time points is based on paired sample t-tests. Significance at follow-up refers to a difference from baseline.

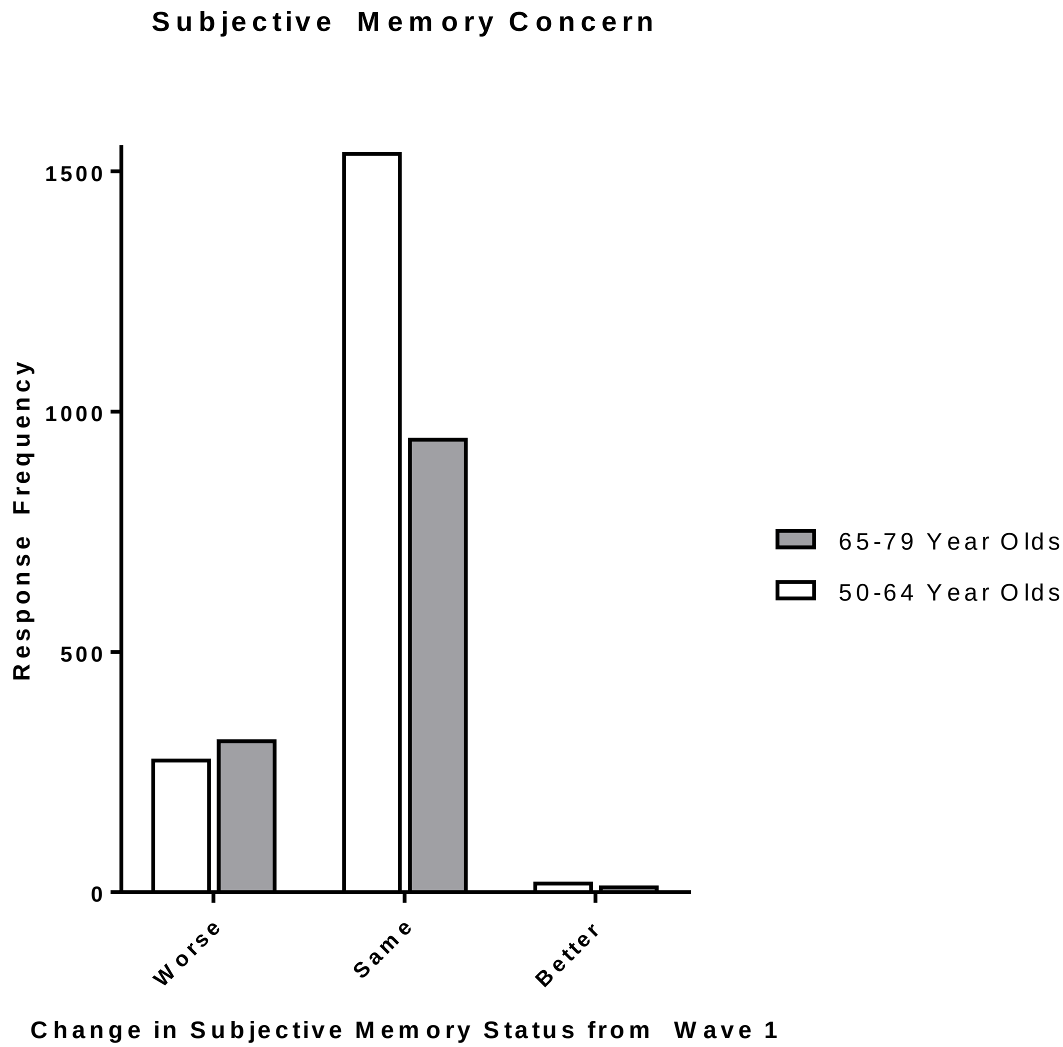


Figure 24. TILDA change in subjective memory status from Wave 1 across age groups (complete cases)

6.4.2 Model 1 – Baseline Model

Goodness of fit was evaluated using χ^2 index of absolute model fit, weighted root mean square residual (WRMR), root mean square error of approximation (RMSEA) and its 90% confidence interval (90% CI), comparative fit index (CFI) and the Tucker-Lewis index (TLI). Model fit was determined by the following criteria: RMSEA (.05–.08) WRMR (≤1.0), CFI (≥.90), and TLI (≥.90). Fit statistics for Model 1 are summarised in *Table 34*. Overall, goodness-of-fit indices suggest that the structural model fits the data well across both age groups.

Table 34. TILDA fit statistics for Model 1 across age-groups

Statistic	**50-64 years**	**65-79 years**
χ^2	259.760	236.980
df	33	33
p	0.000	.0000
RMSEA (90% CI)	0.059 [0.053, 0.066]	0.066 [0.059, 0.074]
CFI	0.942	0.929
TLI	0.921	0.904
WRMR	1.454	1.416

The completely standardised parameter estimates for 50-64 year olds are presented in *Figure 25* (standard errors of the estimates are provided in *Table 35*). All freely estimated unstandardised parameters for the measurement model were statistically significant (*p*s<.001). The significant component weights for EF/PR (5.726) and CCE (-4.615) suggest that each component is an important determinant of CR capacity. There was a correlation of 1.004 between EF/PR and CCE, which calls into question the discriminant validity of these factors. Baseline CR capacity was predictive of baseline scores on MMSE scores, the delayed recall task and ratings of subjective memory (standardised coefficients = 0.548, 0.569 and 0.281 respectively).

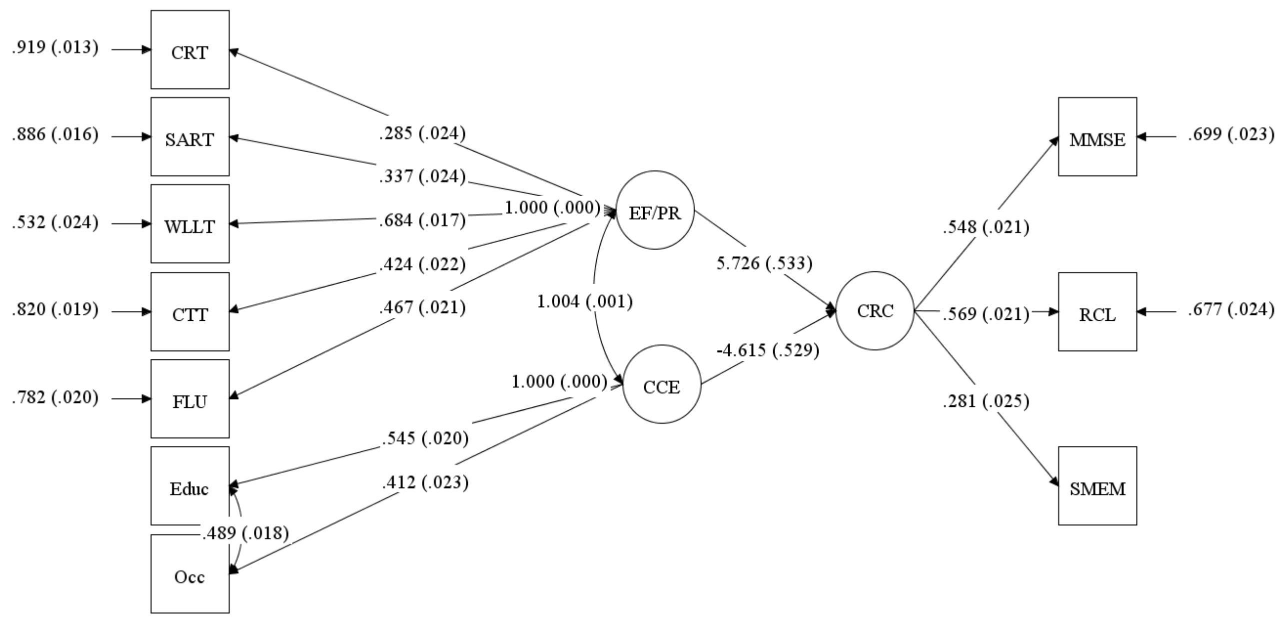


Figure 25. TILDA Model 1: Completely standardised estimates of free parameters in the structural model for healthy adults aged 50-64 years

Note. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

The completely standardised parameter estimates for 65-79 year olds are presented in *Figure 26* (standard errors of the estimates are provided in *Table 35*). All freely estimated unstandardised parameters for the measurement model were statistically significant (*p*s<.001). The significant component weights for EF/PR (14.484) and CCE (-13.437) suggest that each component is an important determinant of CR capacity. There was a correlation of 1.00 between EF/PR and CCE, which calls into question the discriminant validity of these factors. Baseline CR capacity was predictive of baseline scores on MMSE, the delayed recall task and subjective memory (standardised coefficients = 0.596, 0.595 and 0.271 respectively).

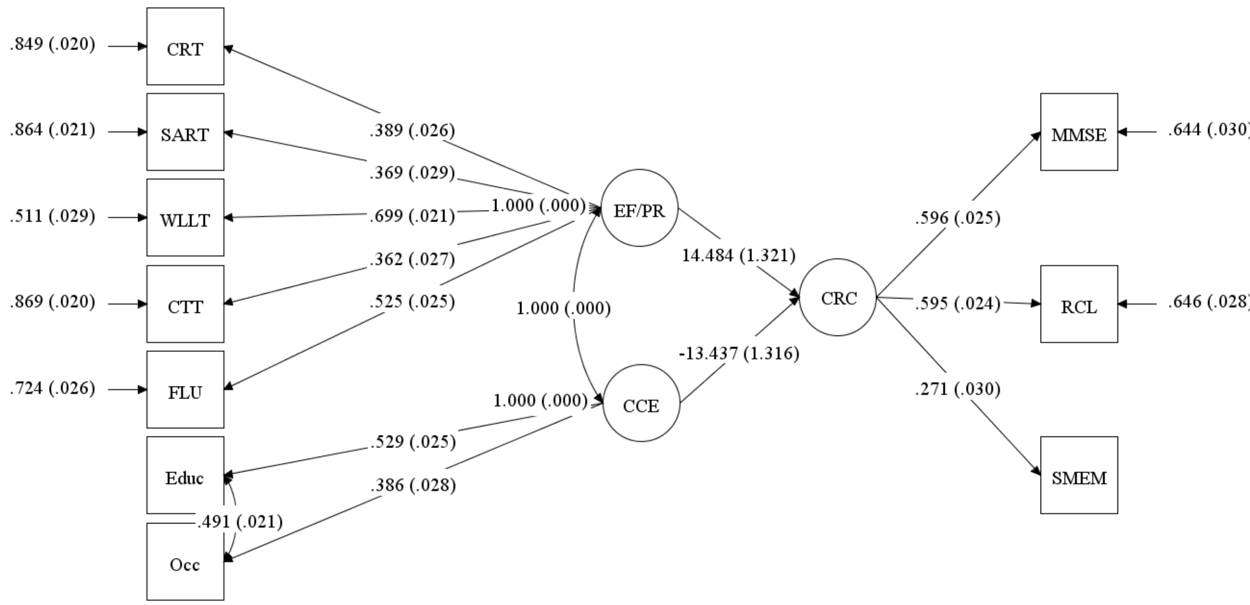


Figure 26. TILDA Model 1: Completely standardised estimates of free parameters in the structural model for healthy adults aged 65-79 years

Note. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

Table 35. TILDA parameter estimates for Model 1

50-64 Year Olds	Estimates	S.E.	Est./S.E.	Std	StdYX	R^2
EF/PR						
Processing Speed	1.00	0.00	999.00	1.27	0.29	0.08
Immediate Working Memory	1.44	0.13	11.02	1.83	0.68	0.47
Response Inhibition	0.73	0.08	9.27	0.92	0.34	0.11
Cognitive Switching	1.46	0.14	10.23	1.85	0.42	0.18
Fluency	0.49	0.05	10.21	0.61	0.47	0.22
CCE						
Education Level	1.00	0.00	999.00	0.55	0.55	0.30
Level of Occupational Attainment	0.76	0.04	20.25	0.41	0.41	0.17
Global Cognition/Memory						
MMSE	1.00	0.00	999.00	0.22	0.55	0.30
Delayed Recall	5.40	0.32	16.82	1.19	0.57	0.32
Subjective Memory	1.27	0.12	10.69	0.28	0.28	0.08
EF/PR → CR Capacity	1.00	0.00	999.00	5.73	5.73	-
CCE → CR Capacity	-1.872	0.20	-9.25	-4.62	-4.62	-
Covariance of EF/PR and CCE	0.69	0.07	10.61	1.00	1.00	-

65-79 Year Olds	Estimates	S.E.	Est./S.E.	Std	StdYX	R^2
EF/PR						
Processing Speed	1.00	0.00	999.00	3.98	0.39	0.15
Immediate Working Memory	0.51	0.04	11.90	2.03	0.70	0.49
Response Inhibition	0.35	0.04	9.26	1.37	0.37	0.14
Cognitive Switching	0.48	0.05	9.61	1.93	0.36	0.13
Fluency	0.17	0.01	11.84	0.67	0.53	0.28
CCE						
Education Level	1.00	0.00	999.00	0.53	0.53	0.28
Level of Occupational Attainment	0.73	0.05	14.42	0.39	0.39	0.15
Global Cognition/Memory						
MMSE	1.00	0.00	999.00	0.28	0.60	0.36
Delayed Recall	4.81	0.33	14.59	1.32	0.60	0.35
Subjective Memory	0.99	0.12	8.26	0.27	0.27	0.07
EF/PR → CR Capacity	1.00	0.00	999.00	14.48	14.48	-
CCE → CR Capacity	-6.98	0.63	-11.14	-13.44	-13.44	-
Covariance of EF/PR and CCE	2.11	0.19	11.21	1.00	1.00	-

Note. Estimates, unstandardised parameter estimate; S.E., standard error; Est./S.E., test statistic (*z* value); Std, standardised parameter estimate; StdYX, completely standardised parameter estimate; R^2, square of the completely standardised parameter estimate.

6.4.3 Model 2 – Longitudinal Model (2-Year Follow-Up)

Goodness of fit was evaluated using χ^2 index of absolute model fit, weighted root mean square residual (WRMR), root mean square error of approximation (RMSEA) and its 90% confidence interval (90% CI), comparative fit index (CFI) and the Tucker-Lewis index (TLI). Model fit was determined by the following criteria: RMSEA (.05–.08) WRMR (≤1.0), CFI (≥.90), and TLI (≥.90). Fit statistics for Model 2 are summarised in *Table 36*. Overall, goodness-of-fit indices suggest that the structural model fits the data very well for both age groups.

Table 36. TILDA fit statistics for Model 2 across age-groups

Statistic	**50-64 years**	**65-79 years**
χ^2	121.262	92.322
df	33	33
p	0.000	0.000
RMSEA (90% CI)	0.037 [0.030, 0.044]	0.036 [0.027, 0.045]
CFI	0.976	0.978
TLI	0.967	0.970
WRMR	1.050	0.904

The completely standardised parameter estimates for 50-64 year olds are presented in *Figure 27*. All freely estimated unstandardised parameters for the measurement model were statistically significant (*p*s<.001). The significant component weights for EF/PR (14.083) and CCE (-13.174) suggest that each component is an important determinant of CR capacity. There was a correlation of 1.00 between EF/PR and CCE, which calls into question the discriminant validity of these factors. Baseline CR capacity was predictive of scores on MMSE and the delayed recall task at two-year follow-up (standardised coefficients = 0.518 and 0.593 respectively). However, baseline CR capacity was not a significant predictor of subjective memory at two-year follow-up.

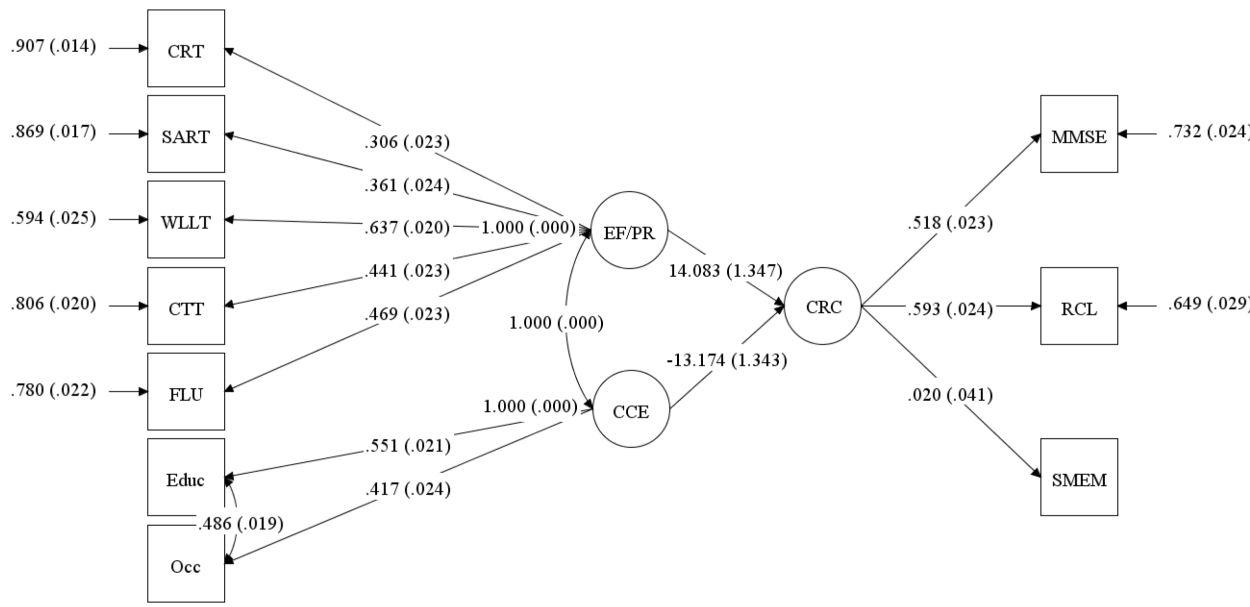


Figure 27. TILDA Model 2: Completely standardised estimates of free parameters in the proposed structural model for healthy adults aged 50-64 years

Note. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

The completely standardised parameter estimates for 65-79 year olds are presented in *Figure 28*. All freely estimated unstandardised parameters for the measurement model were statistically significant (*p*s<.001). The significant component weights for EF/PR (15.166) and CCE (-14.303) suggest that each component is an important determinant of CR capacity. There was a correlation of 0.999 between EF/PR and CCE, which calls into question the discriminant validity of these factors. Baseline CR capacity was predictive of scores on MMSE and the delayed recall task at two-year follow-up (standardised coefficients = 0.632 and 0.623 respectively). However, baseline CR capacity was not a significant predictor of subjective memory at two-year follow-up.

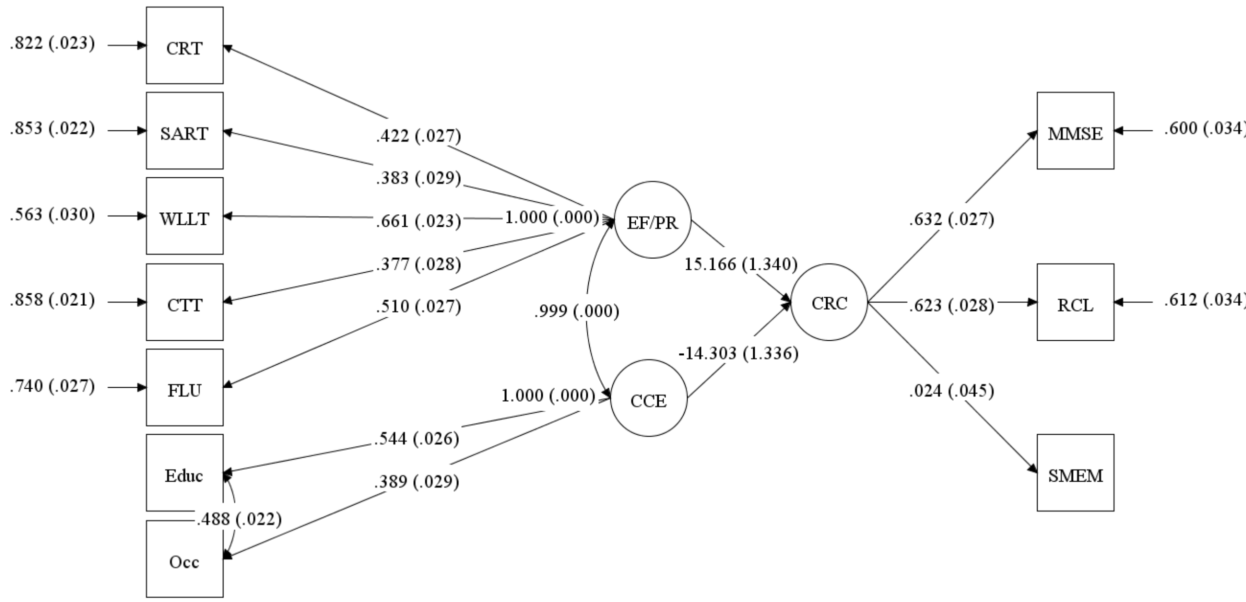


Figure 28. TILDA Model 2: Completely standardised estimates of free parameters in the proposed structural model for healthy adults aged 65-79 years

Note. Standard errors of the estimates for the completely standardised solution are reported in parentheses.

Parameter Estimates When Adjusting for Covariates

Controlling for baseline levels of the outcomes by including them as covariates was necessary in order to investigate change in scores at two-year follow-up. In Mplus v.7.3, missing data is not permitted for observed covariates because they are not part of the model (L. K. Muthén, 2005). Therefore, any observations with missing data on observed exogenous variables were excluded from the analysis. For the 50-64 year age-group, seven participants with missing data on the observed covariates were excluded from analysis (remaining *n*=1,940) and for the 65-79 year age-group 25 participants with missing data on the observed covariates were excluded (remaining *n*=1,379). The model could not be identified when covariates were included so the correlation between the error terms for level of education and level of occupational attainment was removed.

The adjusted parameter estimates including standard errors of the estimates for Model 2 are presented in *Table 37* and a comparison of the completely standardised parameter estimates for the model, before and after adjusting for covariates, are presented in *Table 38*. When the covariates were included in Model 2 for the 50-64 year age group, all freely estimated unstandardised parameters for the measurement model remained statistically significant (*p*s<.001). The significant component weighting for EF/PR (0.645) suggests that this component is an important determinant of CR capacity. However the component weighting for CCE did not reach significance for the 50-64 year olds (*p*=0.071) suggesting that CCE does not contribute to CR capacity in this model. The correlation of 0.528 between the EF/PR and CCE factors suggestst that the factors are moderately related. Baseline CR capacity was predictive of scores on MMSE and the delayed recall task at two-year follow-up (standardised coefficients = 0.484 and 0.609 respectively). Baseline CR capacity was not a significant predictor of subjective memory at two-year follow-up. When the covariates were included in Model 2 for the 65-79 year age group, all freely estimated unstandardised parameters for the measurement model remained statistically significant (*p*s<.001). The significant component weights for EF/PR (0.704) and CCE (-0.205) suggest that each component is an important determinant of CR capacity. The correlation of 0.595 between the EF/PR and CCE factors suggets that the factors are moderately related. Baseline CR capacity was predictive of scores on MMSE and delayed recall at two-year follow-up (standardised coefficients = 0.600 and 0.643 respectively). Baseline CR capacity was not a significant predictor of subjective memory at two-year follow-up.

Table 37. TILDA parameter estimates for Model 2 (adjusting for baseline)

50-64 Year Olds	**Estimates**	**S.E.**	**Est./S.E**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	0.12	0.01	0.00
Immediate Working Memory	5.64	0.82	6.86	0.66	0.33	0.11
Response Inhibition	5.91	0.97	6.09	0.69	0.26	0.07
Cognitive Switching	11.39	1.73	6.57	1.33	0.32	0.10
Fluency	3.64	0.56	6.53	0.43	0.34	0.12
CCE						
Education Level	1.00	0.00	999.00	0.84	0.84	0.71
Level of Occupational Attainment	0.75	0.08	9.94	0.63	0.63	0.40
Global Cognition/Memory						
MMSE	1.00	0.00	999.00	0.18	0.48	0.23
Delayed Recall	7.15	0.42	16.89	1.29	0.61	0.37
Subjective Memory	-0.02	0.02	-1.08	-0.00	-0.03	0.00
EF/PR → CR Capacity	1.00	0.00	999.00	0.65	0.65	-
CCE → CR Capacity	-0.02	0.01	-1.76	-0.11	-0.11	-
Covariance of EF/PR and CCE	0.05	0.01	6.24	0.53	0.53	-

65-79 Year Olds	**Estimates**	**S.E.**	**Est./S.E**	**Std**	**StdYX**	**R^2**
EF/PR						
Processing Speed	1.00	0.00	999.00	0.19	0.02	0.00
Immediate Working Memory	3.76	0.64	5.88	0.72	0.35	0.12
Response Inhibition	4.87	0.95	5.11	0.93	0.26	0.07
Cognitive Switching	6.60	1.29	5.12	1.26	0.25	0.06
Fluency	1.84	0.34	5.36	0.35	0.30	0.09
CCE						
Education Level	1.00	0.00	999.00	0.90	0.90	0.81
Level of Occupational Attainment	0.64	0.08	7.88	0.58	0.58	0.34
Global Cognition/Memory						
MMSE	1.00	0.00	999.00	0.85	0.39	0.36
Delayed Recall	5.67	0.38	14.79	0.25	0.64	0.41
Subjective Memory	-0.00	0.02	-0.23	-0.00	-0.01	0.00
EF/PR → CR Capacity	1.00	0.00	999.00	0.70	0.70	-
CCE → CR Capacity	-0.06	0.03	-2.31	-0.21	-0.21	-
Covariance of EF/PR and CCE	0.10	0.02	5.26	0.60	0.60	-

Note. Estimates, unstandardised parameter estimate; S.E., standard error; Est./S.E., test statistic (*z* value); Std, standardised parameter estimate; StdYX, completely standardised parameter estimate; R^2, square of the completely standardised parameter estimate.

Table 38. TILDA completely standardised parameter estimates for Model 2: Before and after adjusting for baseline

	50-54 Year Olds		**65-79 Year Olds**	
	Model 2	**Model 2 Adjusted**	**Model 2**	**Model 2 Adjusted**
Path				
EF/PR → CR capacity	14.083**	0.645**	15.166**	0.704**
CCE → CR capacity	-13.174**	-0.109	-14.303**	-0.205*
CR capacity → MMSE	0.518**	0.484**	0.632**	0.389**
CR capacity → Delayed Recall	0.593**	0.609**	0.623**	0.561**
CR capacity → Subjective Memory	0.020	-0.032	0.024	0.030
Covariance of EF/PR and CCE	1.000**	0.528**	0.999**	0.595**

Note. ***p*<.01; **p*<.05

Due to the questionable discriminant validity of the EF/PR and CCE factors for the baseline and unadjusted two-year follow-up models, as well as the persisting negative component weighting of CCE on the CR construct, post-hoc analyses were conducted to assess the integrity of the proposed model. The post-hoc analyses followed the same format as that of Chapter 5 and supported the two-factor structure of the CR capacity model as superior to alternative models, while also ruling out suppression effects in the model (see Appendix F for TILDA model integrity tables).

6.5 Discussion

This validation study sought to replicate the CR capacity structural models (SEM) in a secondary, Irish longitudinal ageing dataset, TILDA.

6.5.1 CR Capacity as a Predictor of Cognitive Status Over Time

Results of MAAS structural equation modelling in both baseline and longitudinal models are largely replicated in the TILDA SEMs. Similar to the MAAS SEMs, the models provide support for a strong, positive predictive relationship between CR capacity and global cognition/memory outcomes at baseline and two-year follow-up. Goodness-of-fit indices were very good across both baseline and two-year follow-up models for both age groups. At baseline for both age groups, CR capacity was found to be predictive of scores on MMSE, delayed recall and subjective ratings of memory. At two-year follow-up, when controlling for baseline, CR capacity was predictive of scores on MMSE and delayed recall, but not subjective ratings of memory. Similar to MAAS, the magnitude of the predictive relationship between CR capacity and delayed recall increased over time for the older age group. This pattern was also replicated when compared with the six-year follow-up model in MAAS for the middle-aged group. Patterns of CR capacity relationships with MMSE were also similar to the MAAS six-year follow-up model for the middle aged group, with the magnitude of the relationship decreasing over time. However, this trend was not replicated in the older age group, with the relationship between CR capacity and MMSE scores appearing almost identical at two-year follow-up. As with the MAAS models, the fact that these strong positive relationships hold both cross-sectionally and longitudinally in TILDA supports the theory that CR capacity is involved in sustaining cognitive abilities over time in healthy ageing populations. Support for this finding comes from research linking control processes, the strongest driver of CR capacity, with improved memory performance in older adults (Buckner, 2004). The predictive relationship between CR capacity and subjective memory complaints was unclear in MAAS due to mixed findings across age-groups and across time points. The baseline MAAS model was suggestive of a positive predictive relationship between CR capacity and subjective memory in the older age group, but as model fit was poor, firm conclusions could not be drawn. The baseline TILDA model found a similar strong positive predictive relationship between CR capacity and subjective memory, and as model fit was very good, this finding supports the validity of this relationship. This relationship was also found in the middle-aged group in TILDA, but not MAAS, which may be reflective of a more comprehensive measure of subjective memory used in TILDA. The five-point Likert scale measure of subjective memory used in TILDA may have been able to capture more variance in responses than the binary measure used in MAAS. While a significant predictive relationship between CR capacity and subjective memory was found in the MAAS six-year follow-up model for the older age group, this finding was not replicated in TILDA at two-year follow-up, in either middle-aged or older adults. This may be because the follow-up measure of subjective memory in TILDA was designed to measure changes in subjective opinions of memory by asking participants if they felt their memory was 'better', 'the same', or 'worse' than it was at baseline, and the two-year time lapse may not have been long enough for significant changes to have occurred. Regardless, the finding of a significant predictive relationship at baseline is of importance as it suggests that an engaged CR capacity system is predictive of subjective opinions of memory performance in a positive direction (activation of a CR capacity system leads to better subjective reports of memory performance). Overall, the findings pertaining to predictive relationships in this validation study support the overall findings of the MAAS SEMs and are in keeping with the proposal that CR capacity is predictive of cognitive outcomes in healthy ageing over time.

6.5.2 The CR Capacity Construct

The relative weightings of EF/PR and CCE on CR capacity in the TILDA models are reflective of the MAAS model weightings. EF/PR has a consistently strong, positive weighting, while CCE has a consistently strong negative weighting. These weightings are always significant with regard to EF/PR, however the relationship between CCE and CR capacity in the adjusted model at two-year follow-up for the 50-64 year olds is non-significant. The fact the CCE dropped out of the model in this instance may be due to the lack of a crystallised IQ indicator on the CCE construct. As the CCE weighting on CR capacity was consistently significant in MAAS, having only two indicators on the construct may have resulted in reduced sensitivity to detect a significant relationship. The results of the validation model support the findings of the MAAS SEMs in relation to the formation of the CR capacity construct, which suggested that control and representational processes are differentially involved in CR capacity. As collinearity and suppression effects do not appear to be problematic in the data, and respecification is not suitable, there are some potential theoretical explanations for this finding.

It may be the case that control and representational processes are differentially involved in CR capacity, whereby high CCE levels are related to low activation or engagement of the CR capacity system (as indicated by a negative relationship between CCE and CR capacity), while high EF/PR levels are associated with high activation of this system (as indicated by a positive relationship between EF/PR and CR capacity) in healthy older adults. This idea is related to suggestions made by Stern (2002) regarding differential ability in recruitment of alternative networks. Using the example of expertise, he suggests that when solving a problem a mathematician may rely on the processing efficiency of a typically used system (neural reserve). However, if faced with brain damage, or increased task demands, the mathematician would be expected to have greater flexibility in recruiting alternative systems not typically used to maintain performance (neural compensation). Stern suggests that these two types of CR could be used to form a heuristic framework in the study of CR in healthy individuals in order to investigate how individual differences in skills or intelligence might affect responses to brain damage. Although necessarily speculative, this idea maps on to the CR capacity model, where EF/PR can be viewed as the processing efficiency, or neural reserve, arm of CR capacity and CCE can be viewed as the compensatory arm of CR capacity, as cognitively enriching experiences across the lifespan may facilitate cognitive flexibility and the ability to compensate through recruitment of alternative networks if required. As this model was explored in relation to healthy individuals, it may be the case that direct, damage specific, compensation is not being directly engaged in this group, and CR capacity is primarily activated through a standard EF/PR network, or neural reserve arm. While Stern acknowledges that compensation in the form of recruitment of alternative networks can be seen in healthy individuals who are faced with increasing task demands or decreased efficiency of a standard brain networks, this may not be evident in the MAAS and TILDA models due to the high levels of EF/PR, indicating high neural reserve and processing efficiency. It may be the case that the populations investigated using MAAS and TILDA data are displaying high levels of neural efficiency and this is reflected in the strong positive relationship between the EF/PR factor and the hierarchical CR capacity factor. In a non-compensatory situation for healthy individuals, the CCE representations system may not be engaged, and thus, may not co-activate non-standard CR systems or deactivate the primarily EF driven CR capacity system. If the population was affected by some form of pathology, or processing efficiency was strongly impaired due to advancing age, it is possible that both arms, including the non-standard CCE arm of CR capacity, would be engaged and alternative networks would be recruited to maintain performance. In this case, EF/PR, through its strong reciprocal relationship with CCE, may assist compensation by facilitating greater flexibility in the recruitment of alternative networks. However, the direct strong positive relationship between EF/PR and CR capacity may no longer be evident in populations where control processes are disrupted as a result of pathology. This explanation can be adapted to the current CR capacity model weightings that were established in study 3 and the current study. For standard processing in healthy ageing, high levels of EF/PR result in high activation or engagement of a CR capacity system, and high CCE levels result in low activation or engagement of a CR capacity system. The patterns of activation of CR capacity in a situation where participants have low EF/PR levels due to pathology, is yet to be clarified through future research. These differential roles are in need of further investigation in brain damaged populations before any conclusions in this regard can be drawn.

Another potential explanation focuses on the differential roles of EF/PR and CCE as a function of age. Bouazzaoui et al. (2013) explored the hypothesis that control and representational processes are differentially involved in performance of episodic memory in both young and older healthy adults. They found that while representational processes were the sole predictor of episodic memory performance for young adults, control processes were the main predictor for older adults, with representational processes adding a small contribution. The influential role of control on memory can be explained here as EF engaging in higher order memory strategies in order to sustain memory performance. As the prefrontal cortex sustains EF, and greater prefrontal cortex activation is evident in older rather than younger individuals (Dennis & Cabeza, 2008), it is possible that older adults depend on control processes more than young adults when faced with age-related declines in cognition. This explanation can be applied to the differential involvement of EF/PR and CCE in CR capacity, as EF/PR may be increasingly relied upon in older adults to activate the CR capacity system and maintain performance in age-related decline. Paradoxically, this pattern is evident in older adults despite age-related declines in control processes (Bouazzaoui et al., 2014).

Furthermore, high CCE can be interpreted as resulting in low activation of a CR capacity system when the relationship between EF/PR and CR capacity is controlled for, and this may be because control processes are necessary to access the information stored in representational systems. When the relationship between EF/PR and CR capacity is controlled for, the engagement of CCE with a CR capacity system may be filtered out, resulting in a negative relationship. The contribution of representational processes is likely reflected in the reciprocal relationship between EF/PR and CCE. The correlations between these CR capacity components was consistently high in TILDA. While there was reason to question the discriminant validity of the EF/PR and CCE factors in only one of the MAAS models (adjusted model at 12-year follow-up for 50-64 year olds), both the baseline and unadjusted two-year follow-up SEMs in TILDA had extremely high correlations between the EF/PR and CCE components. However, when controlling for baseline levels of the outcome variables at two-year follow-up these correlations reduced substantially to support the discriminant validity of the factors (the correlation reduced from 1.000 to 0.528 for the 50-64 year olds and from 0.999 to 0.595 for the 65-79 year olds). It is possible that the correlation between the errors of education level and level of occupational attainment artificially inflated the relationship between the EF/PR and CCE factors in the baseline and unadjusted models. The adjusted model could not be identified when the errors were allowed to correlate, therefore this may explain why this effect was not seen in the adjusted models.

Additionally, it is possible that CCE indicators such as education and occupation provide mental demands that may cumulatively engage CR capacity, but only while they are ongoing and once the formal period of training or work ceases, due to completion of studies or retirement, this may result in engagement of alternative systems that activate CR capacity and support cognitive function. Research by Singh-Manoux et al. (2011) investigated factors affecting cognitive decline and found greater decline in global cognitive functioning in a high occupation group at 10-year follow-up. An explanation put forward by the authors for this finding was that the cognitive gains associated with occupation are transient. A study by Reed et al. (2011) also found a negative relationship between education and CR (defined as the residual variance of the regressions of cognitive factors on brain pathology). A proposed explanation by the authors was that education develops mental capacity early in life and after formal education ends, other cognitive activities provide mental exercise to further develop and maintain CR. It may be the case that the cognitive enrichment provided by CCE is also transient and when the strong relationship between EF/PR and CCE is taken into account by controlling for EF/PR, any engagement of a CR capacity system through CCE is no longer evident.

Overall, results broadly support the findings of the CFA and SEMs in MAAS. In TILDA, EF/PR continues to be a strong contributor to CR capacity, suggesting that high EF/PR performance is associated with high activation of the CR capacity system. On the other hand, high CCE levels are associated with low activation of the CR capacity system, but contribute to CR capacity through a strong reciprocal relationship with EF/PR. This validation study supports the structural relationships in a theoretically driven, partially-latent model of the interrelations between a two-factor CR capacity model and global cognition/memory outcomes at both baseline and follow-up. Next steps involve further profiling of the CR capacity model parameters in a small sample of Irish healthy older adults, before investigating the effects of a targeted EF cognitive training intervention aimed at modifying control processes, a key component of CR capacity.

Section II: Modifiability of CR Capacity

The relationships between factors associated with CR capacity and global cognition/memory outcomes have been explored and validated in Section I using data from two longitudinal ageing studies, MAAS and TILDA. Exploratory and confirmatory factor analysis support a two-factor model of CR capacity comprised of control processes (EF/PR) and representational processes (CCE). Results of structural equation modelling, both at baseline and longitudinally, support the strong predictive ability of the CR capacity model, and in particular the large contribution of EF/PR to the model. SEM analysis also supports a strong, positive predictive relationship between CR capacity and measures of global cognition/memory. CR capacity is a strong predictor of delayed recall and MMSE scores at baseline, as well as at two-, six-, and 12-year follow-up in healthy adults aged 50 and over. Subjective memory outcomes were only significantly predicted by CR capacity in the older age group in MAAS at baseline and six-year follow-up. In TILDA, these findings were somewhat validated as subjective memory outcomes were predicted by CR capacity at baseline, and this was observed in both age groups and not just in older individuals. Overall, results of SEM analyses support the hypothesis that CR capacity is positively associated with global cognitive/memory scores in healthy ageing, however the relationship between CR capacity and subjective memory complaints merits further investigation due to mixed findings across models. The strong predictive ability of the CR capacity model, and in particular the consistently large contribution of EF/PR to the model, may have implications for a targeted intervention aimed at modifying EF, an important formative component of CR capacity.

Section II focuses on a targeted cognitive intervention in a small sample of Irish healthy older adults. This section firstly aims to further validate the CR capacity model parameters specificied in MAAS and TILDA cross-sectionally in this small sample, while also exploring model relationships with additional parameters that were beyond the scope of the modelling studies but have a basis in the CR literature. Of particular interest are the relationships between the CR capacity model parameters and subjective memory complaints which literature suggests are an important predictor of decline outcomes in healthy ageing. Secondly, this section aims to explore the modifiability of CR capacity through a targeted control process intervention. Given that CR capacity is positively driven by control processes

(EF/PR, a construct that is considered to be modifiable) across all models in both the Dutch and Irish samples, this lends support to the idea that a cognitive training intervention targeting control processes could potentially boost this formative component of CR capacity in this small sample of healthy older adults.

Chapter 7: Study 5 - Pre-Intervention Profiling of CR Capacity

7.1 Introduction

This chapter focuses on a small sample of healthy Irish older adults recruited for a cognitive intervention study, concentrating on the study participants pre-intervention. Firstly, the CR capacity model relationships are explored in this small Irish sample of healthy older adults to investigate if the specified model relationships hold. Of particular interest is whether the strong relationship between control (EF/PR) and representational processes (CCE), and the relationships between these measures and global cognition/memory measures are observed in this sample. If relationships are replicated, this will help to further validate the CR capacity model. It must be noted, however, that CR capacity was modelled is Section I using latent variables that cannot be measured directly. Therefore, for the purposes of this study, direct relationships between observed measures used in the CR capacity model and global cognition/memory measures are investigated. Secondly, relationships between the CR capacity factors, global cognition/memory outcomes, and additional measures that were unavailable in MAAS and TILDA datasets, are explored. Thirdly, the sample will be profiled based on a subjective report of memory performance in order to clarify whether the CR capacity model measures, as well as additional measures that were unavailable in MAAS and TILDA, differ as a function of these subjective memory. In particular, elucidating the relationships between CCE and EF/PR and subjective memory will help to delineate if high levels of CCE and EF/PR correspond to positive reports of subjective memory functioning. This will further inform the potential impact of a cognitive intervention targeting control processes.

7.1.1 CR Capacity Model Relationships

The findings from SEM analyses in studies 3 and 4 provide support for the argument that modification of control processes through a targeted intervention has the potential to boost CR capacity. EF/PR has a consistently high weighting on the CR capacity construct in both the original MAAS SEMs and the validation study SEMs using TILDA data. As CR capacity is positively predictive of global cognition and memory outcomes, it follows that modifying EF/PR could in turn effect these cognitive abilities. The strong relationship between EF/PR and CCE and their individual contributions to CR capacity were validated in an Irish sample in the TILDA study. For this intervention study, it is important to firstly investigate if these parameters hold in a small sample of healthy Irish older adults pre-intervention. However, it must be noted that the direct relationships between a CR capacity construct and global cognition/memory outcomes that were modelled in studies 3 and 4, cannot be replicated in this small sample as a large n (>100) is required for SEM analysis. Therefore, this study specifically investigated the relationship between EF/PR and CCE, and the predictive relationships between these individual CR capacity components and global cognition/memory measures.

Furthermore, the model relationships with additional parameters that were beyond the scope of the modelling studies but have a basis in the CR literature, are also of interest. In particular, there has been a wealth of research to suggest that maintaining social networks and engaging in mentally stimulating activities have protective effects against cognitive decline, and measures of these are frequently used as proxies of CR (Crowe et al., 2003; Fritsch et al., 2005; Valenzuela et al., 2011). These activities can be viewed as potentially contributing to a representational system that develops over the lifespan and remains relatively stable into older age (Craik & Bialystok, 2006) and therefore their relationships with the CCE component of CR capacity is of particular interest. Additionally, a subjective measure of EF, the Behaviour Rating Inventory of Executive Function-Adult Version (BRIEF-A), was included in the study to determine its relationship with CR capacity, particularly the EF/PR component. Research has suggested that participants with cognitive complaints and MCI have significantly worse self-reports of EF compared to healthy controls, despite normal performance on objective EF tasks (Rabin et al., 2006). It may be the case that self-reports of EF are sensitive to prodromal changes that cannot yet be detected by objective EF measures, therefore the relationship between this subjective EF measure and objective measures of control processes pre-intervention is of particular interest.

The memory measures included in the predictive models in studies 3 and 4 were limited to scores on measures of delayed recall and binary/short Likert-scale ratings of subjective memory. For the purposes of this study, the scope of memory measures was expanded to include prospective and retrospective memory as measured by the Prospective and

Retrospective Memory questionnaire (PRMQ). In a study on how PRMQ scores related to actual memory performance, Kliegel and Jager (2006) found that the PRMQ subscales could successfully differentiate between prospective and retrospective memory task performance. Prospective memory performance has also been shown to be related to prefrontal executive systems involved in EF (Martin, Kliegel, & McDaniel, 2003), therefore the relationships between the CR capacity components and the PRMQ subscales are of interest. It must be acknowledged however that the use of a subjective measure of prospective and retrospective memory as opposed to objective measures of these types of memory may have its limitations. For instance, Uttl and Kibreab (2011) assert that correlations between self-report and objective measures of memory are generally weak, calling into question the validity of self-report measures. However, for some of the self-report measures used in this study, such as EF as discussed above, and subjective memory complaints, which were also expanded for the purposes of this study and are discussed in detail below, objective measures were also utilised.

7.1.2 Profiling in Subjective Memory: Relationships with CR Capacity and Global Cognition/Memory Measures

Research suggests that subjective memory complaints play a role in decline outcomes. A meta-analysis by Mitchell et al. (2014) found that older adults with subjective memory complaints, but no objective memory problems, are twice as likely to develop dementia than those without subjective memory concerns. Imaging studies have also found an association between subjective memory complaints and grey matter atrophy in older adults (Peter et al., 2014). Further links have been drawn between subjective memory complaints and objective measures of cognitive performance. For instance, Steinberg et al. (2013) found that healthy older adults with low ratings of their memory demonstrated poorer performance in EF and delayed recall tasks compared to those with higher self-rated memory. Subjective memory complaints have also been associated with traditional CR proxies. Chen et al. (2014) found that lower levels of education were correlated with subjective memory impairment in otherwise healthy young, middle-aged, and older adults. The relationship between CR and cognitive performance has also been investigated in older adults with subjective memory concerns and it was found that a CR construct comprising education level and lifestyle factors was positively predictive of cognitive performance (Lojo-Seoane et al., 2014). Additonally, traditional CR indicators such as education level have been put forward as an explanation for the discrepancy between subjective memory concerns and objective cognitive performance, in that individuals with higher education levels can functionf or longer before objective cognitive deficits emerge (Steinberg et al., 2013). Given the links in the literature between subjective memory complaints and traditional CR proxies, it is of interest to see whether a traditional questionnaire measure of CR, the Cognitive Reserve Index Questionnaire (CRIq) (Nucci, Mapelli, & Mondini, 2012) varies as a function of memory complaints. This questionnaire is comprised of subscales measuring education, occupation and leisure activities across the adult lifespan. Also, while both MAAS and TILDA CR capacity SEMs showed significant predictive relationships between CR capacity and subjective ratings of memory at baseline, this finding was not consistent across age-groups. In fact, CR capacity was predictive of subjective ratings of memory at six-year follow-up in MAAS for the older age group, but this finding was not validated in the TILDA model at two-year follow-up. It may be the case that different trends observed in MAAS and TILDA models were due to the subjective memory measures employed in each study. As a binary measure of subjective memory was used in MAAS and a five-point Likert scale measure of memory was used in TILDA, neither measure addressed specific types of memory complaints. For instance, Alagoa et al. (2016) have shown that while no relationship was found between level of education and total score on a measure of subjective memory in healthy older adults, relationships were evident with regard to specific memory complaints, such as using notes to avoid forgetting (positive relationship) and complaints of transient confusion (negative relationship). For this reason, subjective memory was assessed in this study using the *Memory Functioning Questionnaire* (MFQ) (Gilewski, Zelinski, & Schaie, 1990). This questionnaire has four factor-derived scales: Frequency of Forgetting, Seriousness of Forgetting, Retrospective Functioning, and Mnemonics Usage. Profiling subjective ratings of memory using the MFQ in this small sample of healthy older adults could help to clarify its relationship with CR capacity as modelled in MAAS and TILDA.

The aim of the present study was to investigate whether the CR capacity relationships modelled in MAAS and TILDA hold in a small sample of Irish healthy adults aged 50 years and over. Specific research questions addressed the following:

1. Are composites[1] of EF/PR and CCE positively correlated?
2. Do EF/PR and CCE composites predict global cognition/memory outcomes?

Additionally, the study profiled hypothesised CR capacity relationships that were beyond the scope of the MAAS and TILDA datasets. Specifically, the study sought to answer the following questions:

3. Are there significant differences in CR capacity in those who profiled as low vs. high memory concerns?

[1] Composites are proxies for the latent constructs of EF/PR and CCE modelled in Section I

7.2 Method

7.2.1 Participants

A total of 37 participants were recruited to take part in targeted EF training intervention study. A convenience sample of healthy older adults were recruited nationally through targeted advertising with various organisations for older adults such as Active Retirement groups, Age Action Ireland, and older adult education programmes (see Appendices G to J for recruitment advertisement, information sheet, consent form, and debrief form). All participants were required to be fluent English speakers, able to read and use/access a computer with internet access. Exclusion criteria included a diagnosis of Dementia, Parkinson's disease, a neurological condition known to impact cognition, a significant psychiatric illness, a depression diagnosis, a learning disability, and/or significant hearing or visual impairment. Participants also completed the Mini Mental State Exam (MMSE) (Folstein et al., 1975) to ensure they did not suffer from cognitive impairment. An MMSE cut-off less than or equal to 24 was considered to be indicative of a significant cognitive impairment, therefore one participant with an MMSE score of 23 was excluded from analysis. The remaining participants had MMSE scores of 25 or greater. Mood was also assessed pre-intervention using the Profile of Mood States (POMS) (McNair, Lorr, & Droppleman, 1971) and was indicative of stable mood profiles across participants. A total of 36 participants (male: 13, female: 23) aged between 51 and 84 years (M=65.42, SD=8.01) were included in the data analysis. Prior to the brain training intervention, all participants completed two-hours of on-site profiling where a battery of neuropsychological tests were administered.

7.2.2 Measures of CR Capacity

The measures of CR capacity selected for this study are in keeping with the CR capacity measures modelled in MAAS and TILDA datasets.

CCE

Level of education was determined by asking participants to indicate their highest level of education completed. The levels of education were defined as follows: 1 (*some primary – not complete*), 2 (*primary or equivalent*), 3 (*intermediate/junior/group certificate or equivalent*), 4 (*leaving certificate or equivalent*), 5 (*diploma/certificate*), 6 (*primary degree*) and 7 (*postgraduate/higher degree*).

Level of Occupation was based on a nine-point scale that estimates the highest level of professional activity. This classification was derived from the ISCO-08 (Ganzeboom, 2010) categories developed for inclusion in an adapted version of the Cognitive Reserve Index Questionnaire (Nucci et al., 2012) developed for the In-MINDD profiler (see below for details on the CRIq-Adapted). Level of occupation was defined as follows: 1 (*Elementary Occupations*), 2 (*Plant and Machine Operators and Assemblers*), 3 (*Craft and Related Trades Workers*), 4 (*Skilled Agricultural*), 5 (*Service and Sales Workers*), 6 (*Clerical Support Workers*), 7 (*Technicians and Associate Professionals*), 8 (*Professionals*), and 9 (*Managers*).

The *Wechsler Adult Intelligence Scale – Version IV* (WAIS-IV) is a frequently used test of general intelligence (Wechsler, Coalson, & Raiford, 2008). The vocabulary subtest of the WAIS-IV (WAIS-Vocabulary) required participants to define a series of 26 words, with a maximum score of 52 and was used as a measure of crystallised IQ.

EF/PR

The *Primed Stroop Task* (pStroop) (Delany, 2015b)was used as a measure of response inhibition. The pStroop is a novel variant of the traditional Stroop task (Stroop, 1935) designed to test the effects of parametrically varying (priming) the cognitive control demands on performance. Each incongruent trial is preceded by a cognitive load level of 0, 1, 4, or 9 congruent trials. The pStroop plays the same as the standard Stroop task in that the user is presented with a series of trials, each of which consists of a single colour word (e.g., "RED") printed onscreen in a particular font colour (e.g., green). The participant is instructed to identify the font colour by pressing the relevant key on the keypad. Once the user responds their reaction time and accuracy are recorded and after a brief delay the next trial begins. It is predicted that the higher the prior load the more difficult the incongruent trial will be to respond to efficiently. As such, the average time taken to complete incongruent trials with a prior load of nine minus the average time taken to complete congruent trials was used as a measure of response inhibition.

The *Fluency* test measures strategy-driven retrieval of information from semantic memory (Lezak et al., 2004). Participants were asked to produce as many animal names as possible in one minute. The number of correct responses was used as a measure of verbal fluency.

Three of the cognitive tasks were run using open source software, the Psychology Experiment Building Language (PEBL) (Mueller & Piper, 2014). The PEBL version of the *Letter-Digit Task* (LDT) is derived from the pen and paper version in the Wechsler Adult Intelligence Scale (Wechsler, 1958). The task is designed to assess associative learning ability and perceptual speed. A row of nine letters and a row of nine digits are arranged on the computer screen so that the digit row is directly underneath the letter row. Each digit corresponds to a given letter. A test letter is then presented beneath the two coding strings. The participant is asked to identify which digit corresponds to that test letter by pressing that key on a numbered keypad. The letter-digit associative pairings remain the same for the entire test. Mean and median response times over three blocks of nine trials each were recorded as well as total number of corrects. Raw gain scores were defined as the difference between best performance (lowest mean RT) and performance at baseline (mean RT for Block 1) and were calculated as follows: Mean RT for Block 1 minus Best Mean RT (best performance out of Blocks 2 and 3). Relativised gain was calculated by compensating for baseline scores in order to alleviate ceiling effects in improvement. The raw gain score was first divided by the maximum gain score of the respective population and was then multiplied by the quotient of the baseline and maximum gain scores (Zihl et al., 2014). A value of zero represents the baseline value, then increases (positive values) or decreases (negative values) with improvement or deterioration in performance gains. Letter Digit relativised gain was used as a measure of processing speed.

Cognitive Switching was measured using the PEBL *Trail Making Task* (TMT). The TMT requires participants to connect as quickly as possible a 26-item sequence of numbers in ascending order (Trail A), a 26-item sequence of letters in alphabetical order (Trail B), and a 26-item sequence of numbers and letters in alternating order (Trail C). A measure of cognitive switching was calculated by subtracting the average time in seconds needed to complete Trail A and Trail B from the time need to complete Trail C.

Immediate working memory was measured using PEBL's *Free Recall Task*. Over three consecutive trials a list of 30 words drawn at random from the Toronto Word Pool were presented on screen (Friendly, Franklin, Hoffman, & Rubin, 1982). Immediately after each trial participants were asked to recall these words by typing them into a blank box on the screen. The total number of correctly recalled words after the three trials was used as a measure of immediate working memory.

7.2.3 Measures of Global Cognition/Memory

The *Mini Mental State Examination* (MMSE) is an internationally accepted dementia screening instrument (Folstein et al., 1975). Total score on the MMSE was used as a measure of global cognitive performance.

Delayed recall was measured using PEBL's *Free Recall Task*. Twenty minutes after presentation and immediate recall, participants were asked to again recall these words. This test of delayed recall was used as a measure of long term memory.

Subjective memory was assessed using the *Memory Functioning Questionnaire* (MFQ) (Gilewski et al., 1990). The 64-items on the questionnaire are rated on seven-point Likert scales and represent four factor-derived scales: Frequency of Forgetting, Seriousness of Forgetting, Retrospective Functioning, and Mnemonics Usage. For ease of comparison across factors, mean ratings can be calculated by summing scores within factors and dividing them by the number of items in each factor to produce four unit-weight factor scores (Lane & Zelinski, 2003).

7.2.4 Profiling Measures

Subjective Memory

Subjective memory was assessed using the *Memory Functioning Questionnaire* (MFQ) (Gilewski et al., 1990). Mean scores on the four factor-derived scales (Frequency of Forgetting, Seriousness of Forgetting, Retrospective Functioning, and Mnemonics Usage) were summed to produce a total score on subjective memory performance. Lower ratings indicate more negative self-reports.

7.2.5 Measures Additional to CR Capacity Model Parameters

Additional CCE

Current Social Activity was measured by summing the number of hours in the previous week a person was engaged in social activities in the context of a club, society or association, and the number of hours in the previous week spent engaging with friends or relatives (Meijer, van Boxtel, van Gerven, van Hooren, & Jolles, 2009).

Current Mental Activity was measured by summing the number of hours in the previous week spent engaging in mental activities such as reading, mental exercise, hobbies or learning new things.

A measure of traditional cognitive reserve was attained using an adapted version of the *Cognitive Reserve Index Questionnaire* (CRIq-Adapted). The adapted version was developed for self-administration as part of the In-MINDD project and is based on a validated CR questionnaire (Nucci et al., 2012). The questionnaire is a compound measure of formal and non-formal education, occupational activity and frequency of participation in leisure time activities over an individual's adult life i.e., since the age of 18. The education section of the CRIq was updated by replacing "Vocational Training" with "Years of Non-Formal Education". The adapted version also contains an alternative classification of occupation derived from ISCO-08 categories (Ganzeboom, 2010) in order to provide an updated scale that is generalizable across countries (see Appendix K for an comparison of the original CRIq occupation categories and the ISCO-08 categories). CRIq scores were calculated by combining the weighted scores for each subscale in a composite score.

Additional EF/PR

Subjective views of EF were captured using the *Behaviour Rating Inventory of Executive Function-Adult Version* (BRIEF-A) (Roth, Isquith, & Gioia, 2005). The BRIEF-A comprises 75 items that can be summarised into nine subscales: Inhibit, Shift, Emotional Control, Self-Monitor, Initiate, Working Memory, Plan/Organise, Task Monitor, and Organisation of Materials. Scores on these scales were used to calculate two broader indices – the Behavioural Regulation Index (BRI) and the Metacognition Index (MI). The sum of these indices form an overall summary score, the Global Executive Composite (GEC), which was used as a measure of subjective EF.

Global Cognition/Memory

Prospective and Retrospective Memory were measured using the *Prospective and Retrospective Memory Questionnaire* (PRMQ) (G. Smith, Del Sala, Logie, & Maylor, 2000). The questionnaire provides a self-report measure of prospective and retrospective memory in everyday life. It consists of sixteen items, eight asking about prospective memory failures, and eight concerning retrospective failures.

Table 39. Measures of CR Capacity and Global Cognition/Memory

CR Capacity Model	**Measure**	**Description**
EF/PR		
Response Inhibition	Primed Stroop Task (pStroop)	The mean RT (ms) difference between the incongruent (trials with a prior load of nine) and congruent conditions
Processing Speed	*PEBL* Letter-Digit Task (LDT)	Relativised Gain=$(X_{raw}/X_{max})*(X_{base}/X_{max})$
Cognitive Switching	*PEBL* Trail Making Task (TMT)	Cognitive Switching=Trail C – (A + B)/2)
Fluency	Verbal Fluency Test – animals (Fludier)	Number of correct animal names listed within one minute
Immediate Working Memory	*PEBL* Free Recall Task	Total reproduction on learning trials 1-3 (max score 30)
CCE		
Education	Level of Education	Seven-point scale of formal education
Occupation	Level of Occupation	Seven-point scale that estimates highest level of professional activity
Crystallised IQ	Wechsler Adult Intelligence Scale – Version IV: Vocabulary Subtest	Series of 26 words to be defined. Total score (max 52)
Global Cognition/Memory	**Measure**	**Description**
Global Cognition	Mini Mental State Examination (MMSE)	Total score (max 30)
Delayed Recall	*PEBL* Free Recall Task	Total reproduction after 20 minutes on learning trials 1-3 (max score 30)
Subjective Memory	Memory Functioning Questionnaire (MFQ)	Mean ratings on four factor-derived scales: Frequency of Forgetting, Seriousness of Forgetting, Retrospective Functioning, and Mnemonics Usage
Profiling Measures	**Measure**	**Description**
Subjective Memory	Memory Functioning Questionnaire (MFQ)	Sum of mean scores on the four factor-derived scales: Frequency of Forgetting, Seriousness of Forgetting, Retrospective Functioning, and Mnemonics Usage
Additional Measures	**Measures**	**Description**
Social Activity	Current Social Activity	No. of hours in past seven days spent engaging with (a) a club or society; (b) friends or relatives
Mental Activity	Current Mental Activity	No. of hours in past seven days spent engaging in (a) reading; (b) mental exercise; (c) hobbies; (d) learning new things
Subjective CR	CRIq-Adapted	Total score=average of the standardised subscores: Education, Occupational Activity, Frequency of participation in leisure activities
Subjective EF	Behaviour Rating Inventory of Executive Function-Adult Version (BRIEF-A)	Global Executive Composite (GEC)=Sum of BRI and MI
Prospective Memory	Prospective and Retrospective Memory Questionnaire (PRMQ)	Sum of items 1, 3, 5, 7, 10, 12, 14, 16
Retrospective Memory	Prospective and Retrospective Memory Questionnaire (PRMQ)	Sum of items 2, 4, 6, 8, 9, 11, 13, 15

7.3 Analysis

7.3.1 Data Screening and Composite Measures

Prior to creating the pStroop interference variable, reaction times from trials with incorrect responses were excluded. Correct reaction times that were faster than 200ms or slower than 4000ms were also excluded (screening procedure based on Balota et al.'s (2010) investigation of Stroop performance in healthy older adults). This screening procedure eliminated 1.86% of correct responses. One extreme outlier (>3SD beyond the mean) was removed for the pre-test Letter Digit Relativised Gain variable. An EF/PR composite variable was created by summing standardised scores for pStroop interference, cognitive switching, processing speed, fluency and immediate recall. Scores for pStroop interference, cognitive switching and processing speed were reverse coded to be commensurate with all other cognitive tasks (i.e., higher score = better performance). A CCE composite variable was created by summing standardised scores for education level, occupation level and crystallised IQ.

The distributions of education level, occupation level, trail making task, current social activity, mental activity, MMSE scores, delayed recall and the retrospective functioning subscale of the MFQ were skewed and required transformations to achieve normality. Log transformations (Log 10 for positive skew) were successfully performed on the trail making task, current social activity, delayed recall and MFQ-retrospective functioning measures. Following transformation these measures satisfied the Shapiro Wilk test for normality (p>.05). However, the log transformation was unsuccessful for the mental activity variable as following transformation it did not satisfy the Shapiro Wilk test for normality (p<.05). A reverse score log transformation was initially performed on the MMSE variable (reverse score Log 10 for negative skew), however following transformation this variable did not satisfy the Shapiro Wilk test for normality (p<.05). Therefore, the raw variables were used for mental activity and MMSE scores and non-parametric analysis was necessary with regard to these variables.

7.3.2 Statistical Analysis

Firstly, predictions based on the CR capacity model parameters were investigated using pre-intervention data. Pearson Product Moment correlations were conducted to investigate the relationships between EF/PR, CCE and global cognition/memory (Spearman's Rho correlations were substituted for non-parametric measures). A series of hierarchical multiple regression analyses were conducted to investigate how well EF/PR and CCE scores predicted global cognition/memory. Secondly, participants were profiled based on subjective ratings of memory in relation to CR capacity model parameters and global cognition/memory. Independent *t*-tests were used to compare groups with low vs. high memory concerns on CR capacity and global cognition/memory outcomes (Mann-Whitney tests were conducted for non-parametric measures). All analyses were conducted using SPSS version 21 (IBM Corp, 2012). A Bonferroni correction was imposed to correct for multiple comparisons and control for false positives. Although an arbitrary alpha level of .01 may be common in the field, a familywise correction was imposed and the alpha level was reduced to .006 (.05/9) based on nine key tests of a priori predictions in the pre-post intervention study. Specifically, with regard to pre-intervention data, these key predictions concerned (1) the relationship between EF/PR and CCE, (2) the predictive relationship between EF/PR and CCE and MMSE scores, (3) the predictive relationship between EF/PR and CCE and delayed recall scores, (4) differences in EF/PR as a function of subjective memory concerns, and (5) differences in CCE as a function of subjective memory concerns, With regard to post-intervention data, these key predictions (which will be discussed in detail in Chapter 7) concerned (1) immediate training gains on the trained task, (2) near transfer effects to a measure of response inhibition, (3) near transfer effects to a measure of cognitive switching, and (4) near transfer effects to a measure of processing speed. Although other relationships were also investigated, they were not predicted a priori and therefore were not taken into account when conducting the Bonferroni correction. To reduce the risk of false negatives, any test with a significance value less than .05 is discussed in terms of trends in the data, particularly if the finding has a basis in previous literature, which may suggest a false negative.

7.4 Results

7.4.1 Descriptive Statistics

Table 40 summarises the demographic and cognitive measures for participants at pre-intervention. Participants (*n*=36) were aged between 51 and 84 years. The mean age of participants was 65.42 years. 13 of the participants were male and 23 were female. The mean education level was ‘certificate/diploma’. The mean occupation level was ‘professionals’. Inspection of the table indicates that, as expected, delayed recall scores were negatively correlated with age ($p<.006$, two-tailed), such that as age increased, scores on this measure decreased. EF/PR, immediate working memory, MMSE score, MFQ-Frequency of Forgetting and MFQ-Retrospective Functioning all displayed trends toward negative correlations with age, such that as age increased, scores on these tasks decreased, although these correlations were not significant at the .006 alpha level. Scores on the CRIq-Adapted positively correlated with age such that as age increased, scores on this task increased, although again, this was not significant at the .006 alpha level. As the CRIq-Adapted measured CR as an accumulation of lifetime experience, a positive correlation with age was expected. Correlations were not significant for the remaining variables ($p>.05$, two-tailed).

Table 40. Descriptive statistics of demographic and neuropsychological measures and their correlations with age

	N	Mean	Range	*SD*	Age *r*
Age (years)	36	65.42	51.00-84.00	8.01	-
EF/PR					
EF/PR Composite	35	0.00	-5.40-6.48	2.54	-0.38*
pStroop	36	299.87	-45.61-914.47	216.83	0.14
Fluency (animals)	36	19.75	10.00-35.00	5.54	-0.29
Free Recall Task	36	12.25	7.00-24.00	3.94	-0.37*
Trail Making Task (seconds) (raw)	36	73.01	10.09-327.80	61.67	-
Trail Making Task (seconds) (LOG)	36	4.76	4.00-5.52	0.30	0.24
Letter Digit Task - Relativised Gains	35	0.59	-1.03-2.10	0.58	0.08
CCE					
CCE Composite	36	0.00	-6.16-3.97	2.14	-0.05
Education Level	36	5.28	2.00-7.00	1.30	-0.22
Occupation Level	36	8.00	6.00-9.00	1.01	0.17
WAIS-Vocabulary	36	35.56	11.00-51.00	9.31	-0.11
Global Cognition/Memory					
MMSE	36	28.67	25.00-30.00	1.24	-0.39*
Delayed Recall (raw)	36	4.42	0.00-13.00	3.06	-
Delayed Recall (LOG)	36	0.66	0.00-1.15	0.27	-0.60**
MFQ-Frequency of Forgetting	34	4.95	3.33-6.73	0.78	-0.36*
MFQ-Seriousness of Forgetting	35	4.58	1.06-6.89	1.35	-0.24
MFQ-Retrospective Functioning (raw)	36	3.23	1.60-6.60	1.26	-
MFQ-Retrospective Functioning (LOG)	36	0.48	0.20-0.82	0.16	-0.39*
MFQ-Mnemonics usage	36	3.29	1.13-5.63	1.25	0.23
Profiling Measures					
MFQ-Total Score	34	16.06	9.72-23.29	2.98	-0.25
Additional Measures					
Current Social Networks (raw)	36	15.39	3.00-91.00	15.26	-
Current Social Networks (LOG)	36	1.07	0.48-1.96	0.30	-0.02
Current Mental Activity	36	18.53	2.00-48.00	10.31	0.29
CRIq-Adapted	36	148.00	117.00-193.00	18.55	0.43*
BRIEF-A	36	107.19	72.00-162.00	21.22	0.15
PRMQ-Prospective Memory	36	18.92	11.00-28.00	3.51	0.04
PRMQ-Retrospective Memory	36	16.94	9.00-24.00	4.18	0.18

Note. * p<.05, two-tailed; ** p<.006, two-tailed. Age *r*=Pearson Product Moment Correlations with age; Spearman's Rho correlations with age were reported for Education Level, Occupation Level, MMSE and Current Mental Activity due to non-normality of data. Scores for Delayed Recall, PTRAILS, MFQ-Retrospective Functioning and Current Social Networks were log transformed. High scores represent better performance for all measures except pStroop, TMT, BRIEF-A, PRMQ and POMS.

7.4.2 Predictions Based on Model Parameters

Correlations

Table 41 summarises the correlations between the CR capacity factors, global cognition and memory for all participants pre-intervention. Log transformations (Log 10 for positive skew) were performed on delayed recall and MFQ-Retrospective Functioning variables and following this they satisfied the Shapiro-Wilk test of normality. MMSE scores still violated normality assumptions following transformation therefore non-parametric Spearman Rho correlations were performed in relation to this variable. Results showed a moderate correlation between CR capacity factors EF/PR and CCE, although this finding was not significant at the Bonferroni corrected alpha level of .006. There was a significant large positive correlation between EF/PR and scores on delayed recall (p<.006, two-tailed). Results showed moderate correlations between EF/PR and scores on MMSE and subjective reports of retrospective memory (MFQ3), however these correlations are not significant at the corrected alpha level of .006. CCE was not significantly correlated with any of the measures of global cognition and memory.

Table 41. Correlations between CR capacity factors, global cognition and memory

	EF/PR	**CCE**
CCE	.34*	-
MMSE	.41*	.32
DR	.59**	.00
MFQ1	.32	.19
MFQ2	.14	.16
MFQ3	.40*	-.10
MFQ4	-.12	-.15

Note. Pearson Product Moment Correlations; Spearman's Rho correlation is reported for MMSE due to non-normality of data; *p<.05 two-tailed, **p<.006 two-tailed. EF/PR=Executive Function/Processing Resources; CCE=Cumulative Cognitive Enrichment; MMSE=Mini Mental State Exam; DR=Delayed Recall (log transformed); MFQ1=MFQ Frequency of Forgetting; MFQ2=MFQ Seriousness of Forgetting; MFQ3=MFQ Retrospective Functioning (Log transformed); MFQ4= MFQ Mnemonics Usage. For all measures, high scores represent better performance.

Hierarchical Multiple Regression

A series of hierarchical multiple regression analyses were conducted to investigate how well EF/PR and CCE scores predicted global cognition and memory and results are summarised in *Table 42*. Log transformed (Log 10 for positive skew) delayed recall and MFQ-Retrospective Functioning variables were used in analyses. MMSE scores still violated the Shapiro-Wilk test of normality following transformation. However, for all variables, examination of scatterplots, histograms and P-P plots indicated heteroscedasticity and normality of residuals. For all variables, Cooks distance was less than one, indicating that outliers were not influencing the model (Tabachnick and Fidell, 2011). Durbin Watson values between one and three showed that the residuals in all models were independent. Tolerance statistics greater than .1 and VIF statistics less than four indicated that there was no problem with multicollinearity in the data.

The CR capacity model developed and validated in Section I suggested that EF/PR is a stronger predictor of global cognition/memory outcomes than CCE due to its consistently strong positive weighting on the CR capacity construct. Consequently, EF/PR was entered into the model at Step 1. EF/PR explained 22% of the variance in MMSE scores {$F(1,34)=10.73$, $p<.01$} and 32% of the variance in scores on delayed recall {$F(1,34)=17.14$, $p<.01$}. 14% of scores on MFQ-Retrospective Functioning {$F(1,34)=6.41$, $p<.05$} were explained by EF/PR, however this prediction was not significant at the .006 alpha level ($p<.05$). CCE was entered at Step 2 following the predictions of the CR Capacity model that this variable would account for the next largest degree of variance explained. CCE did not significantly contribute to the model for any of the global cognition/memory variables.

Table 42. Estimates of the effects of EF/PR and CCE on global cognition and memory

Variable	***B***	***SE B***	***β***	***Adjusted R^2***	***ΔR^2***	***ΔF***
DV: MMSE Score						
Step 1				0.22	.25	10.81**
Constant	28.67	0.18				
EF/PR	0.24	.07	.50**			
Step 2				0.23	0.03	1.12
Constant	28.67	0.19				
EF/PR	0.22	0.08	.44*			
CCE	0.10	0.09	.17			
DV: Delayed Recall						
Step 1				0.32	0.34	17.22**
Constant	0.66	0.04				
EF/PR	0.06	0.02	.59**			
Step 2				0.35	0.04	2.30
Constant	0.66	0.04				
EF/PR	0.07	0.02	.66**			
CCE	-0.03	0.02	-.22			
DV: MFQ – Frequency of Forgetting						
Step 1				0.08	0.10	3.59
Constant	4.95	0.13				
EF/PR	0.10	0.05	.32			
Step 2				0.05	0.01	0.23
Constant	4.95	0.13				
EF/PR	0.09	0.06	.29			
CCE	0.03	0.07	.09			

DV: MFQ – Seriousness of Forgetting						
Step 1				-0.01	0.02	0.62
Constant	4.58	0.23				
EF/PR	0.07	0.09	.14			
Step 2				-0.03	0.01	0.46
Constant	4.58	0.24				
EF/PR	0.05	0.10	.09			
CCE	0.08	0.12	.13			
DV: MFQ – Retrospective Functioning						
Step 1				0.14	0.16	6.44*
Constant	0.48	0.03				
EF/PR	0.03	0.01	.40*			
Step 2				0.18	0.06	2.60
Constant	0.48	0.03				
EF/PR	0.03	0.01	.49**			
CCE	-0.02	0.01	-.27			
DV: MFQ – Mnemonics Usage						
Step 1				-0.02	0.01	0.46
Constant	3.29	0.21				
EF/PR	-0.06	0.09	-0.12			
Step 2				-0.03	0.01	0.42
Constant	3.29	.22				
EF/PR	-0.04	0.09	-.08			
CCE	-0.07	0.11	-.12			

Note. *p<.05 two-tailed; **p<.006 two-tailed; Delayed Recall and MFQ-Retrospective Functioning were log transformed (LOG 10 for positive skew).

7.4.3 Predictions Based on Additional Measures

Correlations

Table 43 summarises the correlations between the CR capacity factors and additional measures potentially implicated in CR capacity: current social activity, current mental activity, subjective CR (CRIq-Adapted), and subjective reports of EF (BRIEF-A). Correlations between the CR capacity factors and prospective and retrospective memory for all participants' pre-intervention scores are also summarised. Subjective reports of EF are negatively correlated with both EF/PR and CCE, although these correlations are not significant at the .006 alpha level (p<.05). This is suggestive of a trend whereby as scores on EF/PR and CCE improve, subjective ratings of EF abilities also improve, as low scores on the BRIEF-A represent better performance. Neither EF/PR nor CCE were significantly correlated with measures of current social and mental activity or measures of prospective and retrospective memory.

Table 43. Correlations between CR capacity factors and additional measures

	EF/PR	**CCE**
SA	-.01	-.02
MA	.06	.24
CRIq-Adapted	.07	.51**
BRIEF-A	-.39*	-.35*
PMEM	.06	-.05
RMEM	-.21	-.17

Note. *p<.05 two-tailed, **p<.006 two-tailed; Pearson Product Moment Correlations; Spearman's Rho correlation is reported for MA due to non-normality of data; EF/PR=Executive Function/Processing Resources; CCE=Cumulative Cognitive Enrichment; SA=Current Social Activity (LOG transformed); MA=Current Mental Activity; CRIq-Adapted=Cognitive Reserve Index-Adapted; BRIEF-A= Behaviour Rating Inventory of Executive Function-Adult Version; PMEM=PRMQ Prospective Memory; RMEM=PRMQ Retrospective Memory; For SA, MA, and CRq-Adapted, high scores represent better performance. For the BRIEF-A and PRMQ measures, lower scores represent better performance.

Hierarchical Multiple Regression

Hierarchical multiple regression analyses were conducted to investigate how well EF/PR and CCE scores predicted scores on the additional memory measures of prospective and retrospective memory (PRMQ). Results are summarised in Table 44. For all variables, examination of scatterplots, histograms and P-P plots indicated heteroscedasticity and normality of residuals. For all variables, Cooks distance was less than one indicating that outliers were not influencing the model (Tabachnick and Fidell, 2011). Durbin Watson values between one and three showed that the residuals in all models were independent. Tolerance statistics greater than .1 and VIF statistics less than four indicated that there was no problem with multicollinearity in the data.

EF/PR was entered into the model at Step 1 and CCE was entered at Step 2. Neither EF/PR nor CCE contributed significantly to the model for either of the prospective and retrospective memory outcome.

Table 44. Estimates of the effects of EF/PR and CCE on Prospective and Retrospective Memory

Variable	***B***	***SE B***	***β***	***Adjusted R^2***	***ΔR^2***	***ΔF***
DV: PRMQ - Prospective Memory						
Step 1				-0.03	0.00	0.10
Constant	18.92	0.60				
EF/PR	0.08	24	.06			
Step 2				-0.05	0.01	0.17
Constant	18.92	0.61				
EF/PR	0.11	0.26	.08			
CCE	-0.13	0.31	-.08			
DV: PRMQ - Retrospective Memory						
Step 1				0.01	0.04	1.46
Constant	16.94	0.70				
EF/PR	-0.34	0.28	-.21			
Step 2				-0.01	0.01	0.41
Constant	16.94	0.71				
EF/PR	-0.27	0.30	-.17			
CCE	-0.23	0.36	-.12			

7.4.4 Profiling a Subjective Measure of Memory Based on Model Parameters

Participants were profiled based on scores on subjective memory to investigate if scores on CR capacity measures and global cognition/memory outcomes based on model parameters differed as a function of these measures.

Correlations between CR Capacity and a subjective measure of memory

Table 45 summarises the correlations between the CR capacity factors and the profiling measure of subjective memory (MFQ-Total Score). Neither CCE nor EF/PR were correlated with MFQ-Total Score.

Table 45. Correlations between CR capacity factors and profiling measures

	EF/PR	**CCE**
MFQ-Total Score	0.24	-0.04

Note. Pearson Product Moment Correlations; Spearman's Rho correlation is reported for MA due to non-normality of data; EF/PR=Executive Function/Processing Resources; CCE=Cumulative Cognitive Enrichment

CR Capacity and Subjective Memory Concerns

Table 46 summarises the baseline CR Capacity and global cognition/memory measures for participants with low and high memory concerns. Groups were determined by performing a median split on the MFQ-Total Score variable. Possible scores on this measure ranged from 4 to 28, with lower scores indicating higher memory concerns. Participant scores varied from high to low concern with scores ranging from 9.72 to 23.29. Independent t-tests and a Mann Whitney U test (for the non-normal MMSE variable) revealed a trend towards a difference between groups in scores on EF/PR, however this difference was not significant at the Bonferroni corrected alpha level of .006 (p=.02, two-tailed).

Table 46. Descriptive statistics of CR capacity, global cognition, and memory in participants with low and high memory concerns

	Low Concern Group			High Concern Group				
	N	Mean	*SD*	*N*	Mean	*SD*	*p*-value*	Cohen's *d*
EF/PR	17	0.99	2.32	16	-1.08	2.43	0.02	-0.90
CCE	17	0.22	2.40	17	-0.23	2.01	0.56	-0.21
MMSE	17	28.82	1.29	17	28.41	1.23	0.22	0.34
DR (raw)	17	5.00	2.83	17	3.76	3.38	-	-
DR (LOG)	17	0.73	0.21	17	0.58	0.32	0.10	-0.60

Note. *two-tailed *p*-value. EF/PR=Executive Functioning/Processing Resources; CCE=Cumulative Cognitive Enrichment. DR=Delayed Recall; DR was log transformed. A non-parametric Mann-Whitney test was conducted for MMSE (High Concern *Mdn*=29; Low Concern *Mdn*=29). For all measures, higher scores reflect better performance.

7.4.5 Profiling a Subjective Measure of Memory Based on Additional Measures

Participants were profiled based on scores on subjective memory to investigate if additional measures that were not included in the CR capacity modelling chapters but are potentially related to the CR capacity factors, differed as a function of this measure.

Additional Measures and Subjective Memory Concerns

Table 47 summarises differences in additional pre-intervention measures for participants with low and high memory concerns as measured by the MFQ-Total Score. As per comparisons based on model parameters, groups were determined by performing a median split on the MFQ-Total Score variable. Independent t-tests and a Mann Whitney U test (for the non-normal Current Mental Activity variable) revealed a significant difference between the low and high concern groups in scores on Retrospective Memory (p=.005, one-tailed), with the low concern group performing better. Analyses also revealed a trend toward differences observed between groups in scores on Prospective Memory, with participants appearing to score better in the low concern group. However, the difference was not significant at the Bonferroni corrected alpha level of .006 (p<.05, two-tailed).

Table 47. Descriptive statistics of additional measures in participants with low and high memory concerns

	Low Concern Group			**High Concern Group**				
	N	Mean	*SD*	*N*	Mean	*SD*	*p*-value*	Cohen's *d*
SA (raw)	17	18.47	19.90	17	13.12	9.46	-	-
SA (LOG)	17	1.14	0.32	17	1.03	0.27	0.32	-0.35
MA	17	17.65	10.33	17	17.47	9.24	0.93	-0.02
CRIq-Adapted	17	146.65	20.21	17	147.00	15.00	0.95	0.02
BRIEF-A	17	103.88	24.30	17	111.29	18.86	0.33	0.35
PMEM	17	17.59	3.69	17	20.18	3.11	0.03	0.78
RMEM	17	15.41	4.32	17	18.88	3.41	0.01**	0.92

Note. *two-tailed *p*-value; **one-tailed *p*-value=0.005; SA=Current Social Activity; MA=Current Mental Activity; CRIq-Adapted=Cognitive Reserve Index-Adapted; BRIEF-A= Behaviour Rating Inventory of Executive Function-Adult Version; PMEM=PRMQ Prospective Memory; RMEM=PRMQ Retrospective Memory; SA was log transformed. A non-parametric Mann-Whitney test was conducted for MA (Low Concern *Mdn*=15; High Concern *Mdn*=14). For all measures, high scores represent better performance with the exception of the BRIEF-A and the PRMQ measures where lower scores represent better performance.

7.5 Discussion

Exploring the CR capacity model parameters in a small sample of Irish healthy older adults helped to further validate the relationships modelled in Section I, as well as to clarify the nature of additional relationships that were beyond the scope of the modelling studies. Results of correlational analysis have provided some support for the previously observed relationship between the CR capacity factors of EF/PR and CCE (r=.34, p<.05), however this relationship was not significant at the conservative Bonferroni corrected alpha level of .006 so must be interpreted with caution. Nevertheless, replication of this trend was unlikely a false positive due to the strong evidence for this relationship in Section I.

The predictive relationship between EF/PR and global cognition/memory outcomes was also replicated in this small sample, thus supporting the findings of the SEM analyses in Section I, and previous research on the link between executive dysfunction and age-related memory loss (Buckner, 2004; Clarys, Bugaiska, Tapia, & Baudouin, 2009). EF/PR explained a moderate amount of the variance in both MMSE and delayed recall scores (22% and 32% respectively) which also supports the argument that an intervention aimed at modifying EF/PR may improve global cognition/memory outcomes. Subjective memory was assessed using the *Memory Functioning Questionnaire* (MFQ) (Gilewski et al., 1990) in order to address different types of memory complaints. EF/PR was not predictive of three out of the four MFQ subscales (Frequency of Forgetting, Seriousness of Forgetting, and Mnemonics Usage). However, while EF/PR did not predict subjective reports of retrospective functioning (MFQ-Retrospective Functioning) at the Bonferroni corrected alpha level, there is a trend toward this (p<.05, two-tailed), such that the higher the scores on EF/PR, the greater the likelihood of positive subjective ratings of retrospective memory performance. This finding supports similar trends from the baseline modelling in Section I as well as previous research linking subjective memory complaints with performance on EF tasks (Steinberg et al., 2013). This finding suggests that boosting EF/PR may also have an impact on subjective reports of retrospective memory functioning.

CCE was not a significant predictor of any of the global cognition/memory scores. This result was somewhat unexpected given that representational processes such as high levels of education, occupational complexity, and vocabulary knowledge have been shown to be protective against cognitive decline in previous studies (Valenzuela & Sachdev, 2009). While CCE was not significantly predictive of any of the global cognition/memory scores, it is of note that the beta weights for the CCE regressions on delayed recall and MFQ-Retrospective Functioning were negative, somewhat mirroring the finding of negative CCE weightings on the CR capacity construct in the MAAS and TILDA SEMs. As in the SEM analyses, one possible explanation for this is that cognitively stimulating activities such as education help to develop mental capacity early in life and once these activities end, other cognitive activities may provide mental exercise to further develop and maintain CR capacity (Reed et al., 2011). As the present study was conducted with a sample aged over 50 years, many of the participants were retired (64% of the sample) and therefore mental stimulation due to occupational activity was no longer acting as a substitute for education for these participants. This may explain why CCE was not significantly predictive of outcomes in this sample. Similarly, as suggested in Section I, it may be the case that older adults depend less on innate/acquired CR than younger adults, and instead depend on functional reorganisation consistent with the definition of neural reserve (Y. Stern et al., 2005). This being the case, it would follow that control processes would be a better predictor of global cognition/memory outcomes than representational processes in this age group. Overall, the CR capacity relationships found in this study have been demonstrated both cross-sectionally and longitudinally in two healthy ageing populations (Dutch and Irish) in Section I and continue to hold cross-sectionally for this small sample of healthy Irish adults aged over 50 years.

This study also aimed to delineate the nature of additional relationships that were beyond the scope of the modelling studies. Of particular interest was the relationship between social and mental activity and the CR capacity factors. It was hypothesised that these measures would be related to the CCE component in particular as they can be viewed as potentially contributing to a similar representational system (Craik & Bialystok, 2006). However, it was found that measures of current social and mental activity did not correlate with either the EF/PR or CCE composites. There are a number of potential explanations for this finding. For instance, it may be the case that measures of current social and mental activity are not important contributors to CR capacity as they do not appear to be related to the core components of the CR capacity model. However, it may also be the case that the measures of current social and mental activity are limited in scope as they do not include indices of cumulative social and mental activity across the lifespan. Cumulative measures have traditionally been used as indicators of CR (Nucci et al., 2012) and may be more reflective of the CCE component than measures of current activity. As such, it is possible that cumulative measures would have demonstrated a correlation with the CCE component, however this is subject to future research. Furthermore, the measures of current social and mental activity were self-report and therefore represent subjective views of recent activity levels. These types of self-report measures are subject to limitations such as social desirability bias and can place strong cognitive demands on memory and recall, particularly in older age groups (Sallis & Saelens, 2000). Additionally, the relationship between subjective reports of EF as measured by the BRIEF-A and the CR capacity factors was explored, as poor ratings on this measure have been shown to be related to cognitive complaints and MCI. A trend was evident whereby better ratings of EF on the BRIEF-A were associated with better scores on the EF/PR and CCE composites, however these correlations were not significant at the .006 alpha level (r=-.39, p<.05; r=-.35, p<.05, respectively). While it was hypothesised that subjective EF would be related to control processes, the finding that it is also related to representational processes is further evidence for a possible reciprocal relationship between these two CR factors (Craik & Bialystok, 2006). Finally, memory measures were expanded in this study to include prospective and retrospective memory as measured by the PRMQ. As prospective memory in particular has been linked with prefrontal executive systems (Martin et al., 2003), the predictive relationship between the CR capacity factors and PRMQ measures of prospective and retrospective memory were of interest. No correlation was found between the PRMQ measures and EF/PR and CCE composites, and neither of the CR factors were significantly predictive of PRMQ scores. This may suggest that CR capacity does not influence these types of memory, however this finding must be interpreted with caution due to the subjective nature of the PRMQ measures, as previously discussed in this chapter, and it is possible that more objective measures of prospective and retrospective memory may yield different results. However, this is subject to future research.

Profiling of the CR capacity model measures as a function of low and high scores on a subjective memory scale (MFQ-Total) was conducted in order to investigate if CR capacity (EF/PR and CCE) and measures of global cognition/memory, differed between low and high scoring groups on this measure. The EF/PR and CCE composite scores and measures of global cognition/memory were compared across those with low vs. high memory concerns. Findings revealed a trend towards a difference between groups in scores on the EF/PR composite, with EF/PR scores being better in the low concern group, however this difference was not significant at the Bonferroni corrected alpha level of .006 (p=.02, two-tailed). This finding suggests that memory concerns may be a marker of decline in control processes, which supports previous research linking subjective memory complaints with poorer performance on EF tasks (Steinberg et al., 2013), as well as research linking subjective memory complaints with grey mater atrophy and increased dementia risk (A. J. Mitchell et al., 2014; Peter et al., 2014; van Oijen, de Jong, Hofman, Koudstaal, & Breteler, 2007). Scores on a measure of Retrospective Memory, as measured by the PRMQ, were found to be significantly worse in the high concern group. A trend was also observed whereby scores on a subjective reports of prospective memory, as measured by the PRMQ subscale, were worse for those with high levels of concern about their memory, but this trend was not significant at the .006 alpha level (p<.05, two-tailed). These findings were somewhat expected as the profiling measure (MFQ-Total Score) and the PRMQ subscales both involved subjective interpretation of memory performance. It is likely that scores on the PRMQ-Retrospective Memory measure were significantly different between groups as the measure of subjective memory used to create the groups was mainly comprised of questions assessing aspects of retrospective memory. No differences were found in other global cognition/memory measures, measures of current social and mental activity, subjective EF, and subjective CR, as a function of low/high subjective memory.

Findings from the modelling studies in Section I were mixed with regard to subjective memory. The MAAS SEMs suggest that a CR capacity model driven by EF/PR is predictive of subjective memory outcomes at baseline and at the six-year follow-up in those aged over 65 years, whereas the TILDA SEMs suggest that CR capacity is predictive of subjective memory outcomes at baseline only in both 50-64 year olds and 65-79 year olds. The findings of this study go some way toward supporting a relationship between subjective memory concerns and EF/PR (rather than a latent CR capacity factor as this could not be modelled here) in those aged over 50 years. Studies suggesting a relationship between traditional CR proxies and subjective memory complaints (S. T. Chen et al., 2014; Lojo-Seoane et al., 2014) have not been replicated in this study as neither CCE scores nor scores on the CRIq-Adapted differ as a function of subjective memory complaints. This suggests that groups who are potentially at risk of MCI or dementia based on their subjective memory profile may benefit more from an intervention targeting control processes rather than representational processes.

Overall, EF/PR was a significant predictor of scores on the MMSE and delayed recall scores which supports the findings of the predictive models in Section I. The finding that CCE was not predictive of any of the outcomes supports the idea of a differential relationship between these two constructs and cognitive outcomes. Although this study could not investigate the direct paths between a latent CR capacity construct and the outcome measures, the indirect relationships between the EF/PR factor, the CCE factor and outcomes is supported here. Profiling based on subjective ratings of memory suggests that individuals with memory concerns may be more vulnerable to the effects of age-related cognitive decline. Pre-intervention analyses support the idea that an intervention targeting EF/PR, an important formative component of CR capacity, may indirectly impact on cognitive outcomes.

Chapter 8: Study 6 – Executive Function Training Intervention

8.1 Introduction

Further investigation of the CR capacity model parameters in study 5 has provided some additional support for the correlational relationship between the CR capacity components of EF/PR and CCE as well as providing further evidence for the predictive relationship between EF/PR and global cognition/memory outcomes in healthy adults aged over 50 years. In the MAAS and TILDA SEMs (studies 3 and 4), a latent EF/PR factor had a strong positive weighting on a CR capacity construct, and therefore an indirect positive relationship with cognitive outcomes. Findings from study 5 provided support for a positive relationship between EF/PR and outcomes, as an EF/PR composite was a strong positive predictor of MMSE and delayed recall scores. Additionally, results from study 5 suggest that EF/PR is a moderate predictor of subjective reports of retrospective memory such that the higher the scores on EF/PR, the greater the likelihood of positive subjective ratings of memory performance. Although this finding was not significant at the .006 alpha level ($p<.05$, two-tailed), it reflects the findings of the modelling studies 3 and 4, where the SEM models at baseline (both MAAS and TILDA) and six-year follow-up (MAAS), found that a CR capacity construct, strongly driven by EF/PR, was predictive of subjective ratings of memory. CCE was not significantly predictive of any of the global cognition/memory scores and non-significant negative beta weights were observed in relation to delayed recall and MFQ-Retrospective Functioning. This supports the assertion that control and representational processes are differentially involved in CR capacity, with high EF/PR levels being associated with high activation of the CR capacity system and high CCE levels being associated with low activation of the CR capacity system. Profiling based on subjective ratings of memory provided further support for an emphasis on control processes in CR capacity. Profiling based on subjective ratings of memory revealed a trend towards differences in scores on the EF/PR composite suggesting that memory concerns may be a marker of decline in control processes. As individuals with memory concerns may be more vulnerable to the effects of age-related cognitive decline, this group may benefit from a targeted intervention designed to boost control processes. As it may be the case that EF/PR is increasingly relied upon in older adults to activate the CR capacity system (Bouazzaoui et al., 2014; Dennis & Cabeza, 2008) this lends support to the idea that a targeted intervention aimed at modifying EF/PR could potentially impact on CR capacity.

8.1.1 Modifying Cognitive Control Processes

A review of cognitive training interventions in healthy elderly and MCI found that cognitive training can have beneficial effects on a broad range of cognitive functions, including memory performance, executive functioning, processing speed, attention and fluid intelligence (Reijnders et al., 2013). Maximal benefit can be achieved if training programmes target higher order cognitive control abilities such as EF and working memory (Buitenweg et al., 2012). Broadly defined, cognitive training can be viewed as repeated engagement in a specific programme or task designed to enhance a cognitive skill or ability (Rabipour & Raz, 2012). Any changes as a result of training can be measured at the behavioural, neuronal and functional levels. Various cognitive training paradigms can be used to improve cognitive performance. For instance, strategy training encourages the use of domain-specific strategies, such as rehearsal or resource allocation, that might improve performance on a particular type of cognitive task. This type of training can be viewed as the acquisition of skills that have limited applicability beyond the trained task (Schmiedek, Lövdén, & Lindenberger, 2010). For example, McNamara and Scott (2001) used strategy training in the form of story formation to improve performance on a working memory task. Strategy training is useful in contexts that require retention of information and this type of training is expected to increase performance in tasks very similar to the trained strategy, but not more disparate tasks (Morrison & Chein, 2011). Alternatively, core training paradigms involve repetition of demanding tasks using an adaptive difficulty method to target domain-general mechanisms (Klingberg, Forssberg, & Westerberg, 2002). Core training can be viewed as the improvement of abilities that could potentially improve performance across a wide range of tasks (Schmiedek et al., 2010). Core training studies typically involve high intensity cognitive engagement on process-based cognitive control tasks and require participants to maintain performance in the face of interference. While some core training studies utilise varying stimuli in order to target a number of cognitive components simultaneously, this approach can be problematic when it comes to identifying which particular aspects of the training are driving observed cognitive improvements (Morrison & Chein, 2011). To overcome this problem, a single task approach can be implemented whereby one particular cognitive task is trained and therefore observed cognitive gains can be directly attributed to this task. This approach can help to delineate specific mechanisms that might underlie the training effect. For instance, a study on working memory (WM), the ability to actively control attention and maintain information, trained participants on a specific aspect of the n-back task rather than using several WM tasks such as backward digit span and location memory (Verhaeghen, Cerella, & Basak, 2004). Similarly, as EF can be characterised as a general purpose control mechanism that modulates the cognitive sub-processes of switching, updating and inhibition (Miyake et al., 2000), it is a candidate for core training using a single task approach. This type of training has the potential to increase performance in not only tasks very similar to the trained task, but in a diverse range cognitive tasks. If broad cognitive abilities can be improved through core training this could lead to benefits in everyday intellectual competence, and potentially prolong independent living (Schmiedek et al., 2010).

8.1.2 Efficacy of Control Training

The efficacy of cognitive control training is assessed with regard to transfer. Near transfer effects refer to the generalisation of training effects to cognitive tasks that are similar to those used in training, whereas far transfer effects refer to generalisation to domains more distant from the trained task (Buitenweg et al., 2012). While strategy training paradigms are expected to yield near transfer effects, far transfer effects are not theoretically predicted with this approach (Morrison & Chein, 2011). Core training approaches, however, have previously demonstrated both near and far transfer effects. For example, using a core WM training protocol, Jaeggi et al. (2008) found improved performance in trained participants (young adults) on a measure of general fluid intelligence. Using a similar core WM training protocol, Chein and Morrison (2010) found that trained participants (young adults) improved on measures of cognitive control and reading comprehension, but not general fluid intelligence or reasoning abilities. Smith et al. (2009) used an adaptive speed and accuracy training protocol with healthy older adults and found that the experimental group improved on measures of memory and attention to a larger degree than the active control group.

At the root of cognitive control training interventions is the concept of neuroplasticity, or the brain's ability to modify neural connectivity and adapt to environmental changes (Knaepen, Goekint, Heyman, & Meeusen, 2010). There is evidence to suggest that neuroplasticity may decline with age (Burke & Barnes, 2006) which would call into question the potential benefits of a cognitive control training intervention in elderly participants. Patterns of improvements for young and older adults have varied across studies, and while many have not found significant transfer effects (Colom et al., 2013; Lampit, Hallock, & Valenzuela, 2014; Redick et al., 2013) there has also been research to support the efficacy of cognitive control training in elderly populations. For instance, Karbach and Kray (2009) demonstrated that older adults who were trained on multiple cognitive control mechanisms (switching, interference control and goal maintenance) improved on tasks measuring cognitive switching and interference, but also spatial and verbal working memory and fluid intelligence. Furthermore, both young and older adults trained using an adaptive WM training protocol demonstrated near transfer effects to a more demanding WM task and performance was maintained three months following post-test (Li et al., 2008). Additionally, there has been evidence to suggest that age effects diminish after extensive training on an EF task targeting cognitive switching (Kramer et al., 1999) as well as evidence for more pronounced training gains in older compared with younger adults in dual-task performance (Bherer et al., 2005). In a review of the trainability of healthy older adults, Buitenweg et al. (2012) suggest that in order for training to be successful it must focus on tailoring the training adaptively to the level and progress of the individual. Transfer and maintenance of cognitive intervention effects in healthy older adults are reported more frequently when training is adaptive with at least ten intervention sessions (Kelly et al., 2014). In a review on the efficacy of working memory training, Conway and Getz (2010) raise questions regarding the neural mechanisms that are being trained in order to produce transfer effects. While advocating the use the adaptive and high dose training, they suggest that in order to avoid ambiguity, cognitive training approaches should specifically define a mechanism and adjust measurements and training protocols to target that particular mechanism. In this way, the precise mechanisms underlying transfer effects will be apparent. Furthermore, it has been shown that motivational incentive mechanisms such as feedback on correct and incorrect responses and keeping track of high scores, improved performance on a cognitive control task in both healthy and pathological ageing populations (Harsay, Buitenweg, Wijnen, Guerreiro, & Ridderinkhof, 2010). These findings support the potential efficacy of cognitive control training targeting healthy older participants.

8.1.3 Response Inhibition Training and Cognitive Reserve Capacity

EF is a general-purpose control mechanism that has been shown to modulate various cognitive sub-processes, and is a potential candidate for core cognitive training. EF has been classified, based on latent factor analysis, into three separate but related domains: shifting, updating and inhibition (Miyake et al., 2000). Inhibition refers to the ability to deliberately inhibit automatic or prepotent responses and has been linked to activation of the frontal lobes (Jahanshahi et al., 1998). Miyake et al. (2000) also suggest that EFs like updating and switching involve inhibitory processes, suggesting inhibition may be core to general EF. Previous research has shown that both the Stroop task and the anti-saccade task are sensitive measures of inhibition and frontal lobe dysfunction (Miyake et al., 2000). Prior work on inhibition training suggests it can be improved with short- to medium-term training using a core training approach. For instance, Berkman, Kahn and Merchant (2014) investigated whether response inhibition could be improved with adaptive training on the stop-signal task (SST), and how associated neural systems changed as a result of training. It was found that following three weeks of training, SST performance improved significantly more for the training group than the active control group, while inhibitory improvement correlated with increased activation in the dorsolateral prefrontal cortex. Similar results were found by Chavan et al. (2015) following two weeks of training with an Go/NoGo task as improvements were observed in both the trained task and a 2-back working memory task. EF training studies have noted that successful training protocols involved high dosage and adapted to the level and progress of the individual in order to sustain engagement and challenge (Berkman et al., 2014; Buitenweg et al., 2012). Additionally, it has been hypothesised that patterns of improvements on inhibition-related behavioural tasks may result from improvements in the speed of inhibition processes (Chavan et al., 2015; Hartmann, Sallard, & Spierer, 2015). Given the shared mutual variance between processing speed, inhibition and other EFs, already established in studies 1- 4, and elsewhere (Albinet, Boucard, Bouquet, & Audiffren, 2012; McAuley & White, 2011; Salthouse, 1994), it is expected that targeted inhibition training may improve speed of information processing as well as other closely overlapping constructs. For instance, cognitive switching is also hypothesised to involve inhibition-related functions and has been found to be highly related to response inhibition (Friedman & Miyake, 2004).

These studies support the modifiability of response inhibition through targeted cognitive control training. Furthermore, findings from the modelling studies (studies 1- 4) support the assertion that response inhibition is a good candidate for a targeted training intervention. The CR capacity model is comprised of control processes that include processing speed, response inhibition, cognitive switching, fluency and immediate working memory, each of which load on the EF/PR factor. Given the consistent moderate to strong loading of response inhibition, as measured by the Stroop task (MAAS) and the SART (TILDA), in the CR capacity model and the demonstrated predictive validity of the model with regard to cognitive outcomes at baseline and follow-up at all time points, it follows that an intervention designed to boost response inhibition in older adults may in turn impact on CR capacity. This could potentially have implications for the trajectory of cognitive abilities over time. The EF/PR factor is highly correlated with the CCE factor, a set of representational processes that are accumulated across the lifespan such as education and occupation and crystallised abilities such as vocabulary knowledge, and these remain relatively constant over time (Schottenbauer, Momenan, Kerick, & Hommer, 2007) and are therefore not good candidates for a targeted cognitive training intervention. The modelling studies (studies 3 and 4) also show that CCE does not appear to activate a standard CR capacity system and may represent a non-standard, alternative system that is recruited to maintain cognitive function in the face of pathology. Therefore, an intervention targeting CCE in healthy elderly is unlikely to yield transfer effects.

The current research programme has shown that response inhibition, as measured by Stroop interference (MAAS) and SART errors of commission (TILDA), is an EF that consistently loads highly on the EF/PR factor across multiple analyses (EFA, CFA, and SEM) in two longitudinal datasets – MAAS and TILDA. Moreover, latent has shown in two separate studies (Friedman & Miyake, 2004; Miyake et al., 2000), and more generally with the literature outlined above, that response inhibition is core to EF, is implicated in global cognition and is therefore a candidate for cognitive training on the predicted basis of transfer of training (Conway & Getz, 2010). Therefore, it was predicted that adaptive response inhibition training would result in significant direct effects on the trained task compared to an active control group (Berkman et al., 2014). Indirect effects of adaptive response inhibition training were also hypothesised in relation to constructs similar to the trained task, specifically EF related measures that loaded on the EF/PR factor in the modelling studies (response inhibition, processing speed, and cognitive switching) (Albinet et al., 2012; Chavan et al., 2015). Given the predictive relationship between EF/PR and global cognition/memory outcomes, it is possible that inhibition training may result in far transfer effects to objective and subjective measures of memory such as delayed recall, subjective memory complaints and reports of prospective and retrospective memory performance.

Three primary research questions were investigated with regard to response inhibition training in healthy older adults:

(1) Does adaptive response inhibition training lead to improved performance on the trained task (direct training effects)?

(2) Does adaptive response inhibition training improve performance on tasks highly related to the trained task (near transfer); and

(3) Does adaptive response inhibition training gain transfer to untrained tasks (far transfer)?

8.2 Method

8.2.1 Participants

A total of 37 healthy older adults were recruited for the brain training intervention study. A convenience sample was recruited nationally through targeted advertising with various organisations for older adults such as Active Retirement groups, Age Action Ireland, and older adult education programmes. All participants were fluent English speakers and able to read and use/access a computer with internet access. Exclusion criteria included a diagnosis of Dementia, Parkinson’s disease, a neurological condition known to impact on cognition, a significant psychiatric illness, a depression diagnosis, a learning disability, and/or significant hearing or visual impairment. Participants also completed the Mini Mental State Exam (MMSE) (Folstein et al., 1975) to ensure they were not cognitively impaired. An MMSE cut-off of 24 was considered to be indicative of a significant cognitive impairment, and one participant with an MMSE score of 23 was therefore excluded from analysis. The remaining participants had MMSE scores of 25 or greater. Mood was also assessed at the pre-intervention using the Profile of Mood States (POMS) (McNair et al., 1971) and indicated stable mood profiles across all participants. During the course of the study one participant withdrew participation due to technical difficulties accessing the training exercise, thus a total of 35 participants (male: 12, female: 23) aged between 51 and 79 years (M=64.89, SD=7.46) were included in the data analysis.

8.2.2 Design

The study was a double-blind, two-block (AB) randomisation design that consisted of three parts: (a) a pre-intervention test assessment (study 5), (b) a response inhibition training regime where participants were allocated to one of two treatment conditions: active control or experimental, and (c) a post-intervention test assessment. A member of the research team not involved in recruitment or testing conducted the randomisation to active control and experimental conditions. Participants were required to complete on-site testing on two occasions, for two hours each time: once before and once after five weeks of training. A battery of neuropsychological tests was administered at both pre- and post-test. Task order was counterbalanced at pre-test both within groups and between groups to minimise fatigue effects, and was also counterbalanced at post-test. All tasks except one (CRIq-Adapted – see measures section for details) were administered at both pre- and post-test, and where available, alternative forms of tasks were administered at post-test. Participants were required to play either a low dose (active control) or high dose (experimental) version of the training game for up to 25 minutes a day, five days a week, over a five-week period.

8.2.3 Cognitive Training Programme

The co-design of a response inhibition training programme with Dr David Delany, Waterford Institute of Technology, involved a review of the cognitive training literature in order to establish the key components of effective training tasks. As outlined in the introduction, it was found that successful training paradigms frequently included the following elements: difficulty that adapts to individual performance (Buitenweg et al., 2012), motivational elements in the form of performance feedback (Harsay et al., 2010), and training duration of at least 10 sessions (Kelly et al., 2014). The cognitive training task selected for this intervention incorporated all of the above elements. The Complex Sustained Attention Trainer (CSAT; Delany, 2015a) task is an adaptive variant of the high Go/low No-Go category of the Go/No-Go attentional control paradigm (Donders, 1969). The CSAT uses patterned shapes instead of alphanumeric symbols. Each CSAT item is given by three levels: Shape, Colour, and Pattern Fill. For example, a CSAT No-Go (or No Press) item could be a red square filled with dots. The aim is simply to inhibit pressing to No-Go items, and press to all other Go items, regardless how similar they appear to the No-Go item.

CSAT was designed to boost response inhibition through sustained attention training under progressively increasing working memory load and distractor interference levels. Errors of commission in high Go/low No-Go sustained attention tasks have been shown to be better measures of failures of response inhibition than measures of sustained attention (Carter et al., 2013). For the high dose version of the CSAT, each game lasted approximately 4.5 minutes and participants were required to play five games per training session. Each game comprised of serially presented items that differed in terms of shape type (e.g., square, triangle, etc.), colour (e.g., blue, green, etc.), and pattern fill (e.g., striped, polka-dot, etc.). The sequence of presented items was randomly generated from a set of ten shape types, nine colours and six patterns to give a total of 810 possible objects. Each item was displayed in the centre of the screen for 300ms before being replaced by a '+' symbol mask for 700ms to give an interstimulus interval (ISI) of 1000ms (see *Figure* 29 for schematic diagrams of high and low dose versions of the task). At the beginning of each game the participant was presented with the “no-go” target on which to withhold their response. The “no-go” target comprised a specific combination of shape, colour and pattern (e.g., a blue striped triangle). The same “no-go” target was used across all games within a given training session but was randomly varied across daily sessions. For every “go” object the user was required to press the space bar on the keypad. When a “no-go” object was presented the user was required to withhold pressing. If the user mistakenly responded to a “no-go” item, or failed to respond to a “go” target, feedback, in the form of a flashed red warning circle, was presented. The low dose version of the CSAT follows the same presentation as the high dose game, however each game lasted approximately two minutes and participants were required to play three games per training session. The low dose game also had fewer trials (60) and a longer ISI (1800ms) than the high dose version. Each item was displayed in the centre of the screen for 700ms before being replaced by a '+' symbol mask for 1100ms. Participant feedback in the form of individual scores, a progress bar and indication of correct/incorrect responses was provided during game play in order to increase motivation and engagement with the task (see *Figure 30*).

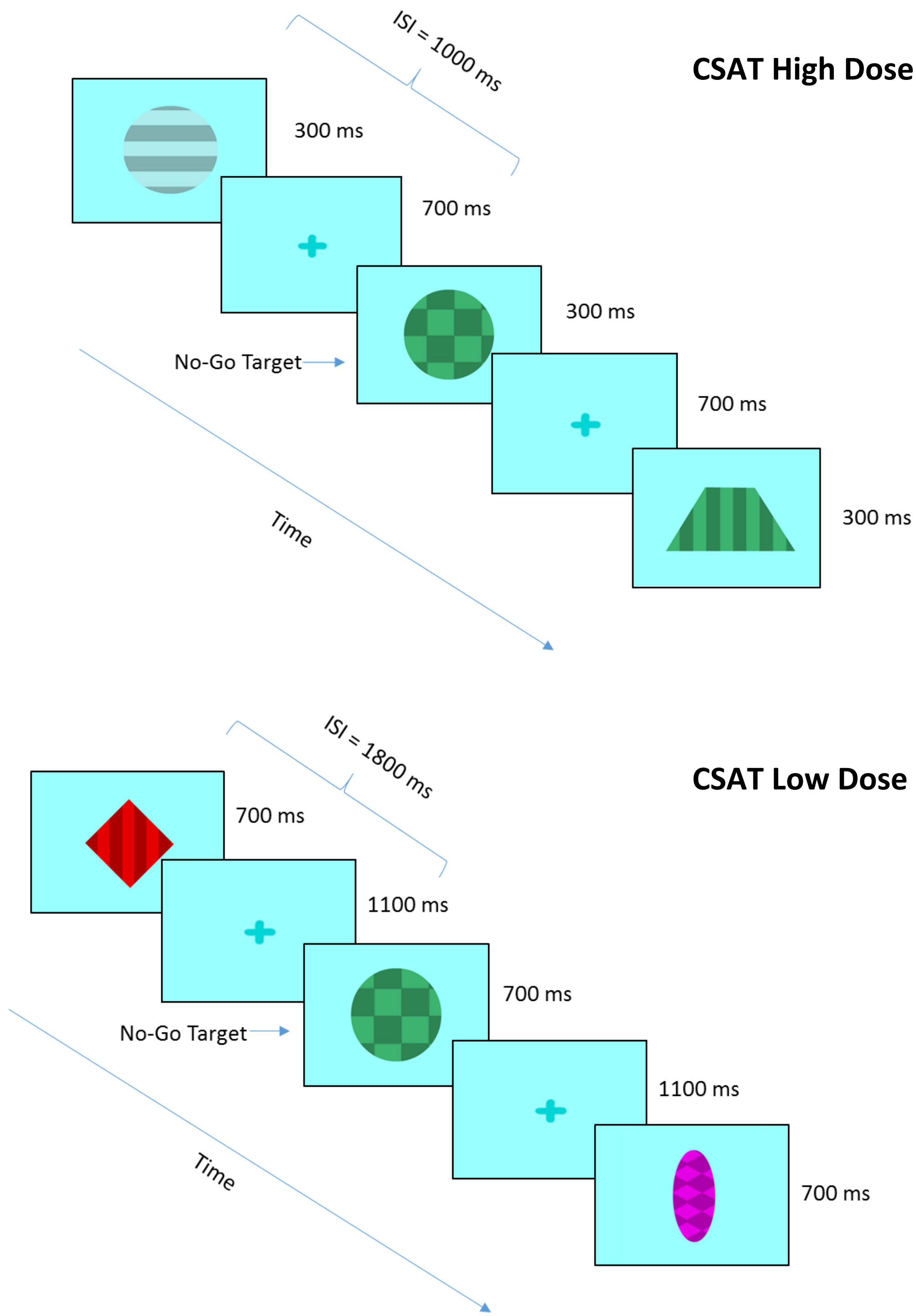
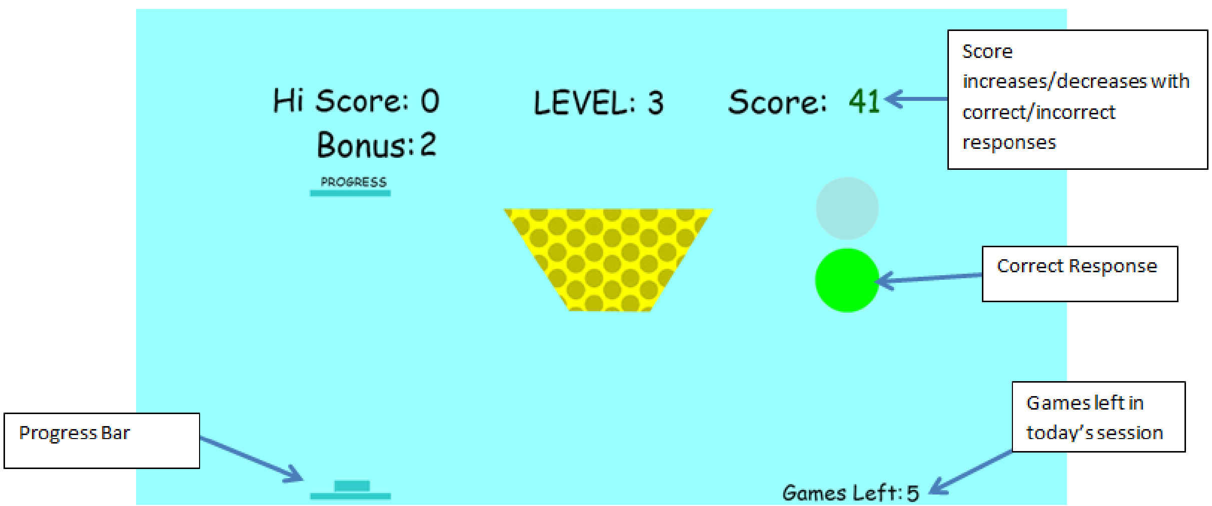


Figure 29. Schematic diagrams of high and low dose versions of the CSAT

Panel A



Panel B

Figure 30. CSAT gameplay screenshots

Note. Panel A is the home screen. Panel B is the gameplay screen.

CSAT Adaptive Training

All objects that were presented during game play were defined by three dimensions. The "go" targets overlapped with the "no-go" targets to varying degrees. For instance, if the "no-go" target was a blue striped triangle, an example of a zero-dimension overlap (0-D) would be a green polka-dot square. Similarly, an example of a one-dimension overlap (1-D) would be a blue polka-dot square and a two-dimension overlap (2-D) would be a blue striped square. These are examples of lures that share 0, 1, and 2 dimensions in common with the no-go target. In total, there were four classes of objects, one "no-go" class and three "go" classes. The probability of encountering each class of stimuli was dynamically varied. Task difficulty was adaptive based on the probability of encountering a "no-go" target (with increased rarity associated with increased difficulty) and the properties of the "go" target (0D-2D). The initial probability was 0.45 for the "no-go" stimulus and zero for 1D and 2D lures. The user progressed within the task by withholding a key-press when presented with a "no-go" object. Each time the participant successfully withheld a response the game automatically became more difficult. For the high dose version of the game, difficulty was manipulated in a systematic fashion by incrementally increasing the probability of a 1D lure by 0.01 to a maximum value of 0.2. When this value was reached the 1D lure probability was reset to zero and the same incremental process was applied to the 2D lure probability. Once the 2D lure probability reached the maximum it was reset to zero, the no-go target probability was reduced by 0.005, and the 1D lure probability was activated again and the cycle repeated. The inverse process applied in the case of an error but with probability decrement values of 0.02 and 0.01 for the lure and no-go probabilities respectively. Training was terminated when the participant completed a game where the target "no-go" probability had reached the minimum value of 0.01. The low dose version of the game had a higher final no-go target probability (0.4).

8.2.4 Measures of CR Capacity

The CCE and EF/PR measures used in this study are the same as those used in the study 5 (pre-intervention profiling). Please see Chapter 7 for a more detailed description of the measures.

Briefly, the CCE measures included level of education, level of occupation, and the vocabulary subtest of the WAIS-IV (WAIS-Vocabulary), which was used as a measure of crystallised IQ.

Briefly, the EF/PR measures used in this study included the following: The *Primed Stroop Task* (pStroop) (Delany, 2015b) was used as a measure of response inhibition. *Fluency* was measured by asking participants to produce as many animal names as possible in one minute. The PEBL version of the *Letter Digit Task* (LDT) was used as a measure of processing speed. Cognitive switching was measured using the PEBL *Trail Making Task* (TMT). Immediate working memory was measured using PEBL's *Free Recall Task*.

8.2.5 Measures of Global Cognition and Memory

The measures of global cognition/memory used in this study are the same as those used in the study 5 (pre-intervention profiling). Please see Chapter 7 for a more detailed description of the measures.

Briefly, the measures included the following: The *Mini Mental State Examination* (MMSE) was used as a measure of global cognitive performance. Delayed recall was measured using PEBL's *Free Recall Task*. Subjective memory was assessed using the *Memory Functioning Questionnaire* (MFQ).

8.2.6 Measures Additional to CR Capacity Model Parameters

The additional measures included in this study were also broadly the same as those used in study 5 (pre-intervention profiling), with the inclusion of a working memory measure under additional EF/PR.

Additional CCE

As change over time is unlikely to be reflected in CCE variables (education level, occupation level, crystallised IQ), measures believed to reflect current cognitive enrichment were included in the study. Briefly, the additional CCE measures were as follows: *Current Social Activity* was measured by summing the number of hours in the previous week a person was engaged in social activities in the context of a club, society or association, and the number of hours in the previous week spent engaging with friends or relatives (Meijer et al., 2009). *Current Mental Activity* was measured by summing the number of hours in the previous week spent engaging in mental activities such as reading, mental exercise, hobbies or learning new things. A measure of traditional cognitive reserve was attained using an adapted version of the *Cognitive Reserve Index Questionnaire* (CRIq-Adapted) (Nucci et al., 2012).

Additional EF/PR

As in study 5, subjective views of EF were captured using the *Behaviour Rating Inventory of Executive Function-Adult Version* (BRIEF-A) (Roth et al., 2005).

The *Digit Span Backwards* subtest of the Wechsler Adult Intelligence Scale (WAIS-DSB) was included as a measure of working memory, a cognitive ability related to control processes. WAIS-DSB involved a series of trials where the examiner read a sequence of numbers aloud and asking the participant to recall the numbers in reverse order. The total number of correct trials was used as a measure of working memory.

Additional Global Cognition/Memory

As in study 5, Prospective and Retrospective Memory were measured using the *Prospective and Retrospective Memory Questionnaire* (PRMQ) (G. Smith et al., 2000).

8.3 Analysis

8.3.1 Data Screening and Composite Measures

PStroop data was screened as per the procedure outlined in Chapter 6 and 1.86% of correct responses were removed. One extreme outlier was removed from the post-test delayed recall variable (>3 SD beyond the mean), the pre-test Letter Digit Relativised Gain variable (>3 SD beyond the mean), and the post-test fluency variable (>2.5 SD beyond the mean). An EF/PR composite variable was created by summing standardised scores for measures of response inhibition, cognitive switching, processing speed, fluency and immediate recall. A CCE composite variable was formed by summing standardised scores for education level, occupation level and crystallised IQ. When computing standardised scores when there are two or more time points it is necessary to use a common mean and standard deviation, as standardising within a time point removes any change in scores over time (Anglim, 2009). As lower scores on measures of response inhibition (pStroop) and cognitive switching (TMT) were indicative of better performance, this was taken into account when compiling the composite scores. The standardised scores for both pStroop and TMT were subtracted from zero (0-z) (Anglim, 2009) in order to reverse the direction prior to summing the EF/PR composite.

8.3.2 Statistical Analysis

Independent *t*-tests were used to compare groups at baseline on all demographic and neuropsychological variables. T-values and degrees of freedom were used to calculate the effect size of group differences, Cohen's *d*. Cohen's *d* was reported as an index of effect size as it shows the standardised difference in baseline scores between the experimental and active control groups. Cohen (1988) defined effect sizes as small (d=.2), medium (d=.5) and large (d=.8). Effect-size analysis was also used to determine the size of the training effect for both the experimental and the active control groups. Size of effect was expressed as the mean standardised difference between pre- and post-test scores and was calculated as follows: the mean of pre-test scores minus the mean of post-test scores, divided by the pooled standard deviation (calculated using the original standard deviations for the two means). Dunlap, Cortina, Vaslow, and Burke (1996) argue that for repeated measures designs the original standard deviations should be used to compute effect size from pre- to post-test, rather than using the paired *t*-test value.

Any differences between the groups were assessed at baseline using independent groups t-tests and Mann Whitney U tests for variables that violated normality assumptions. Direct training effects on the trained task were assessed by conducting 2 (Group: active control, experimental) x 2 (Time: mean level achieved in first two training sessions, mean level achieved in last two training sessions) repeated measures ANOVAs. To assess near transfer to untrained tasks, scores on measures of response inhibition, processing speed and cognitive switching were analysed separately with 2 (Group: active control, experimental) x 2 (Time: pre-intervention, post-intervention) repeated measures ANOVAs. To assess far transfer to untrained tasks, all other tasks were analysed separately with 2 (Group: active control, experimental) x 2 (Time: pre-intervention, post-intervention) repeated measures ANOVAs. As findings from study 5 suggest that subjective memory complaints may be a marker of decline in control processes, controlling for subjective memory scores in the repeated measures ANOVAs was considered. However, as there were no significant relationships between scores on subjective memory and the DVs in this study (*p*s>.05), the subjective memory measure was not suitable for covariate analysis (Tabachnick & Fidell, 2006). All analyses were conducted using SPSS version 21 (IBM Corp, 2012).

8.4 Results

8.4.1 Descriptive Statistics

Table 48 summarises the baseline demographic and cognitive measures for both the active control and experimental groups. Participants (n=35) were aged between 51 and 79 years at baseline. There were 19 participants in the experimental group (male: n=7; female: n=12), and 16 participants in the active control group (male: n=5; female: n=11). The mean education level for both groups was 'certificate/diploma'. The mean occupation level for both age groups was 'professionals'. There were no significant differences between the groups on any of the demographic and neuropsychological variables (p>0.05).

Table 48. Demographic and neuropsychological characteristics of the participants in the active control and experimental groups at baseline

	Active Control Group (m=5; f=11)				Experimental Group (m=7; f=12)					
	N	Mean	Range	*SD*	N	Mean	Range	*SD*	*p*-value	Cohen's *d*
Age (years)	16	63.75	51.00-79.00	7.99	19	65.84	56.00-78.00	7.06	.417	-0.29
EF/PR										
EF/PR Composite	16	0.76	-2.02-6.5	2.29	18	-0.54	-5.51-2.75	2.65	.141	0.53
pStroop (ms)	16	234.21	-45.61-610.15	213.38	19	355.11	113.09-914.47	215.46	.230	-0.58
Fluency (animals)	16	21.44	10.00-35.00	6.31	19	18.68	12.00-29.00	4.49	.142	0.52
Immediate Working Memory	16	11.50	7.00-19.00	3.69	19	12.89	7.00-24.00	4.23	.311	-0.36
Trail Making Task – (raw) (s)	16	60.08	10.09-132.91	34.30	19	73.41	15.28-327.81	66.77	-	-
Trail Making Task (LOG) (s)	16	4.71	4.00-5.12	0.29	19	4.77	4.18-5.52	0.28	.559	-0.21
Letter Digit Task – Relativised Gains	16	0.67	-0.27-1.87	0.53	18	0.49	-1.03-2.10	0.63	.773	0.10
BRIEF-A	16	106.19	78.00-137.00	16.30	19	107.47	72.00-162.00	25.43	.863	-0.06
Digit Span Backwards	16	8.63	5.00-12.00	1.89	19	9.47	6.00-13.00	2.39	.259	-0.40
CCE										
CCE Composite	16	0.09	-4.75-3.97	2.09	19	-1.25	-6.16-2.79	2.23	.717	0.13
Education Level	16	5.19	3.00-7.00	1.05	19	5.32	2.00-7.00	1.53	.556	-0.10
Occupation Level	16	7.94	6.00-9.00	1.12	19	8.00	6.00-9.00	0.94	.957	-0.06
WAIS-Vocabulary	16	37.63	26.00-51.00	7.66	19	33.63	11.00-47.00	10.55	.217	0.44
CRIq-A	16	148.88	117.00-193.00	23.09	19	146.00	123.00-176.00	13.71	.651	0.15
Current Social Activity (raw)	16	16.88	3.00-91.00	20.53	19	14.53	4.00-40.00	9.79	-	-

Current Social Activity (LOG)	16	1.08	0.48-1.96	0.32	19	1.07	0.60-1.60	0.29	.908	0.04
Current Mental Activity	16	15.56	6.00-41.00	9.13	19	20.74	2.00-48.00	11.07	.048	-0.52
Memory/Global Cognition										
MMSE	16	28.63	26.00-30.00	1.15	19	28.74	25.00-30.00	1.37	.624	-0.09
DR	16	4.44	0.00-13.00	3.41	19	4.63	1.00-11.00	2.71	.852	-0.07
MFQ-Frequency of Forgetting	15	4.71	3.58-6.18	0.76	18	5.24	3.88-6.73	0.65	.041	-0.77
MFQ-Seriousness of Forgetting	15	4.63	2.11-6.44	1.21	19	4.55	1.06-6.89	1.51	.869	0.06
MFQ – Retrospective Functioning (raw)	16	3.18	1.80-2.00	1.26	19	3.35	1.60-6.60	1.29	-	-
MFQ-Retrospective Functioning (LOG)	16	0.47	0.26-0.75	0.17	19	0.50	0.20-0.82	0.16	.651	-0.16
MFQ-Mnemonics usage	16	3.17	1.50-5.63	1.20	19	3.41	1.13-5.50	1.34	.590	-0.19
PRMQ-Prospective Memory	16	19.38	12.00-26.00	3.36	19	18.37	11.00-28.00	3.67	.407	0.29
PRMQ-Retrospective Memory	16	17.69	11.00-24.00	4.05	19	16.16	9.00-23.00	4.32	.291	0.37

Note. Alpha=0.006 corrected for nine comparisons. EF/PR=Executive Functioning/Processing Resources; CCE= Cumulative Cognitive Enrichment. Trail Making Task, MFQ-Retrospective Functioning and Current Social Activity were log transformed (LOG 10 for positive skew) and descriptive statistics for both raw and transformed variables are reported. For all tasks a higher score represents better performance, with the exception of the following: pStroop; Trail Making Task; Brief-A and PRMQ. Independent t-tests were conducted and *p*-values and effect sizes (Cohen's *d*) are reported. Non-parametric Mann-Whitney tests were conducted for Education Level (Active Control *Mdn*=5.00; Experimental *Mdn*=5.00), Occupation Level (Active Control *Mdn*=8.00; Experimental *Mdn*=8.00, pStroop (Active Control *Mdn*=262.72; Experimental *Mdn*=281.06), MMSE (Active Control *Mdn*=29.00; Experimental *Mdn*=29.00) and Current Mental Activity (Active Control *Mdn*=13.50; Experimental *Mdn*=16.00)

8.4.2 Repeated Measures ANOVA

Three primary research questions were investigated with regard to response inhibition training in healthy older adults: (1) Does adaptive response inhibition training lead to improved performance on the trained task (direct training effects)? (2) Does adaptive response inhibition training improve performance on tasks highly related to the trained task (near transfer)? and (3) Does adaptive response inhibition training gains transfer to untrained tasks (far transfer)? To address these questions, repeated Measures ANOVAs were conducted and the results are summarised in Figures 31 and 32, and Tables 49 and 50. Effects were considered significant at the Bonferroni corrected alpha level of .006. Effects with a *p*-value less than .05 are considered near-significant and are discussed in terms of trends in the data.

Direct Training Effects

Training Gain

A repeated measures ANOVA with time as a within factor (mean level obtained in first two training sessions, mean level obtained in last two training sessions) and group as a between factor (active control, experimental) revealed a significant interaction between Time x Group, $F(1,33)=126.99$, $p<.006$, $\eta_p^2= 0.794$. There was also a significant main effect of time, $F(1,33)=334.99$, $p<.006$, $\eta_p^2=0.910$. In the active control group there were large training gains from pre- ($M=7.16$, $SD=0.81$) to post-test ($M=129.67$, $SD=35.61$), Cohen's $d=-4.88$. The experimental group had larger training gains from pre- ($M=10.05$, $SD=2.41$) to post-test ($M=39.26$, $SD=5.46$), Cohen's $d=-6.92$. Figure 31 (Panel A) presents a graph of direct training gains for both groups. At first glance it may appear that the active control group outperformed the experimental group in terms of level obtained over the course of the training period. It must be noted however that the active control group were playing a low dose version of the training task which provided less challenge and therefore allowed participants to more easily progress to higher levels than the experimental group who were playing a high dose version of the task (see figure 29 for a schematic diagram illustrating the differences between the high and low dose versions of the task). While the active control group did indeed attain a higher mean level than the experimental group on completion of training, there was also much larger variance in the level attainted within the active control group compared to the experimental group. As effect size (Cohen's *d*) was calculated by dividing the difference between mean pre-test and post-test scores by the pooled standard deviation, as explained earlier in this chapter, the effect size was larger for the experimental group due to a lower pooled standard deviation.

Near Transfer Effects

Stroop Interference

Stroop Interference score pre-intervention in the experimental group violated the assumptions of normality using the Shapiro Wilk test at the 5% alpha level. However, further investigation found that the data appeared normal based on the Kolmogorov-Smirnov test and therefore no data transformation was conducted.

A repeated measures ANOVA with time as a within factor (pre-intervention, post-intervention) and group as a between factor (active control, experimental) revealed a near significant main effect of time, $F(1,33)=4.398$, $p<.05$ ($p>.006$ corrected alpha), $\eta_p^2=0.118$. There was no significant interaction between Time x Group. In the active control group there was an improvement in Stroop Interference scores from pre- (M=234.21, SD=213.38) to post-test (M=198.80, SD=152.37), Cohen's d=0.19. In the experimental group there was a greater improvement in Stroop Interference scores from pre- (M=355.11, SD=215.46) to post-test (M=259.44, SD=166.55), Cohen's d=0.50.

Processing Speed

A repeated measures ANOVA with time as a within factor (pre-intervention, post-intervention) and group as a between factor (active control, experimental) revealed a significant main effect of time, $F(1,32)=13.392$, $p<.006$, $\eta_p^{2=}0.295$. There was no significant interaction between Time x Group. In the active control group there was an improvement in Processing Speed scores from pre- (M=0.67, SD=0.53) to post-test (M=1.20, SD=1.17), Cohen's d=-0.58. In the experimental group there was a greater improvement in Processing Speed scores from pre- (M=0.49, SD=0.63) to post-test (M=1.46, SD=1.08), Cohen's d=-1.10.

Cognitive Switching

Cognitive Switching scores pre-intervention in both the active control and the experimental groups, and scores post-intervention in the experimental group violated the assumptions of normality using the Shapiro Wilk test at the 1% alpha level. Log transformations (Log 10 for positive skew) were performed on pre and post cognitive switching scores in the active control and experimental conditions and all conditions satisfied the Shapiro Wilk test of normality (e.g., $p>.05$).

A repeated measures ANOVA with time as a within factor (pre-intervention, post-intervention) and Group as a between factor (active control, experimental) revealed a significant main effect of time, $F(1,33)=9.446$, $p<.006$, $\eta_p^2=0.223$. There was no significant interaction between Time x Group. In the active control group there was an improvement in Cognitive Switching scores from pre- ($M=4.71$, $SD=0.29$) to post-test ($M=4.61$, $SD=0.28$), Cohen's $d=0.35$. In the experimental group there was a greater improvement in Cognitive Switching scores from pre- ($M=4.77$, $SD=0.28$) to post-test ($M=4.63$, $SD=0.35$), Cohen's $d=0.44$.

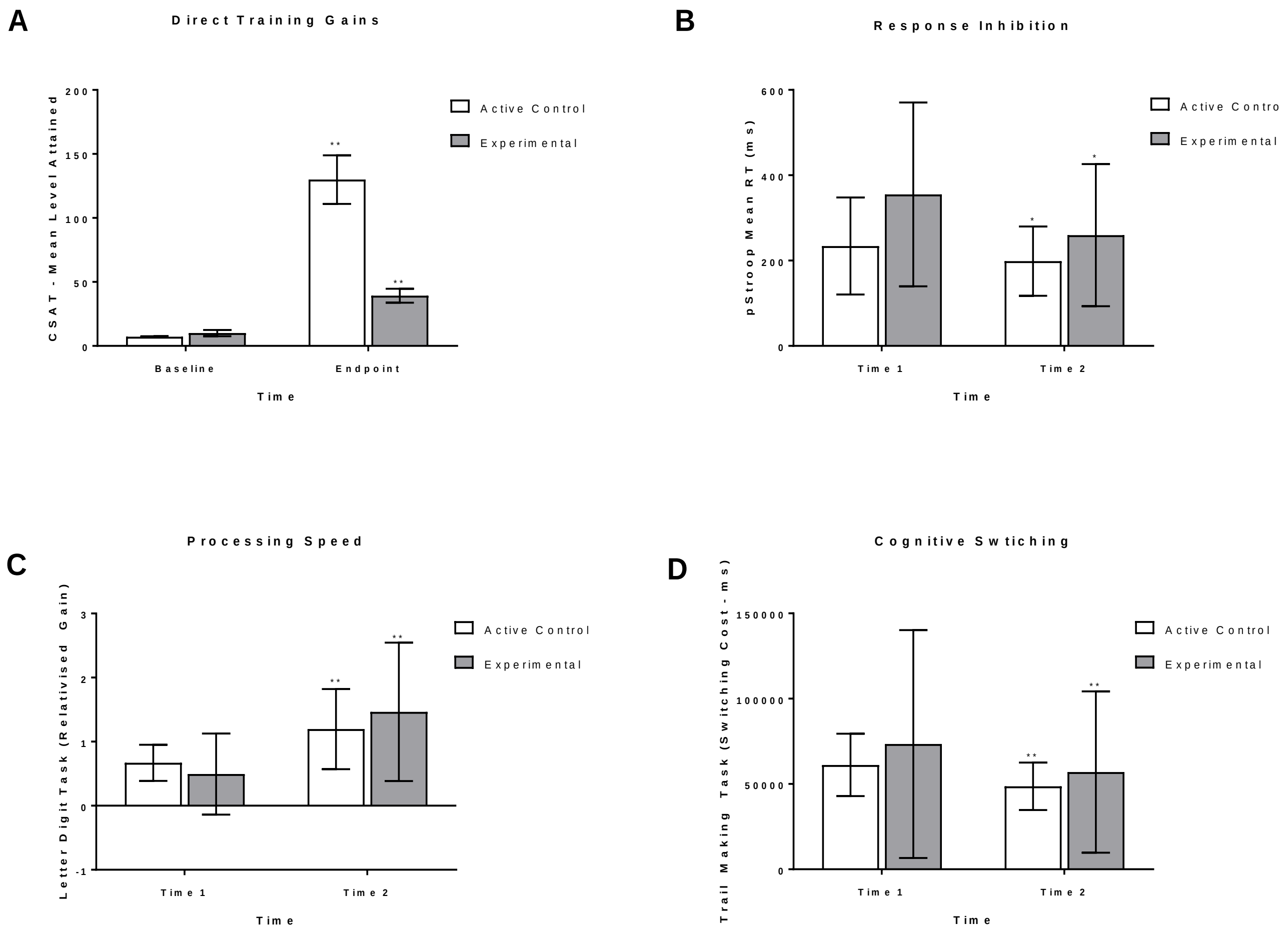


Figure 31. Direct (panel A) and near transfer (panels B, C, and D) effects across groups as a function of CSAT training.

Note. Error bars are standard deviations. Significance is noted where means differed from baseline (**p*<.05, ***p*<.006).

Table 49. Performance on direct and near transfer tasks as a function of training

	Active Control			**Experimental**							**Mixed ANOVA Time Effect**		**Mixed ANOVA Group Effect**		**Mixed ANOVA Interaction Effect**	
Transfer Task	*Pre M* (*SD*)	*Post M* (*SD*)	*d*	*Pre M* (*SD*)	*Post M* (*SD*)	*d*	*F (Time)*	*F (Group)*	*F (Inter-action)*	*df*1, *df*2	*p*-value	η_p^2	*p*-value	η_p^2	*p*-value	η_p^2
Training Gain	7.16 (0.81)	129.97 (35.61)	-4.88	10.05 (2.41)	39.26 (5.46)	-6.92	334.99	112.92	126.99	1,33	.000	0.91	.000	0.77	.000	0.79
PStroop	234.20 (213.38)	198.80 (152.37)	0.19	355.11 (215.16)	259.44 (166.55)	0.50	4.40	2.62	0.93	1,33	.044	0.12	.115	0.07	.342	0.03
TMT (LOG)	4.71 (0.29)	4.61 (0.28)	0.35	4.77 (0.28)	4.63 (0.35)	0.44	9.45	0.15	0.26	1,33	.004	0.22	.698	0.01	.613	0.01
LDT	0.67 (0.53)	1.20 (1.17)	-0.58	0.65 (0.93)	1.40 (1.09)	-1.10	13.39	0.16	1.18	1,32	.001	0.30	.688	0.01	.285	0.04

Note. pStroop=Primed Stroop Task (ms); TMT (LOG)=Trail Making Task (Log Transformed); LDT=Letter Digit Task (Relativised Gains); M=mean; SD=Standard Deviation; *d*=Cohen's *d*; *F*=ANOVA test statistic; η_p^2=partial eta squared; For % Training Gain and LDT a higher score indicates better performance. For the pStroop and the TMT a lower score indicates better performance

Far Transfer Effects

EF/PR Composite

A repeated measures ANOVA with time as a within factor (pre-intervention, post-intervention) and group as a between factor (active control, experimental) revealed a significant main effect of time, $F(1,31)=22.613$, $p<.001$, $\eta_p^2=0.422$. There was no significant interaction between Time x Group. In the active control group there was an improvement in EF/PR scores from pre- (M=-0.46, SD=1.78) to post-test (M=1.33, SD=2.57), Cohen's d=-0.81. In the experimental group there was also an improvement in EF/PR scores from pre- (M=-1.43, SD=2.63) to post-test (M=0.49, SD=2.94), Cohen's d=-0.69, but to a lesser degree than the active control group.

Fluency

A repeated measures ANOVA with time as a within factor (pre-intervention, post-intervention) and group as a between factor (active control, experimental) revealed a near significant main effect of time, $F(1,32)=7.225$, $p<.05$, $\eta_p^2= 0.184$. There was no significant interaction between Time x Group. In the active control group there was an improvement in Fluency scores from pre- (M=20.73, SD=5.85) to post-test (M=23.47, SD=5.82), Cohen's d=-0.47. In the experimental group there was also an improvement in Fluency scores from pre- (M=18.68, SD=4.49) to post-test (M=20.32, SD=5.60), Cohen's d=-0.32, but to a lesser degree than the active control group.

Working Memory

A repeated measures ANOVA with time as a within factor (pre-intervention, post-intervention) and Group as a between factor (active control, experimental) revealed a near significant main effect of time, $F(1,33)=6.459$, $p<.05$, $\eta_p^2=0.164$. There was no significant interaction between Time x Group. In the active control group there was an improvement in Digit Span Backwards scores from pre- (M=8.63, SD=1.89) to post-test (M=9.00, SD=2.03), Cohen's d=-0.19. In the experimental group there was a greater improvement in Digit Span

Backwards scores from pre- (*M*=9.47, *SD*=2.39) to post-test (*M*=10.63, *SD*=2.56), Cohen's *d*=-0.47.

Current Social Activity

Current Social Activity scores pre-intervention in both the active control group and the experimental group, as well as post-intervention in the experimental group violated the assumptions of normality using the Shapiro Wilk test at the 5% alpha level. Log transformations (Log 10 for positive skew) were performed on pre and post Current Social Activity scores in the active control and experimental conditions and all conditions satisfied the Shapiro Wilk test of normality (e.g., $p>.05$).

A repeated measures ANOVA with time as a within factor (pre-intervention, post-intervention) and Group as a between factor (active control, experimental) revealed a near significant main effect of time, $F(1,33)=7.99$, $p<.01$, $\eta_p^2=0.195$. There was no significant interaction between Time x Group. In the active control group there was an improvement in Current Social Activity scores from pre- (*M*=1.08, *SD*=0.32) to post-test (*M*=1.22, *SD*=0.33), Cohen's *d*=-0.43. In the experimental group there was a greater improvement in Current Social Activity scores from pre- (*M*=1.07, *SD*=0.29) to post-test (*M*=1.23, *SD*=0.26), Cohen's d =-0.58.

Current Mental Activity

Current Mental Activity scores pre-intervention in the active control group violated the assumptions of normality using the Shapiro Wilk test at the 5% alpha level. Log transformations (Log 10 for positive skew) were performed on pre and post Current Mental Activity scores in the active control and experimental conditions. However, normality is still violated.

A repeated measures ANOVA with time as a within factor (pre-intervention, post-intervention) and Group as a between factor (active control, experimental) revealed a significant interaction between Time x Group, $F(1,33)=11.572$, $p<.01$, $\eta_p^2=0.260$. There was also a significant main effect of time, $F(1,33)=14.301$, $p<.01$, $\eta_p^2=0.302$. In the active control group there was an improvement in Current Mental Activity scores from pre- (*M*=15.56, *SD*=9.13) to post-test (*M*=28.5, *SD*=15.09), Cohen's *d*=-1.04. In the experimental group there was also an improvement in Current Mental Activity scores from pre- (*M*=20.74, *SD*=11.07) to post-test (*M*=21.42, *SD*=9.78), Cohen's *d*=-0.07, but to a lesser degree than the active control group.

There were no significant effects of training on the CCE composite, crystallised IQ, subjective EF, immediate working memory, MMSE, delayed recall, subjective memory, prospective memory and retrospective memory.

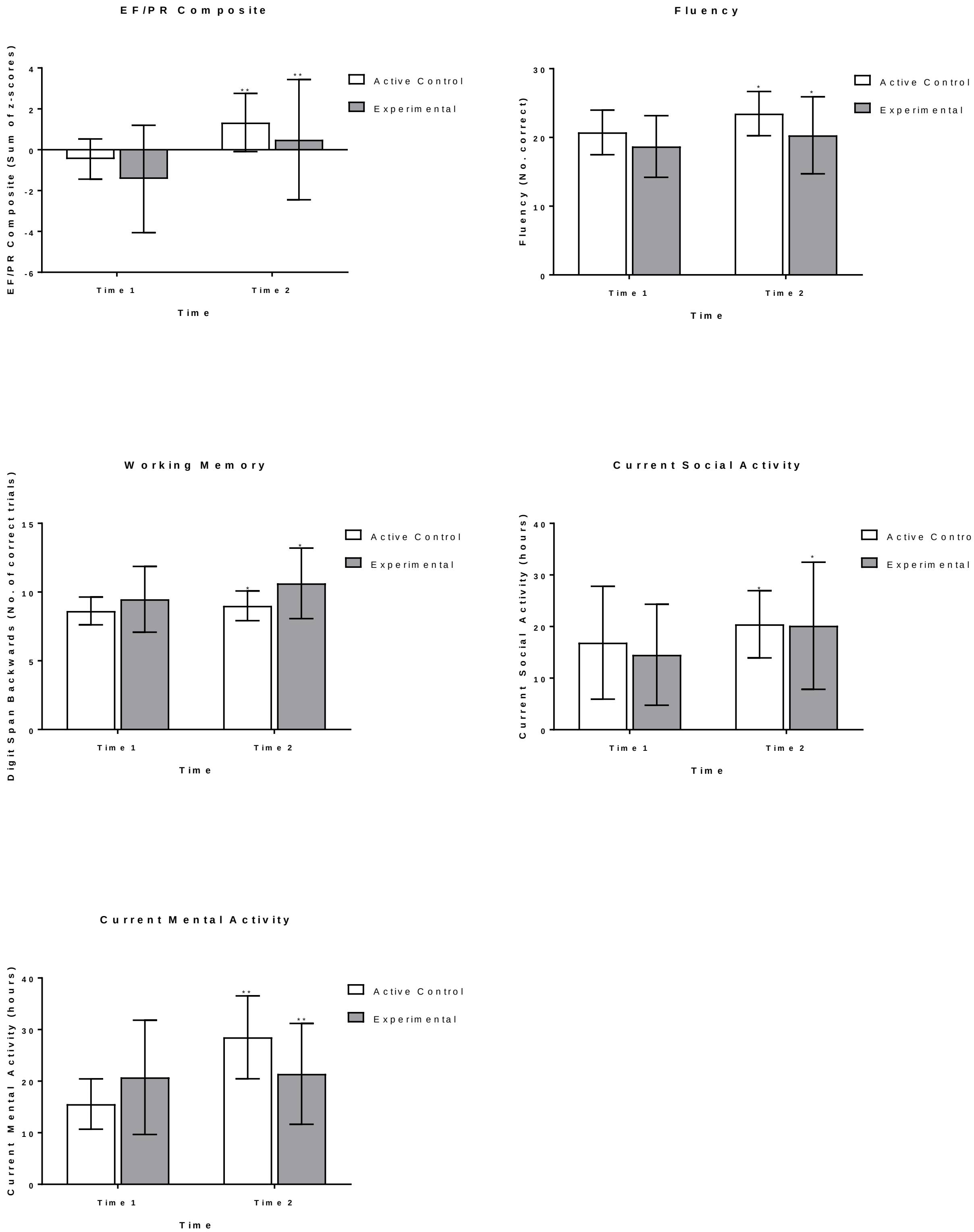


Figure 32. Far transfer effects across groups as a function of CSAT training.

Note. Error bars are standard deviations. Significance is noted where means differed from baseline (*p<.05; **p<.006).

Table 50. Performance on far transfer tasks as a function of training

	Active Control			Experimental							Mixed ANOVA Time Effect		Mixed ANOVA Group Effect		Mixed ANOVA Interaction Effect	
Transfer Task	*Pre M* (*SD*)	*Post M* (*SD*)	*d*	*Pre M* (*SD*)	*Post M* (*SD*)	*d*	*F (Time)*	*F (Group)*	*F (Inter-action)*	*df*1, *df*2	*p*-value	η_p^2	*p*-value	η_p^2	*p*-value	η_p^2
EF/PR																
EF/PR (comp.)	-0.46 (1.78)	1.33 (2.57)	-0.81	-1.43 (2.63)	0.49 (2.94)	-0.69	**22.61**	13.44	0.03	1,31	**.000**	0.42	.265	0.04	.868	0.00
Immediate WM	11.5 (3.69)	12.19 (4.69)	-0.16	12.89 (4.23)	12.42 (4.82)	0.10	0.03	0.36	0.84	1,33	.867	0.00	.551	0.01	.366	0.03
Fluency	20.73 (5.85)	23.47 (5.82)	-1.47	18.68 (4.49)	20.32 (5.60)	-0.32	7.23	2.38	0.46	1,32	.011	0.18	.133	0.07	.502	0.01
WAIS-DSB	8.63 (1.89)	9.00 (2.03)	-0.19	9.47 (2.39)	10.63 (2.56)	-0.47	6.46	3.10	1.69	1,33	.016	0.16	.088	0.09	.203	0.05
BRIEF-A	106.19 (16.30)	106.37 (16.61)	-0.01	107.22 (26.14)	105.17 (24.28)	0.08	0.20	0.00	0.29	1,32	.660	0.01	.990	0.00	.567	0.01
CCE																
WAIS-vocab.	37.63 (7.66)	36.69 (7.15)	0.13	33.63 (10.55)	36.00 (7.82)	-0.26	0.38	0.79	2.03	1,33	.541	0.01	.381	0.02	.163	0.06
Current Social Activity (LOG**)**	1.08 (0.32)	1.22 (0.33)	-0.43	1.07 (0.29)	1.23 (0.26)	-0.58	7.99	0.00	0.05	1,33	.008	0.20	.993	0.00	.827	0.00
Current Mental Activity	15.56 (9.13)	28.5 (15.09)	-1.04	20.74 (11.07)	21.42 (9.78)	-0.07	**14.30**	0.08	**11.57**	1,33	**.001**	0.30	.783	0.00	**.002**	0.26

Memory/Global Cognition Outcomes																
MMSE	28.63 (1.15)	28.75 (1.29)	-0.10	28.74 (1.37)	28.53 (1.26)	0.16	0.03	0.02	0.50	1,33	.858	0.00	.878	0.00	.486	0.02
Delayed Recall	3.87 (2.61)	3.93 (1.71)	-0.03	4.63 (2.71)	5.32 (3.20)	-0.23	1.03	1.63	0.70	1,32	.318	0.03	.211	0.05	.410	0.02
MFQ:																
MFQ1	4.71 (0.76)	4.84 (0.88)	-0.16	5.28 (0.64)	5.25 (0.87)	0.04	0.13	3.81	0.36	1,30	.718	0.00	.060	0.11	.551	0.01
MFQ2	4.63 (1.21)	4.13 (1.16)	0.42	4.69 (1.43)	4.74 (1.45)	-0.03	2.36	0.57	3.69	1,31	.135	0.07	.455	0.02	.064	0.11
MFQ3	0.47 (0.17)	0.47 (0.13)	-0.02	0.50 (0.16)	0.46 (0.12)	0.28	0.70	0.03	0.89	1,32	.408	0.02	.858	0.00	.352	0.03
MFQ4	3.17 (1.20)	3.12 (1.15)	0.04	3.36 (1.36)	3.02 (1.11)	0.27	2.31	0.01	1.21	1,32	.138	0.07	.907	0.00	.280	0.04
PRMQ: PMEM	19.37 (3.36)	19.93 (4.27)	-0.15	18.37 (3.67)	18.21 (2.55)	0.05	0.17	1.59	0.53	1,33	.684	0.01	.217	0.05	.470	0.02
PRMQ: RMEM	17.69 (4.05)	18.25 (3.81)	-0.14	16.16 (4.32)	16.47 (4.02)	-0.07	0.73	1.67	0.06	1,33	.398	0.02	.205	0.05	.812	0.00

Note. EF/PR (comp.)=EF/PR Composite; Immediate WM=Immediate Working Memory; WAIS-DSB=WAIS Digit Span Backwards; WAIS-vocab.=WAIS-vocabulary; MFQ=Memory Functioning Questionnaire; MFQ1=Frequency of Forgetting; MFQ2=Seriousness of Forgetting; MFQ3=Retrospective Functioning; MFQ4=Mnemonics Usage; PMEM=Prospective Memory; RMEM=Retrospective Memory; M=mean; SD=Standard Deviation; *d*=Cohen's *d*; *F*=ANOVA test statistic; η_p^2=partial eta squared; Significant effects are highlighted with bold font. For all tasks a higher score indicates better performance, with the exception of the BRIEF-A and the PRMQ measures of prospective and retrospective memory where a lower score indicates better performance.

8.5 Discussion

The present study investigated whether adaptive response inhibition training could improve performance on the trained task as well as inhibition-related (near transfer) and untrained tasks (far transfer). Results of RM ANOVAs on training gains and near transfer effects are summarised in *Table 49*. It was found that following participation in a five-week computerised training programme, there was a main effect of time with both active control and experimental groups significantly improving on the trained task, $F(1,33)=334.99$, $p<.001$, $\eta_p^2=0.910$, as well as on measures of processing speed, $F(1,32)=13.392$, $p<.006$, $\eta_p^2=0.295$ and cognitive switching, $F(1,33)=9.446$, $p<.006$, $\eta_p^2=0.223$. There was also a trend towards improvement in response inhibition, $F(1,33)=4.398$, $p<.05$, $\eta_p^2=0.118$, however this result was not significant at the .006 alpha level. Although there were no significant interaction effects for near transfer measures, the magnitude of the improvements from pre- to post-test (Cohen's *d*) indicates that the experimental group experienced larger performance gains than the active control group with regard to respective training gains (d=-6.92 vs. d=-4.88), response inhibition (d=0.50 vs. d=0.19), processing speed (d=-1.10 vs. d =-0.58), and cognitive switching (d=0.44 vs. d=0.35). These results suggest that, as predicted by core training paradigms (Morrison & Chein, 2011), improvement on the trained task also generalised to improved performance on a range of closely related, but untrained, tasks.

Far transfer effects were investigated in relation to the ER/PR composite, the remaining EF/PR indicators (immediate working memory and fluency), the CCE crystallised IQ indicator (WAIS-vocabulary), current cognitive enrichment as measured by current social and mental activity, working memory as measured by the digit span backwards, as well as measures of global cognition and memory (see Table 50 for summary of far transfer effects). The EF/PR composite showed significant improvement over time in both groups, $F(1,31)=22.613$, $p<.001$, $\eta_p^2=0.422$, however the magnitude of the effect (Cohen's *d*) was greater for the active control group. Similarly, the Fluency measure saw a trend towards improvement over time in both groups, $F(1,32)=7.225$, $p<.05$, $\eta_p^2=.014$, with the magnitude of the effect being greater for the active control group. While not predicted a priori, transfer effects of response inhibition training to a composite measure of EF/PR were expected as three of the five measures comprising this composite were hypothesised to experience near transfer effects (processing speed, cognitive switching, and response inhibition). Although there was not a significant difference between the groups at pre-intervention with regard to EF/PR composite scores, the active control group appeared to be performing better than the experimental group, pre-intervention (Active Control *M*=0.76 vs. Experimental *M*=-0.54), and therefore this may have impacted on the magnitude of the training effects. Transfer effects of training to the measure of Fluency were not expected. As fluid abilities are related to EF it is possible that response inhibition training improved this ability. However, this measure, which involved asking participants to name as many animals as they can in one minute, has previously been found to be prone to practice effects in healthy older adults (Cooper et al., 2001) and therefore this finding must be interpreted with caution. As this measure was also used to calculate the EF/PR composite, it is possible that practice effects also influenced the composite score variable.

Following participation in the response inhibition training programme, both active control and experimental groups showed a trend towards improvement on a measure of Current Social Activity, $F(1,33)=7.99$, $p<.05$, $\eta_p^2=0.195$. Additionally, there was a trend toward improved performance for both active control and experimental groups on a measure of working memory (WAIS-DSB), $F(1,33)=6.46$, $p<.05$, $\eta_p^2=0.164$. There were no significant interaction effects, however the magnitude of the training effect (Cohen's *d*) indicates that the experimental group experienced larger gains than the active control group on both of these measures. While far transfer effects were not hypothesised a priori, improvements on a measure of working memory were unsurprising due to research demonstrating that executive control abilities contribute to working memory performance (Kane, Conway, Hambrick, & Engle, 2008; McVay & Kane, 2012). Improvements in Current Social Activity, however, were not expected. There has been research to suggest that social interactions promote cognitive functioning (Ybarra et al., 2008), however as much of this research is correlational, the causal direction is unclear. It is possible that a reciprocal relationship exists between cognitive functioning and social activity whereby improvements in cognitive functioning lead to improved social cognition and greater levels of engagement, which in turn leads to greater gains in social cognition. However, as there is no pre-intervention correlation between Current Social Activity and measures of EF, changes as a result of EF training are unlikely and findings cannot be directly attributed to the intervention.

There was a significant group x time interaction for Current Mental Activity, $F(1,33)=11.572$, $p<.006$, $\eta_p^2=0.26$, with the active control group experiencing significantly larger gains following training than the experimental group. Again, this finding was unexpected, in particular the significantly larger improvement in the active control group. Similar to unexpected improvements in social activity discussed above, it may be the case that a reciprocal relationship exists, whereby improvements in control processes lead to greater engagement in mental activities, which in turn further boosts control processes. However, as with social activity, there was no pre-intervention correlation between control processes and mental activity and therefore this finding must be interpreted with caution. There were no significant effects of training on immediate working memory, crystallised IQ, subjective EF, or any of the measures of global cognition and memory.

The failure to find a significant time x group interaction effect for the majority of near and far transfer measures means that performance improvements cannot be explicitly attributed to the intervention. There are a number of possible explanations for the lack of an interaction effect, and also larger gains in the active control group for some of the measures. In a review of the trainability of healthy older adults, Buitenweg et al. (2012) suggested that training was likely to be successful if it focused on tailoring the training adaptively to the level and progress of the individual. The core training strategy applied in this study adhered to this recommendation, yet no significant interaction effects were observed for the majority of measures (with the exception of current mental activity). For the near transfer measures (training gains, processing speed, cognitive switching and response inhibition), the larger effects sizes in the experimental group suggest that the adapted training was more beneficial than the non-adaptive training, and perhaps with a larger sample size the interaction effects would have been significant, although further research will need to be conducted before firm conclusions can be drawn in this regard. The fact that effects sizes appeared larger in the active control group for many of the far transfer measures suggests that for tasks not directly related to response inhibition, low level training may be sufficient to see an effect. Future research could potentially benefit from the addition of a no-contact control group in order to determine if low-level training is as effective as adaptive training with regard to far transfer. Additionally, a quantified approach to decomposing the transfer effect from low levels (e.g. motor speed) to higher integration levels (e.g. decision making) should be adopted (see Poreh, 2000 for details of how this approach can be used in functional assessment).

Other possible explanations for the lack of an interaction effect, as well as the lack of transfer effects to measures of global cognition/memory, include waning of participant arousal due to the repetitive nature of the training task (Richmond, Morrison, Chein, & Olson, 2011). According to Richmond, Morrison and Chein (2011) learning is a U-shaped function of arousal and the repetitive nature of a training task may result in the waning of participant arousal over the course of the training sessions. While the training regime was adaptive and controlled for motivation across both groups through the use of performance feedback, the task itself was repetitive as the objective did not change over the course of training. It may be the case that the experimental group, who had considerably longer training sessions than the active control group, may have experienced reduced arousal levels toward the end of the training period and learning effects may have diminished. Over the course of the training period, the active control group also engaged in more training sessions than the experimental group, training between 19 and 55 times over the course of the study compared to the experimental group who trained between 24 and 33 times, although it must be noted that this difference was not statistically significant. Due to heterogeneity of regression slopes across groups for the number of training sessions in relation to training gains, number of training sessions could not be included as a covariate in the analysis (see Field, 2009). The lack of a significant relationship between number of training sessions and the remaining near transfer measures meant that this could not be controlled for in the analysis by inclusion as a covariate. It is possible that engagement in low level, non-adaptive training is sufficient to result in similar or greater performance gains to that of the experimental group, but as a no-training control group was not included in the study this remains unclear.

A review of computerised cognitive training interventions in healthy elderly supports the assertion that fatigue effects may have reduced training efficacy as it was found that training more than three times per week has a neutralising effect on training gains (Lampit et al., 2014). It is suggested that there is perhaps a maximal dose for cognitive training, after which the effects of fatigue may hinder training. Furthermore, the fact that the training did not generalise to CCE or global cognition/memory measures may be related to the training dose, as Lampit et al. (2014) found that training session of less than 30 minutes may be ineffective. A possible explanation for this is that the level of synaptic plasticity required for far transfer effects is more likely to occur after 30-60 minutes of cognitive stimulation (Luscher, Nicoll, Malenka, & Muller, 2000). Training duration of this size, however, can be problematic with regard to motivation and adherence in home-based training and may be more suited to a group-based training environment. Group-based training programmes, although not a practical as home-based interventions, may be better equipped to ensure adherence and provide motivational and technical support due to direct supervision by a trainer (Lampit et al., 2014).

It is also possible that differences were not found between groups due to ceiling effects. All participants were highly educated (77.1% indicated some form of third level education) and had a current/previous occupation high in complexity (77.2% fell into the top two categories of "professionals" or "managers"). Research suggests that individuals high in CR (as measured by the CRIq which includes measures of education and occupation) do not benefit from cognitive training as much as those with low CR levels (Mondini et al., 2016). As both experimental and active control groups are high in CR according to the Nucci classification (Nucci et al., 2012), improvements may not have been as steep as for individuals with low CR.

Overall findings demonstrate the plasticity of EF and support the assertion that a core component of CR capacity can be boosted through targeted EF training. The training programme, however, did not result in improvements on measures of CCE (crystallised IQ) or measures of global cognition/memory. Improvements in crystallised IQ, as measured by the WAIS-vocabulary, following a training intervention that targeted cognitive control abilities, were unlikely as the demands of the training task did not involve an overt shared strategy with cyrstallised abilities (Thompson et al., 2013). The modelling studies in Section I found that a CR capacity model driven by EF/PR was predictive of global cognition/memory outcomes both at baseline and longitudinally. It is possible that gains in global cognition/memory measures were not observed in this small sample as measures were not sensitive enough to detect changes after a five-week period. Descriptively, the experimental group improved slightly on delayed recall scores (Pre: M=4.63, SD=2.71; Post: M=5.32, SD=3.20), but this improvement was not statistically significant. It may also be the case that plasticity was limited to the trained cognitive control system. It is also possible that gains in global cognition/memory measures were not observed in this small sample as training duration was not sufficient to result in the synaptic plasticity required for far transfer to these domains. Far transfer to these measures was not expected as a lack of generalisation of training gains is common in the field of cognitive training and findings of far-transfer effects in ageing populations have been limited (Brehmer, Westerberg, & Bäckman, 2012). In sum, targeted response inhibition training improved performance on the trained task as well as performance on related measures of processing speed, cognitive switching and response inhibition, with the experimental group experiencing larger effect sizes than the active control group.

Chapter 9: Summary and Synthesis of Findings

This chapter provides a general discussion of the research programme. Study findings are outlined and are critically assessed in light of current literature in the field. The implications of this research, both theoretical and practical, are discussed and limitations of the research are considered. Finally, future directions for research are suggested.

9.1 Study Rationale and Objectives

CR capacity can be viewed as the cognitive processing potential of neural systems that support adaptive cognitive performance in the face of age-related decline. In this sense, CR capacity can predict cognitive performance across the lifespan in healthy ageing populations, as well as cognitive performance in response to neural stress. Traditionally, lifestyle and environmental enrichment variables have been used as proxy measures of CR. However, it is likely that these representational indicators do not capture all of the elements involved in CR capacity. For instance, recent research has suggested that biological mechanisms, such as the repeated activation of the noradrenergic system in response to environmental influences may be implicated in CR capacity (I. H. Robertson, 2013). NA activation may facilitate networks for arousal, novelty, sustained attention, awareness and working memory (Greene, Bellgrove, Gill, & Robertson, 2009; I. H. Robertson, 2014), which highlights the role of cognitive control processes as a potential mechanism by which the brain adapts to age-related changes. Research has also supported a strong relationship between traditional CR proxy measures and cognitive variables such as EF, PR, and IQ (M. B. Mitchell, Shaughnessy, et al., 2012; Satz et al., 2011; Siedlecki et al., 2009). These strong relationships again point towards the important role of control processes in CR capacity and support the expansion of definitions of CR based on representational processes to include these control indicators.

As CR cannot be measured directly, the a priori groupings of variables purported to contribute to CR capacity were in need of construct validation to clarify the convergent and discriminant validity of the proposed indicators. Furthermore, demonstrating empirically that cognitive factors such as EF contribute to CR capacity has implications for the modifiability of CR capacity. Traditional CR measurement paradigms draw on cognitive enrichment proxies that accumulate across the lifespan, such as education, a complex occupation and crystallised abilities such as vocabulary knowledge. As these CR proxies reflect lifetime experience they are not suitable targets for a short-term intervention aimed at boosting CR capacity. However, if modifiable factors such as EF are implicated in CR capacity, targeted EF training could potentially provide a means of increasing CR capacity in a timely and accessible manner.

Therefore, the objectives of this research programme were twofold. Firstly, the modelling section of the research programme explored the construct validity of a novel, a priori, model of CR capacity and its relationship with cognitive decline outcomes, both cross-sectionally and longitudinally. This objective is predicated on both theoretical and empirical linkages between traditional CR proxies and cognitive functions such as fluid executive abilities (Siedlecki et al., 2009), however prior to this research programme, these constructs have not been empirically tested as mutual components of CR capacity. Secondly, this novel operationalisation of CR capacity allowed for investigation of its modifiability through a targeted EF training intervention study. This objective encompassed the EF training intervention section of the research programme. There is evidence for the beneficial effects of EF training interventions in healthy older adults (Reijnders et al., 2013), hence targeting the modifiable control processes component of CR capacity through EF training could potentially impact on the CR capacity construct in this population.

9.2 Summary of Findings

Section I of the Research Programme: Construct Validity of CR Capacity

The construct validity of CR capacity and its relationship with cognitive decline outcomes in healthy older adults was explored in studies 1-4. In study 1, Satz et al.'s (2011) a priori four-factor model of CR capacity was refined through EFA and a two-factor underlying structure was established. The first factor grouping was comprised of the cognitive control processes of EF and PR and was labelled EF/PR. The second factor grouping reflected representational processes built up over the lifespan and was labelled CCE. This dual framework is evidenced in previous research on cognitive change over the lifespan. For instance, Kennedy and Raz (2009) linked performance on processing speed tasks with frontal-parietal brain areas similar to the substrates of EF, while a CFA conducted by Mitchell et al. (2012) supported convergent validity of a factor represented by both EF and processing speed indicators. The CCE indicators (education level, level of occupational attainment, and crystallised IQ) are experiential resources that have been frequently used as proxy measures of CR (Meng & D'Arcy, 2012; Valenzuela & Sachdev, 2006). These two factors can also be considered representative of two types of cognition – *process* measures reflective of more efficient information processing and cognitive function, and *product* measures reflective of cumulative processing across the lifespan (Salthouse, 2006). These factors can also be interpreted in light of a similar framework put forward by Craik and Bialystok (2006) that addresses the mechanisms of cognitive change across the lifespan. Under this framework, the EF/PR factor comprises control processes that can be viewed as the set of fluid operations that facilitate intentional processing and adaptive cognitive performance. The CCE factor comprises representational processes that can be viewed as crystallised schemas reflecting knowledge of the world. Central to this framework is the proposition by the authors that these two systems are interactive in the sense that representations of the world are selected based on needs and desires, and in turn, these representations demonstrate control through their influence on the selection of schema-relevant information.

CFA was also used in study 1 to evaluate the EFA factor solution in terms of how well the measurement model of CR capacity fits the data. Goodness-of-fit indices suggested that the measurement model fits the data reasonably well when looking at the full age range sample, and very well when the sample is broken out into age groups. Convergent validity of the latent variables was established due to the moderate to high factors loadings of indicators. Discriminant validity was established through examination of the correlations between the factors across age models. The moderate to large correlations between the dimensions of EF/PR and CCE across age groups (*r* range: 0.595-0.816) supports the theory that a strong relationship exists between executive processing abilities and traditional enrichment CR proxies. In study 2, this measurement model was validated using CFA in a secondary Irish ageing dataset, TILDA. The validation study yielded further support for convergent validity of the EF/PR and CCE factors due to the moderate to high factor loadings of indicators. Although again a strong relationship was observed between EF/PR and CCE, discriminant validity was also supported as correlations between the latent factors across age groups ranged from 0.581 to 0.617. Stern's (2009) theory of neural reserve posits that greater flexibility in network selection, an ability believed to be captured by executive processing tasks, underpins protection against cognitive decline, and thus a relationship between these abilities and traditional CR proxies was expected. Craik and Bialystok's (2006) framework of control and representational processes can also be applied here as an explanatory framework in the sense that the relationship between these systems can be viewed as reciprocal, i.e., control processes determine the construction of representations, which in turn play a role in further controlled processing. When applied to the two-factor CR capacity model, EF/PR can be viewed as a driver of CCE which in turn feeds back into EF/PR, and their mutual evolution across the lifespan may contribute to a CR capacity system that is predictive of cognitive ability over time. This strong relationship however, is not large enough to call into question the discriminant validity of these two factors, and therefore both EF/PR and CCE can theoretically be viewed as separate contributors to CR capacity.

The findings of the EFA and CFA in MAAS, and the CFA validation in TILDA, support the findings of previous CR research linking control and representational processes. For instance, although relationships were not modelled within a CR capacity framework, a similar strong relationship was found between a CR factor comprising Education and premorbid IQ and a separate factor comprised of executive function/processing speed indicators in both healthy ageing and aMCI populations (M. B. Mitchell, Shaughnessy, et al., 2012). Although it was not possible to model CR capacity in a population with brain atrophy due to screening for healthy elderly at baseline in MAAS and the small number of dementia converters at follow-up, the fact that similar relationships between control and representational processes were seen in this study in both healthy and aMCI populations suggests that the CR capacity model may hold in populations affected by brain pathology. This, however, is subject to future research. Also, Siedlecki et al. (2009) found evidence for a strong relationship between a latent 'CR' construct (education, vocabulary, literacy) and an EF construct in healthy older adults, but concluded that there was sufficient evidence to argue for discriminant validity. Furthermore, as the factor loadings of indicators were similar in strength across healthy ageing models, this suggests that vulnerability factors in relation to decline outcomes may remain similar from youth into older age.

In study 3, the structural relationships between the CR capacity indicators, CR capacity, and cognitive decline outcomes in healthy older adults were investigated in MAAS data. The relationships were assessed in two age groups (50-64 years; 65-82 years) using outcomes at baseline, six-year, and 12-year follow-up. The CR capacity construct, comprised of baseline EF/PR and CCE latent factors, was predictive of global cognition/memory outcomes at all time-points. This suggests an association between higher baseline activation of the CR capacity system and higher global cognition/memory scores over time. The EF/PR factor had a consistent strong, positive weighting on the CR capacity component suggesting that this factor is a strong driver of CR capacity. This finding supports previous research linking control processes to CR. For instance, a study that measured CR as the residual variance in episodic memory scores found that CR modified rates of longitudinal decline in EF (Reed et al., 2010). CR as measured by traditional proxy indicators was also found to be highly predictive of a cognitive performance latent variable indicated by EF, attention, and abstract thought (Lojo-Seoane et al., 2014).

Conversely, CCE had a negative weighting on CR capacity across models which suggests that this factor is related to lower activation of a CR capacity system. This negative weighting was unexpected as previous research has indicated a direct protective effect of representational processes with regard to decline outcomes (Bosma et al., 2002; Crowe et al., 2003; Scarmeas et al., 2001; Valenzuela & Sachdev, 2009; Wilson et al., 2013). Further exploration with regard to multicollinearity and suppression effects was necessary in order to rule out a potential statistical explanation for this finding. CCE was found to be neither collinear nor a suppressor. The model was also respecified, firstly as a one-factor model, secondly, with EF/PR as a mediator of the relationship between CCE and the cognitive outcomes, and finally, with CCE as a moderator of the relationship between EF/PR and the outcomes. These respecified models were assessed in terms of fit and theoretical suitability. It was also noted whether or not a negative relationship persisted with regard to CCE. Following respecification, CCE continued to display negative relationships with outcomes in some of the models, which supports the integrity of the negative CCE weighting on CR capacity in the original two-factor model.

In study 4, the SEM findings in both baseline and longitudinal models were largely replicated in TILDA data which demonstrates the generalisability of the CR capacity model to a healthy Irish ageing population. The TILDA models provide support for a strong, positive predictive relationship between CR capacity and global cognition/memory outcomes. The negative weighting of the CCE factor on CR capacity was also replicated in this study. In the two-year follow-up model for the 50-64 year old age group, the relationship between CCE and CR capacity became insignificant when controlling for baseline values of the outcomes. The fact the CCE dropped out of the model in this instance could potentially be explained by the lack of a crystallised IQ indicator on the CCE construct. The CCE weighting on CR capacity was consistently significant in MAAS, therefore having only two indicators on the construct may have resulted in reduced sensitivity with regard to detection of a significant relationship.

A potential explanation for these findings is the differential involvement of control and representational processes in CR capacity. It may be the case that high EF/PR levels are associated with high activation of a CR capacity system, while high CCE levels are related to low activation of a CR capacity system in healthy ageing populations. In this sense, similar to suggestions made by Stern (2002) regarding differential ability in the recruitment of alternative networks, EF/PR can be viewed as the processing efficiency, or neural reserve, arm of CR capacity and CCE can be viewed as the compensatory arm of CR capacity. It is possible that in healthy individuals, direct, damage specific, compensation is not engaged and CR capacity is instead activated through the EF/PR, or neural reserve arm. In populations affected by brain pathology, it is possible that the CCE arm of CR capacity would be directly engaged and alternative networks would be recruited in order to maintain performance. The strong relationship between EF/PR and CCE may assist compensation by facilitating greater flexibility in the recruitment of alternative networks, however the direct strong positive relationship between EF/PR and CR capacity may no longer be evident in populations where pathology has affected control processes. In healthy ageing populations, under this dual framework, high EF/PR levels will result in recruitment of standard networks to support function, and this is aided by a reciprocal relationship with CCE. In populations affected by pathology, and therefore deficits in EF/PR, patterns of activation may deviate from the standard system to recruit alternative networks supported by CCE, however this is yet to be clarified through future research.

Another potential explanation considers the differential roles of EF/PR and CCE as a function of age. There may be a greater dependence on control processes in older adults in order to compensate for age related declines in cognition (Bouazzaoui et al., 2013). High CCE levels can be interpreted as resulting in low activation of a CR capacity system when the relationship between EF/PR and CR capacity is controlled for, and this may be the case as control processes are utilised to access the information stored in representational systems. Controlling for the relationship between EF/PR and CR capacity may have resulted in any engagement of CCE with CR capacity being filtered out.

It may also be the case that the cognitive enrichment provided by CCE indicators like education and occupation are transient, and therefore are not the most important proxies of CR capacity. For instance, Wilson et al. (2005) found that lifetime engagement in cognitively enriching activities was not a useful index in quantifying CR capacity as their association with current cognitive performance was not strong after accounting for the effects of current activity. Furthermore, research has shown that a CR latent construct comprised of representational variables was highly predictive of general cognitive performance in participants with subjective memory complaints, but this effect became insignificant when working memory, a cognitive control indicator, was included as a mediator (Lojo-Seoane et al., 2014). These findings suggest that representational processes may not be the strongest proxies of CR capacity.

The longitudinal modelling section of this research programme (studies 1 to 4) demonstrated a novel approach to modelling CR capacity by the inclusion of both control and representational processes in a model of CR capacity. Established neuropsychological measures were used throughout which facilitated the reproducibility of the model in the Irish TILDA dataset. While findings support the novel claim that both control and representational processes are involved in CR capacity, a potential limitation to the modelling studies, common within the field, was the unavailability of some of the measures specified by Satz et al.'s (2011) a priori four-factor CR model. For instance, measures of social networks and mental activity were not captured in the MAAS longitudinal dataset, and the measure of literacy was only administered to a small cohort. It is likely, however, that these variables would load on the CCE factor as they can be considered representational processes that contribute to crystallised abilities, and are frequently used traditional CR proxies (Lojo-Seoane et al., 2014; M. B. Mitchell, Shaughnessy, et al., 2012; Siedlecki et al., 2009). Similarly, other indicators specified by Satz et al. (2011), such as measures of divided attention and reasoning, were not suitable for SEM analyses as they were administered to only a small subsection of participants in MAAS. Measures of selective attention, error monitoring and fluid IQ were also removed from analyses during the iterative processes of EFA. Based on previous research, it is likely that indicators such as divided/selective attention, reasoning and error monitoring would load on the EF/PR factor given the previously demonstrated relationships between these indicators and control processes (Kyllonen & Christal, 1990; Salthouse & Davis, 2006; Süß et al., 2002). Fluid IQ has also been found to be related to both control processes and representational processes such as executive abilities, crystallised IQ, education, and occupation (Schooler et al., 1999; Sternberg et al., 2001) so it is likely this indicator would cross-load on both constructs. In fact, the MAAS measure of fluid IQ (GIT3) was found to cross-load on both the EF/PR and CCE factors, however as the factor loadings were small (<.4) it was removed from the final EFA. Future research, however, should aim to include these measures in a more comprehensive model of CR capacity to clarify these relationships.

Despite this limitation, the CR capacity model tested using MAAS and TILDA data included a large number of the indicators suggested by the Satz model and represented all four of the specified factors. The CR capacity model advances our understanding of how both control and representational processes relate to CR capacity, and in turn, are indicators of cognitive decline over time. The negative relationship between CCE and CR capacity was unexpected and called into question the direct contribution of representational processes with regard to the activation of a CR capacity system. However, it is in line with arguments made by Stern (2002) regarding differential abilities in the recruitment of alternative networks. With regard to the modifiability of CR capacity, this brings control processes to the fore as a promising target for intervention aimed at boosting an important component of CR capacity.

Section II of the Research Programme: Modifiability of CR Capacity

In Section I of the research programme, CR capacity was modelled in terms of control and representational processes, and a consistently strong and positive relationship between the modifiable control processes factor (EF/PR) and CR capacity was found. A further aim of the research programme was to design an intervention targeting a modifiable component of CR capacity. Response inhibition, as measured by Stroop interference, is an EF that consistently loads moderately to strongly on the EF/PR factor across multiple analyses (EFA, CFA and SEM) in two longitudinal datasets, MAAS and TILDA, and is therefore an important indicator of the EF/PR factor, and indirectly, CR capacity.

The EF training intervention targeted healthy Irish adults aged 50 and over. The sample consisted of individuals with variable CR capacity and variable memory concerns. The study was a double-blind, two block (AB) randomisation design that consisted of three parts: (a) a pre-intervention test assessment, (b) a response inhibition training regime where participants were allocated to one of two treatment conditions: active control or experimental, and (c) a post-intervention test assessment. A battery of neuropsychological tests was administered before and after five weeks of online response inhibition training. The study aimed to investigate whether the CR capacity model would continue to hold in a small sample of healthy Irish older adults, some of whom had concerns about their memory.

Firstly, pre-intervention data was explored to investigate if the CR capacity parameters from the modelling studies held in this sample. Additional parameters that could not be explored through the longitudinal modelling studies were also investigated, such as associations between CR capacity indicators and measures of social and mental activity, prospective/retrospective memory and subjective ratings of EF. While not all findings were significant at the Bonferroni corrected alpha level of .006, relationship trends appear to support the CR capacity model relationships from the modelling studies. CR capacity was measured using composite measures of EF/PR and CCE and there was a trend toward a moderate relationship between these measures. This somewhat supports the finding of moderate to large correlations between the EF/PR and CCE factors in Section I. Predictive relationships between EF/PR and MMSE scores and scores on delayed recall were statistically significant and supported the findings of the modelling studies. The finding that CCE was not significantly predictive of any of the global cognition/memory scores, and the observation of non-significant negative beta weights in relation to delayed recall and MFQ-Retrospective Functioning, went some way toward supporting the findings of the modelling studies and literature suggesting the experiential resources like education may not be the best proxies of CR (Reed et al., 2011; Singh-Manoux et al., 2011). This finding again points to differences between control and representational processes with regard to activation of a CR capacity system. It may be the case that EF/PR is increasingly relied upon in healthy older adults to activate the CR capacity system, despite paradoxical age-related declines in control processes (Bouazzaoui et al., 2014; Dennis & Cabeza, 2008). A further explanation for these findings is that for many participants the elements that contribute to representational processes, such as education and occupation, were no longer ongoing, and perhaps the cognitive stimulation incurred by these activities had not been replaced with alternatives (Reed et al., 2011). These findings lend further weight to the argument that representational processes may not be useful predictors of global cognition and memory in healthy ageing populations.

With regard to parameters that were beyond the scope of the modelling studies, it was found that measures of current social and mental activity, which can be viewed as potentially contributing to a representational system that develops over the lifespan and remains relatively stable into older age (Craik & Bialystok, 2006), were not related to the EF/PR and CCE composites. This suggests that these measures may not be important contributors to CR capacity. This was unexpected due to previous literature highlighting the protective role of these frequently used CR proxies against cognitive decline (Crowe et al., 2003; Fritsch et al., 2005; Valenzuela et al., 2011). However, this finding accords with the findings from the modelling studies in section I, where further research was recommended to explore the activation of CR capacity under this dual framework.

The relationship between subjective reports of EF as measured by the BRIEF-A and the CR capacity factors was also explored, as poor ratings on this measure have been shown to be related to cognitive complaints and MCI (Rabin et al., 2006). There was a trend toward a positive relationship between subjective EF scores and scores on both the EF/PR and CCE composites. This suggests that subjective reports of EF may be an indicator of CR capacity and the fact that scores on this measure are related to both arms of the CR capacity model provides further evidence for a reciprocal relationship between these factors (Craik & Bialystok, 2006).

Secondly, the pre-intervention data was used to profile CR capacity model measures as a function of subjective ratings of memory. Profiling revealed a significant difference between the low and high concern groups in scores on Retrospective Memory (p=.005, one-tailed), with the low concern group performing better, and also revealed a trend toward differences between the low vs. high concern groups in scores on EF/PR and Prospective Memory. Although these differences were not significant at the .006 alpha level (ps<.05, two-tailed), they provided additional support for the assertion that memory concerns may be a marker of decline in control processes. This finding supports previous research linking poorer performance on EF tasks with increased subjective memory complaints (Steinberg et al., 2013). As this group also performed poorly on the PRMQ measures of prospective and retrospective memory relative to those with low memory concerns, this group may be particularly vulnerable to the effects of age-related decline. Therefore, this group may benefit most from a targeted intervention aimed at boosting control processes, rather than representational processes which did not differ as a function of memory concerns.

Finally, the effects of a novel, adaptive response inhibition training on performance on the trained task, as well as inhibition-related (near transfer) and untrained tasks (far transfer) was investigated. The modelling studies in Section I and the pre-intervention profiling in Section II both provide support for the important role of control processes in CR capacity. As the modelling studies suggest CR capacity is driven by control processes, it follows that an intervention targeting control processes may also impact on CR capacity. Given the observed predictive relationship between control processes and global cognition/memory outcomes in study 5, and the finding that EF/PR explained a moderate amount of the variance in both MMSE and delayed recall scores (22% and 32% respectively), this also supports the argument that an intervention aimed at modifying EF/PR may improve global cognition/memory outcomes. It was found that following five weeks of computerised training on the novel training task, participants in both the active control and experimental groups significantly improved on the trained task, as well as on measures of processing speed and cognitive switching (near transfer). There was a trend towards improvement on a measure of response inhibition although these findings were not significant at the .006 alpha level (*p*=.04). Nevertheless, this finding suggests that inhibition may be modifiable in older adulthood through this novel computerised training task. The failure to find a significant time x group interaction effect means that improvements cannot be explicitly attributed to the intervention. However, it is of note that the differences in magnitude of the improvements from pre- to post-test (Cohen's *d*) in both groups indicate that the experimental group experienced larger performance gains than the active control group with regard to near transfer. This suggests that the adaptive training was more effective than the active control training in producing near transfer effects.

Far transfer effects in relation to the ER/PR composite, the remaining EF/PR indicators (immediate working memory and fluency), the CCE crystallised IQ indicator (WAIS-vocabulary), current cognitive enrichment, working memory, as well as measures of global cognition and memory were also investigated. Significant improvements were observed on the EF/PR composite for both groups, with effect sizes being larger for the active control group. A trend toward improvement was seen in both groups on the measure of current social activity (*p*=.008), with effect sizes appearing larger in the experimental group. Trends toward improvement were also seen in both groups on measures of working memory and fluency (*p*s<.05), with fluency gains appearing larger for the active control group. There was only one significant group x time interaction and this was in relation to current mental activity. Again, the active control group experienced larger gains than the experimental group. Training had no significant effects on measures of immediate recall, crystallised IQ, subjective EF or any of the measures of global cognition and memory.

A number of explanations have been put forward for the larger training gains in the active control group for some measures, as well as for the lack of interaction effects and far transfer effects. For the near transfer measures (training gains, processing speed, cognitive switching and response inhibition), the larger effects sizes observed in the experimental group suggest that the adapted training was more effective than the non-adaptive training, and perhaps if a larger sample size had been employed the interaction effects would have been significant, although this cannot be concluded until further research has been conducted in this regard. Larger effect sizes observed in the active control group for many of the far transfer measures suggests that for tasks not directly related to response inhibition, low level training may be sufficient to see an effect. The addition of a no-contact control group in future research could potentially help to clarify if this is the case. Other possible explanations for the lack of an interaction effect, as well as the lack of transfer effects to measures of global cognition/memory, include reduction in participant arousal levels due to the repetitive nature of the training task (Richmond et al., 2011). As the experimental group had considerably longer training sessions than the active control group, they may have experienced a dip in arousal toward the end of the training period and learning effects may have diminished. Furthermore, far transfer effects to measures of CCE and global cognition/memory measures may be related to the training dose, as Lampit et al. (2014) found that training session of less than 30 minutes may be ineffective.

Overall, this novel response inhibition training programme improved performance on the trained task as well as performance on related cognitive control measures of processing speed, cognitive switching and response inhibition on the EF/PR axis of CR capacity, with the experimental group experiencing larger effect sizes than the active control group. These findings demonstrate the plasticity of control processes and support the assertion that an important formative component of CR capacity can be boosted through targeted EF training. However, the training programme did not result in improvements on measures of CCE or global cognition/memory. The modelling studies in Section I found that a CR capacity model driven by EF/PR was predictive of global cognition/memory outcomes both at baseline and longitudinally. It is possible that gains in global cognition/memory measures were not observed in this small sample as training duration was not sufficient to result in the synaptic plasticity required for far transfer to these domains.

9.3 Theoretical and Practical Implications

The findings of both the modelling and training intervention sections of the research programme contribute to the existing literature on CR in several ways. In terms of theoretical implications, the modelling studies are of particular importance. Firstly, the modelling studies sought to expand on CR measurement paradigms, that drew solely on environmental enrichment based CR proxies, by including a range of indicators, hypothesised by Satz et al.

(2011) to be involved in CR capacity in an a priori four-factor model. The construct validity of CR has been questioned due to multiple reserve indicators used across studies and the lack of an organisational structure in which to group these indicators (Jones et al., 2011; Satz et al., 2011). Exploratory analysis in the form of an EFA elucidated the organisation of a range of these hypothesised CR indicators and produced a two-factor solution comprised of EF/PR and CCE. This two-factor structure was confirmed in a CFA in the same dataset (MAAS) and was also validated in a secondary dataset (TILDA). Inclusion of a factor representing control processes together with a factor representing more traditional CR proxy measures reflective of cognitive enrichment over the lifespan in a CR capacity model has implications for the theoretical framework surrounding CR.

Previous research has called into question the protective role of traditional CR proxy measures with regard to cognitive decline and dementia due to the possibility that protective effects may be the result of differences in cognitive functioning (Tucker-Drob et al., 2009). A study on the construct validity of CR as indicated by traditional proxy measures, called into question the discriminant validity of CR and EF which suggests CR may be highly related to fluid executive abilities (Siedlecki et al., 2009). Stern's theory of neural reserve emphasises the potential role of higher order executive processes in CR as neural reserve operates by allowing greater flexibility in network selection, an ability believed to be captured by EF tasks (Tucker & Stern, 2011). Barulli and Stern (2013) also point out that the extent to which CR is based on acquired knowledge (e.g., crystallised abilities) versus cognitive processes (e.g., fluid abilities) remains an outstanding question in CR research. Despite research such as this linking EF and CR, thus far, the hypothesis that executive processes are directly involved in CR capacity has not been tested empirically. The modelling studies have contributed to the CR literature in this regard by firstly supporting previous findings of a strong relationship between EF and traditional CR proxy measures, and secondly demonstrating that this two-factor CR capacity model is predictive of global cognition/memory outcomes over time. The modelling studies also helped to clarify the extent of the contribution of each factor to CR capacity. It appeared that when EF/PR and CCE were both specified as direct contributors to CR capacity in a predictive model, CCE had a negative relationship with CR capacity. The role of EF/PR however is consistently strong and significant across models, which supports the idea that, in healthy ageing populations, CR capacity may be based more strongly on executive processes than cognitively enriching experiences across the lifespan.

The modelling studies in Section I have helped to develop a clearer understanding of the mechanisms involved in CR capacity in healthy ageing populations, and the contribution of control processes in particular. This could have important implications for primary prevention of cognitive decline and dementia in healthy ageing, as well as for health policy. For instance, an important practical implication of these findings relates to the potential modifiability of CR capacity. Research has suggested that EF training can have beneficial effects in healthy older adults, therefore targeted EF training has the potential to boost an important component of CR capacity in this population. Targeting EF in mid- to late-life healthy adults could potentially improve cognitive outcomes in this group as there is evidence that executive processes negatively decline from mid-life onwards (Zelazo et al., 2004). The response inhibition training study aimed to demonstrate the modifiability of this particular EF and related functions. While results did not find significant differences in EF/PR measures for the active control and experimental groups, the magnitude of training gains was larger in the experimental group for measures of response inhibition, processing speed and cognitive switching. This suggests that EF may represent an important target for intervention in those aged 50 and over. The finding that EF appears to contribute to CR capacity in healthy ageing populations and has the potential to be modified through targeted cognitive training could have broader societal implications in terms of primary prevention and policy development. For instance, the current consensus on boosting CR stresses the importance of staying cognitively active. The findings from this research programme have helped to narrow the scope in terms in what activities in particular might be most beneficial, for instance, tasks designed to target control processes. Practical implications of this could involve further research to developtimely and easily accessible short-term cognitive training interventions aimed at boosting this important component of CR capacity and improving cognitive outcomes over time. Furthermore, clear and simple public messages on the important role of EF in cognitive health could be developed along with advice on the kinds of activities that might target this core component of CR capacity in daily life. In its focus on healthy ageing, the research programme predominantly speaks to primary prevention, however it represents an important first step in understanding the role of EF/PR and CCE in clinical populations. Given the incurable nature of dementia, future research could examine the modifiability of EF in populations affected by pathology and this could then inform secondary and tertiary prevention by potentially reducing the impact of disease processes.

9.4 Future Research

A future programme of research could benefit from the inclusion of measures implicated in CR capacity by Satz et al. (2011), but that were beyond the scope of the modelling studies. Inclusion of these measures in a more comprehensive model could help elucidate their influence on the factor structure of the two-factor CR capacity measurement model, as well as the fit and structure of the longitudinal predictive models. Measures of social networks and mental activity were not captured in the MAAS longitudinal dataset, and a measure of literacy was administered to a very small participant pool. As discussed above, it was hypothesised that these variables would load on the CCE factor. Similarly, measures of divided attention and reasoning were not suitable for SEM analyses as they too were administered to a small subsection of MAAS participants. As a consequence of the iterative process of EFA, measures of selective attention, error monitoring and fluid IQ were removed from the analyses at an early stage. As discussed earlier in the chapter, it was hypothesised that indicators such as divided/selective attention, reasoning and error monitoring would load on the EF/PR factor and fluid IQ may cross-load on both constructs. Future research, however, should aim to include these measures in a more complete model of CR capacity in order to clarify these relationships.

Furthermore, while the longitudinal models succeeded in capturing performance on cognitive outcome measures that have demonstrated predictive ability with regard to clinically significant decline (i.e., global cognition, long-term memory, and subjective memory) (Jacobs et al., 1995; Jessen et al., 2010; A. J. Mitchell et al., 2014; Tombaugh & McIntyre, 1992), future research could benefit from expansion of these measures to include a broader range of memory outcomes. For instance, episodic memory performance has been shown to be impaired in participants with subjective memory complaints (Erk, S. et al., 2011) and is a known predictor of conversion to dementia in MCI (Landau et al., 2010). Future research should also seek to model CR capacity longitudinally in participants with varying degrees of memory concern/pathology (e.g., subjective cognitive decline, MCI, and dementia) in order to see if the model holds in these populations and continues to demonstrate predictive ability. Model investigation in populations with brain pathology would also allow for investigation of the differential roles of EF/PR and CCE in this group compared to healthy ageing. This could help to clarify the exact nature of the negative weighting of CCE on CR capacity that was observed in healthy individuals. Specifically, it would be of interest to see if the role of CCE in CR capacity activation becomes more prominent in populations with EF/PR deficits due to pathology. Replication of the CR capacity model relationships in a population affected by pathology could help to elucidate this.

Another approach, similar to that of Stern et al. (2009), could investigate differences in CR capacity in young and older individuals using imaging techniques. For instance, it is hypothesised that individuals with higher CR capacity will demonstrate patterns of task-related activation that are more efficient than those with lower CR capacity. Efficiency can be quantified as the amount of task-related activation as a function of task load. An efficient cognitive network will show less activation while demonstrating the same or better task performance. Differences in efficiency are expected to differ in young and older individuals as a function of CR capacity. Additionally, it is likely that individuals with high CR capacity will demonstrate greater network expression under high load conditions compared to low CR capacity individuals. This higher expression would likely correspond to better performance on tasks.

With regard to the modifiability of CR capacity, future research could benefit from the expansion of response inhibition training to include both young and older adults. Efficacy of training could then be investigated in individuals profiled as high vs. low CR capacity. Furthermore, investigation of training efficacy in varying populations such as subjective memory concerns and MCI/dementia could help to clarify the breadth of near and far transfer effects. The addition of a no-contact control group in future research could also help in determining if low-level training is as effective as adaptive training. Furthermore, as it was beyond the scope of the intervention study to re-test participants at varying intervals following training (days, weeks, months), it is unclear whether training gains were maintained following training. Future research could involve longer term follow-up assessments, as well a systematic quantified approach to decomposing training effects from low to high levels to aid the understanding of immediate and longer-term effects.

9.5 Conclusion

The findings of the present research programme provide evidence for a two-factor CR capacity model comprised of the control processes of EF and PR (EF/PR) and also a factor representing traditional enrichment CR measures (CCE). The predictive relationships between this CR capacity model and global cognition/memory outcomes were demonstrated both cross-sectionally and longitudinally in healthy adults in mid- and later-life. The modifiability of response inhibition which is a core indicator of EF/PR, an important formative component of CR capacity, was demonstrated in a small sample of healthy Irish participants aged over 50 years through a five-week online training programme, suggesting that control processes represent an important target for intervention in this group.

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Appendix A: DCU Research Ethics Approval for Studies 1-6

Appendix A (i). Ethics approval for studies 1 and 3

Ollscoil Chathair Bhaile Átha Cliath
Dublin City University

DCU

Dr. Kate Irving
School of Nursing and Human Sciences

1st July 2013

REC Reference: DCUREC/2013/178

Proposal Title: **Cognitive Risk and Protective Factors in Dementia**

Applicants: Dr. Kate Irving, Dr. Lorraine Boran, Ms. Lisa McGarrigle

Dear Kate,

This research proposal qualifies under our Notification Procedure, as a low risk social research project. Therefore, the DCU Research Ethics Committee approves this research proposal. Materials used to recruit participants should note that ethical approval for this project has been obtained from the Dublin City University Research Ethics Committee. Should substantial modifications to the research protocol be required at a later stage, a further submission should be made to the REC.

Yours sincerely,

DCU Research & Innovation

Dónal O'Mathúna

Dr. Donal O'Mathuna
Chairperson
DCU Research Ethics Committee

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Appendix A (ii). Ethics approval for studies 2 and 4

Ollscoil Chathair Bhaile Átha Cliath
Dublin City University

Ms Lisa McGarrigle
School of Nursing and Human Sciences

2nd July 2014

REC Reference: **DCUREC/2014/166**

Proposal Title: **Cognitive Risk and Protective Factors in Dementia**

Applicants: Ms Lisa McGarrigle, Dr Lorraine Boran, Dr Kate Irving

Dear Lisa,

This research proposal qualifies under our Notification Procedure, as a low risk social research project. Therefore, the DCU Research Ethics Committee approves this research proposal. Materials used to recruit participants should state that ethical approval for this project has been obtained from the Dublin City University Research Ethics Committee. Should substantial modifications to the research protocol be required at a later stage, a further submission should be made to the REC.

Yours sincerely,

DCU
Research & Innovation

Dr. Donal O'Mathuna
Chairperson
DCU Research Ethics Committee

Taighde & Nuálaíocht Tacaíocht
Ollscoil Chathair Bhaile Átha Cliath,
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Research & Innovation Support
Dublin City University,
Dublin 9, Ireland

T +353 1 700 8000
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E research@dcu.ie
www.dcu.ie

Appendix A (iii). Ethics approval for studies 5 and 6

Oliscoil Chathair Bhaile Átha Cliath
Dublin City University

14th April 2015

Dr Lorraine Boran
School of Nursing and Human Sciences

REC Reference:	**DCUREC/2015/033**
Proposal Title:	**Exploring the relationship between cognitive reserve and function in healthy older adults.**
Applicant(s):	**Dr Lorraine Boran; Dr Kate Irving; Ms Lisa Garrigle**

Dear Lorraine,

Further to Expedited Review, the DCU Research Ethics Committee approves this research proposal.

Materials used to recruit participants should note that ethical approval for this project has been obtained from the Dublin City University Research Ethics Committee.

Should substantial modifications to the research protocol be required at a later stage, a further submission should be made to the REC.

Yours sincerely,

Dónal O'Mathúna

Dr Dónal O'Mathúna
Chairperson
DCU Research Ethics Committee

DCU Research & Innovation

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Appendix B: MAAS Kolmogorov-Smirnov (K-S) Test Statistics and Associated *p*-Values across Age Groups

	24-82 year olds			*24-49 year olds*			*50-64 year olds*			*65-82 year olds*		
	N	**K-S**	***p*-value**	***N***	**K-S**	***p*-value**	***N***	**K-S**	***p*-value**	***N***	**K-S**	***p*-value**
EF/PR Indicators												
Stroop Colour Word Test	1500	.102	.000	784	.085	.000	379	.132	.000	345	.098	.036
Fluency (animals)	1568	.062	.000	796	.060	.000	392	.090	.000	389	.073	.200
Concept Shifting Test	1528	.091	.000	788	.077	.000	381	.128	.000	368	.096	.045
Letter Digit Modalities Test	1568	.045	.000	800	.038	.079	392	.067	.016	385	.048	.200
Verbal Learning Test	1554	.052	.000	789	.188	.000	280	.098	.000	385	.119	.004
CCE Indicators			.000									
Education Level	1578	.149	.000	801	.176	.000	394	.195	.000	392	.183	.000
Level of Occupational Attainment (LOA)	1578	.173	.000	801	.179	.000	394	.177	.000	392	.183	.000
Groningen Intelligence Test (Vocabulary)	1561	.110	.000	795	.135	.000	389	.106	.000	386	.155	.000

Appendix C: MAAS CFA Fit Statistics for Males and Females

Appendix C (i). Fit statistics for a two-factor CFA model of EF/PR and CCE for male participants (n=860) aged 24-82 years

Statistic	Result
χ^2	67.147
df	18
p	.0000
RMSEA (90% CI)	0.056 (0.042-0.071)
CFI	0.978
TLI	0.965
WRMR	0.739

Appendix C (ii). Fit statistics for a two-factor CFA model of EF/PR and CCE for female participants (n=718) aged 24-82 years

Statistic	Result
χ^2	69.514
df	18
p	.0000
RMSEA (90% CI)	0.063 (0.048-0.079)
CFI	0.975
TLI	0.960
WRMR	0.771

Appendix C (iii). Fit statistics for a two-factor CFA model of EF/PR and CCE for male participants (n=403) aged 24-49 years

Statistic	Result
χ^2	46.209
df	18
p	.0003
RMSEA (90% CI)	0.062 (0.040-0.085)
CFI	0.970
TLI	0.954
WRMR	0.639

Appendix C (iv). Fit statistics for a two-factor CFA model of EF/PR and CCE for female participants (n=398) aged 24-49 years

Statistic	Result
χ^2	22.333
df	18
p	.2175
RMSEA (90% CI)	0.025 (0.000-0.054)
CFI	0.995
TLI	0.993
WRMR	0.482

Appendix C (v). Fit statistics for a two-factor CFA model of EF/PR and CCE for male participants (n=224) aged 50-64 years

Statistic	Result
χ^2	27.433
df	18
p	.0712
RMSEA (90% CI)	0.048 (0.000-0.083)
CFI	0.983
TLI	0.974
WRMR	0.457

Appendix C (vi). Fit statistics for a two-factor CFA model of EF/PR and CCE for female participants (n=169) aged 50-64 years

Statistic	Result
χ^2	23.659
df	18
p	.1665
RMSEA (90% CI)	0.043 (0.000-0.086)
CFI	0.992
TLI	0.988
WRMR	0.466

Appendix C (vii). Fit statistics for a two-factor CFA model of EF/PR and CCE for male participants (n=233) aged 65-82 years

Statistic	Result
χ^2	14.061
df	18
p	.7251
RMSEA (90% CI)	0.000 (0.000-0.044)
CFI	1.000
TLI	1.013
WRMR	0.359

Appendix C (viii). Fit statistics for a two-factor CFA model of EF/PR and CCE for female participants (n=151) aged 65-82 years

Statistic	Result
χ^2	34.503
df	18
p	.0109
RMSEA (90% CI)	0.078 (0.037-0.117)
CFI	0.950
TLI	0.922
WRMR	0.606

Appendix D: TILDA Kolmogorov-Smirnov (K-S) Test Statistics and Associated *p*-Values across Age Groups

	50-79 year olds			***50-64 year olds***			***65-79 year olds***		
	N	**K-S**	***p*-value**	***N***	**K-S**	***p*-value**	***N***	**K-S**	***p*-value**
EF/PR Indicators									
Sustained Attention to Response Task	3153	.176	.000	1896	.178	.000	1257	.157	.000
Fluency (animals)	3321	.064	.000	1929	.055	.000	1392	.083	.000
Colour Trials Test	3276	.066	.000	1931	.063	.000	1345	.053	.000
Choice Reaction Time	3239	.065	.000	1918	.068	.000	1321	.054	.00
Verbal Learning Test	3337	.100	.000	1941	.104	.000	1396	.092	.000
CCE Indicators									
Education Level	3351	.162	.000	1947	.146	.000	1404	.187	.000
Occupation Level	3351	.216	.000	1947	.215	.000	1404	.216	.000

Appendix E: MAAS SEM Correlation Matrices for latent variables

Baseline

	EF/PR	CCE
50-64 Year Olds		
EF/PR	1.000	
CCE	0.881	1.000
CR	0.967	0.731
65-82 Year Olds		
EF/PR	1.000	
CCE	0.706	1.000
CR	0.955	0.465

6-Year FU

	EF/PR	CCE
50-64 Year Olds		
EF/PR	1.000	
CCE	0.904	1.000
CR	0.923	0.671
65-82 Year Olds		
EF/PR	1.000	
CCE	0.752	1.000
CR	0.942	0.486

12-Year FU

	EF/PR	CCE
50-64 Year Olds		
EF/PR	1.000	
CCE	0.931	1.000
CR	0.929	0.730
65-82 Year Olds		
EF/PR	1.000	
CCE	0.749	1.000
CR	0.913	0.414

Appendix F: TILDA Model Integrity Tables

Appendix F (i). Fit statistics for the respecified one-factor and mediator models across age-groups compared to fit of original two-factor model

	One-Factor Model		**EF/PR as Mediator**		**Original Two-Factor Model**	
Model 1	50-64 years	65-79 years	50-64 years	65-79 years	50-64 years	65-79 years
χ^2	258.043	231.091	223.872	191.262	259.760	236.980
df	31	31	28	28	33	33
p	0.000	0.000	0.000	0.000	0.000	.0000
RMSEA	0.061	0.068	0.060	0.064	0.059	0.066
(90% CI)	[0.055, 0.068]	[0.060, 0.076]	[0.053, 0.067]	[0.056, 0.073]	[0.053, 0.066]	[0.059, 0.074]
CFI	0.942	0.931	0.950	0.943	0.942	0.929
TLI	0.916	0.899	0.919	0.909	0.921	0.904
WRMR	1.450	1.394	1.331	1.247	1.454	1.416
Model 2						
χ^2	115.794	134.500	91.990	83.306	121.262	92.322
df	40	40	36	36	33	33
p	0.000	0.000	0.000	0.000	0.000	0.000
RMSEA	0.069	0.078	0.063	0.058	0.037	0.036
(90% CI)	[0.055, 0.084]	[0.064, 0.093]	[0.047, 0.079]	[0.042, 0.075]	[0.030, 0.044]	[0.027, 0.045]
CFI	0.943	0.899	0.958	0.949	0.976	0.978
TLI	0.921	0.861	0.935	0.923	0.967	0.970
WRMR	0.869	1.013	0.759	0.764	1.050	0.904

Appendix F (ii). Summary of three-pronged approach to suppression testing

	Model 1	**Model 2**
1. Relationships between IVs and DVs	*IV's*: - Significant correlations between all IV's for both age groups. *DV's*: - Significant correlations between all IV's and all DV's.	*IV's:* As per Model 1 *DV's:* - Both EF/PR and CCE indicators, for both age-groups, have non-significant correlations with subjective memory
2. *spc* > *r*	None of the *spc*'s, whether significant or non-significant, were greater than *r*.	In relation to the subjective memory outcome measure, some of the *spc*'s were greater than *r*, however none of these correlations were significant (*p*s>.05).
3. Delta Method (CCE as mediator)	- Indirect effect of EF/PR on delayed recall < 0 for both age groups	- No significant indirect effect of EF/PR on any of the outcome variables for both age groups.

Appendix F (iii). AIC fit statistics for moderation model and two-factor model (re-run using MLR estimator)

	CCE as moderator		**Original Two-Factor model**	
Model 1	50-64 years	65-79 years	50-64 years	65-79 years
AIC	75986.83	55925.16	76247.04	56141.09
Model 2				
AIC	72486.15	53888.68	72656.19	54072.54

Appendix G: Recruitment Advertisement

Cognitive Reserve Training Study

PRINCIPAL INVESTIGATORS AND RESEARCHERS

Dr. Lorraine Boran, Dr. Kate Irving, Ms Lisa McGarrigle

School of Nursing and Human Sciences, DCU

CALL FOR VOLUTEEERS: THE COGNITIVE RESERVE TRAINING STUDY

We are looking to recruit healthy adults (aged 50 or over), including adults who believe they are experiencing memory loss (aged 50 or over), to take part in a brain training study. The goal of the study is to investigate the effects of an innovative type of computerised brain training on cognitive reserve. Cognitive reserve can be understood as the ability of the brain to cope with brain damage or age-related cognitive decline. This study predicts general improvements in cognitive reserve and broader cognitive abilities as a result of regular training using an online brain trainer we have developed.

As the training phase of the study will involve training online we are specifically looking for older adults with access to a computer and the internet. Participants will be required to play the brain training game online at home for approximately 30 minutes per day, 5 days a week, for 5 weeks in total. We will assess aspects of cognitive functioning in Dublin City University before and after training.

To find out more please contact:
Lisa McGarrigle: Phone – XXXXXXXX; email: XXXXXXXXX

Please note:

1. Only those who provide informed consent will be eligible to take part in the study. You will be asked to sign a consent form that will then be linked to your study data through a unique numerical code.
2. This study is not a comprehensive medical and psychological assessment and therefore you cannot receive a diagnosis about your memory as a result of your participation. However, should you have any concerns about your memory, you can request a copy of your test scores for the attention of your GP.

If, for any reason, you have any concerns about your memory, you should consider consulting your GP for advice.

Appendix H: Participant Information Sheet

Cognitive Reserve Training Study

PRINCIPAL INVESTIGATORS AND RESEARCHERS

Dr. Lorraine Boran, Dr. Kate Irving, Ms Lisa McGarrigle

School of Nursing and Human Sciences, DCU

Introduction:

We invite you to participate in a research study in the School of Nursing and Human Sciences in Dublin City University (DCU).This research is being funded by the European Community's Framework Programme Seven (FP7) as part of the In-MINDD project (www.in-mindd.eu) and is being carried out by Lisa McGarrigle, a PhD candidate in part fulfilment of a PhD. If you are interested in participating, please read the following information carefully. If you need additional information please contact Lisa or a member of the research team (see above contact details).

Background and aims of the study:

Cognitive reserve (CR) is a measure of the brain's ability to cope with brain damage and keep functioning at normal levels. Research suggests that a person's level of cognitive reserve should not be viewed as a fixed trait determined early in life, but as something that may be actively enhanced in mid and late life through participation in cognitively stimulating activities. The aim of this study is to investigate the effects of a new type of brain training on the cognitive reserve of healthy adults. This study predicts general improvements in cognitive reserve and broader cognitive abilities as a result of regular training using an online brain trainer we have developed.

This study will:

- help us understand the relationship between cognitive reserve and other cognitive abilities such as memory

- help us discover if targeted CR brain training can boost cognitive reserve and broader cognitive abilities

Am I eligible to take part in the study?

To participate in this study you must be a healthy adult aged 50 years or older, living independently in the community. You must be a fluent English speaker and be able to read and use/access a computer with internet access. You must have no history of dementia or other neurological conditions such as Parkinson's disease; and no significant psychiatric illness, depression diagnosis, learning disability, significant hearing or visual impairment.

What does participation in the study involve?

If you agree to participate in this study you will be required to visit Dublin City University on two occasions, for approximately 2 hours each time: once before and once after 5 weeks of brain training. In DCU you will participate in a number of computerised and pen and paper test sessions. The brain training will be performed online at home and will take approximately 30 minutes a day, 5 days a week for 5 weeks. There are two versions of the brain training program, and you will be randomised to one of them. Depending on the program to which you will be invited, time commitment and challenge levels may vary.

Please note: Motivated compliance with the training is vital to the success of this study.

Research has shown that effective improvements in brain performance only occur when the brain is constantly pushed to improve on past performance. Consequently, the training task is designed to adapt to your current performance level (i.e., it gets harder as you improve, or easier if your performance drops). The goal of training is to advance through as many levels of difficultly as possible. To perform at the higher task levels your brain will need to physically change and this takes effort.

Participation in this study is voluntary and you may withdraw at any time.

Are there any risks?

There are no known risks associated with brain training. The duration of the testing in DCU (up to 2 hours) may involve some degree of subjective boredom but you will be given short regular breaks between tasks. However, as this study will investigate aspects of your memory and mood there is a possibility you may become concerned about your memory or performance on the various tasks. Please note that you are free to withdraw from the study at any time and without any consequences. Additionally, you are advised to discuss your concerns with your local general practitioner (GP). Performance on any of the tests may be the result of a number of possible reasons and poor performance should not be considered evidence of a significant medical problem.

What are the benefits of participating in this research?

Your participation in the study will help us understand the relationship between cognitive reserve and other cognitive abilities such as memory and help us discover if targeted brain training can boost cognitive reserve and broader cognitive abilities. The 5 weeks of brain training may potentially benefit you directly by increasing CR and boosting protection against cognitive decline. Please be aware that this study is for research purposes only and is not a comprehensive medical and psychological assessment. You will not receive any diagnosis as a result of participation in this study. However, if you have any concerns about your memory or performance on any of the tests you can request feedback from Dr Lorraine Boran and a copy of your test scores can be made available for your GP.

How will my information and identity be protected?

Your identity will remain confidential. All information collected in this study will be used exclusively for research purposes. Participant data will be fully anonymised in any scientific publication. We ensure proper safeguards so that participation is confidential and data are securely stored and protected. This study will be run with the approval of DCU Research Ethics Committee (Decision Number: DCUREC/2015/033).

What will happen to the data?

The data will be used for the purposes of dissertation writing for PhD. Findings from this research may be published in academic journals and reports, however, these publications will not contain any identifying information. In accordance with standard research data management practices, data belonging to you will be securely retained for 5 years in Dublin

City University after the study is completed. This material will not be used in future unrelated studies without obtaining further specific permission from you. If requested, a one-page summary of the research will be available following submission and examination of the thesis. Individual feedback will not be offered as a routine part of the research; however, you may request feedback on your test performance for the attention of your GP if you have concerns about your memory.

How is this study being funded?

This study is being funded by the European Community's Framework Programme Seven (FP7) as part of the In-MINDD project (www.in-mindd.eu). All materials developed as part of this study have been funded from this project.

Further Information

If you would like further information, please contact Lisa McGarrigle: email: XXXXXXX; Phone – XXXXXX

If participants have concerns about this study and wish to contact an independent person, please contact: The Secretary, Dublin City University Research Ethics Committee, c/o Research and Innovation Support, Dublin City University, Dublin 9. Tel 01-7008000

Appendix I: Participant Consent Form

Cognitive Reserve Training Study

PRINCIPAL INVESTIGATORS AND RESEARCHERS

Dr. Lorraine Boran, Dr. Kate Irving, Ms Lisa McGarrigle

School of Nursing and Human Sciences, DCU

Background and Aims of the Research

Cognitive reserve (CR) is a measure of the brain's ability to cope with brain damage and keep functioning at normal levels. Research suggests that a person's level of cognitive reserve should not be viewed as a fixed trait determined early in life, but as something that may be actively enhanced in mid and late life through participation in cognitively stimulating activities. The aim of this study is to investigate the effects of a new type of brain training on the cognitive reserve of healthy adults. This study predicts general improvements in cognitive reserve and broader cognitive abilities as a result of regular training using an online brain trainer we have developed.

This study will:

- help us understand the relationship between cognitive reserve and other cognitive abilities such as memory
- help us discover if targeted CR brain training can boost cognitive reserve and broader cognitive abilities

Confidentiality

Your identity will remain confidential. All information collected in this study will be used exclusively for research purposes. Participant data will be fully anonymised in any scientific publication. This material will not be used in future unrelated studies without obtaining further specific permission from you. (Note: confidentiality of information provided can only be protected within the limitations of the law - i.e., it is possible for data to be subject to subpoena, freedom of information claim or mandated reporting by some professions)

Potential Concerns about Memory and/or Well-Being

Answering questions about memory and mood and taking part in cognitive testing may cause you to feel anxious or concerned about your performance. Please discuss any concerns with your GP and please note that this study is not a comprehensive medical or psychological assessment. Therefore, you will not receive any form of diagnosis as a result of participation in this study

Participant – please complete the following (<u>Circle Yes or No</u> for each question)

I have read the Information Sheet (or had it read to me)	*Yes/No*
I understand the information provided	*Yes/No*
I have had an opportunity to ask questions and discuss this study	*Yes/No*
I have received satisfactory answers to all my questions	*Yes/No*
I understand I may withdraw from the study at any time	*Yes/No*
I am aged 50 or above	*Yes /No*
I have not been diagnosed with dementia	*Yes/No*
*Can you confirm that you do **<u>not</u>** suffer from a neurological condition such as Parkinson's disease, significant psychiatric illness, depression diagnosis, learning disability, significant hearing or visual impairment*	*Yes/No*

Signature

I have read and understood the information in this form. My questions and concerns have been answered by the researchers, and I have a copy of this consent form. Therefore, I consent to take part in this research project

Participants Signature: ______________________________

Name in Block Capitals: ______________________________

Witness: ______________________________

Date: ______________________________

Appendix J: Debriefing Sheet

Debrief Statement

Why is this study being conducted?

This study is being conducted to help us understand the relationship between cognitive reserve and other cognitive abilities such as memory and to help us discover if targeted brain training can boost cognitive reserve and broader cognitive abilities

How were the aims of this study achieved?

Taking part in this study involved completing a number of tasks relating to memory, mood, lifestyle and cognitive functioning both before and after 5 weeks of computerised brain training.

Why is this important to study?

This study is important as it predicts general improvements in cognitive reserve and broader cognitive abilities as a result of regular training using an online brain trainer we have developed.

What if I want to know more?

If requested, a one-page summary of the research will be available following submission and examination of the thesis. Individual feedback will not be offered as a routine part of the research; however, you may request feedback on your test performance for the attention of your GP if you have concerns about your memory. Please be aware that this study is for research purposes only and is not a comprehensive medical and psychological assessment. You will not receive any diagnosis as a result of participation in this study. However, if you have any concerns about your memory or performance on any of the tests you can request feedback from Dr Lorraine Boran and a copy of your test scores can be made available for your GP.

If you would like to request a one-page summary of the research findings when it is completed and submitted for examination, please contact XXXXXXXXX

If you have any concerns about this study and wish to contact an independent person, please contact: The Secretary, City University Research Ethics Committee, c/o Office of the Vice-President for Research, Dublin City University, Dublin 9, You may also contact project supervisors, Dr. Lorraine Boran (Tel: 01700XXXX) and Dr Kate Irving (Tel: 01 700XXXX).

Appendix K: Comparison of Original CRIq Occupation and ISCO-08 Categories

CRIq levels	CRIq categories	ISCO-08 categories
Level 1	Low skilled manual work (e.g., agricultural worker, gardener, housekeeper (hotel), waiter, driver, mechanic, plumber, call center operator, electrician, etc.)	Plant and machine operators, and assemblers (for example: machine operator, van driver)
		Elementary occupations (for example: cleaner, farm labourer, building construction labourer)
Level 2	Skilled manual work (e.g., craftsman, clerk, cook, shop assistant, tailor, nurse, professional soldier, barber/hairdresser, etc.)	Service and sales workers (for example: shopkeeper, chef, child care worker, hairdresser, waitress)
		Skilled agriculture, forestry and fishery workers (for example: forestry worker, vegetable grower, farmer)
		Craft and related trades workers (for example: carpenter, builder, jewellery maker, baker)
Level 3	Skilled non-manual work (e.g., shopkeeper, white-collar worker, priest or monk/nun, sales representative, real estate agent, nursery school teacher, musician, etc.)	Technicians and associate professionals (for example: engineering technician, photographer, ICT operations technician)
		Clerical support workers (for example: receptionist, office supervisor, clerical worker)
Level 4	Professional occupation (e.g., CEO of a small company, qualified freelancer, teacher, contractor, lawyer, engineer, etc.)	Professionals (for example: medical doctor, teacher, engineer, artist, accountant)
Level 5	Highly responsible or intellectual occupation (e.g., CEO of a large company, judge, university professor, top manager, politician, surgeon, etc.)	Managers (for example: managing director, senior government official, hotel or restaurant manager)