Executive Function Abilities, Cognitive Ageing, and Cognitive Decline

A thesis submitted for the degree of Doctor of Philosophy

by

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Dedication

This PhD degree is dedicated to my mother,

Mrs Titilayo Omowunmi (Shofolahan) Idowu,

who went to heaven during its completion,

and for who this degree would not have been possible.

Thank you mummy.

"All that I am, or hope to be, I owe to my angel mother. - Abraham Lincoln"

Abstract

Decline in cognitive abilities is a predominant feature of cognitive ageing and neuropathological conditions, which is attributed to the decline of executive functions (EFs). Four EFs are suggested to be particularly important, dual-tasking (DT), inhibition, shifting, and working memory (WM) updating. As part of the research completed in this thesis, two studies sought to determine the age-associated trajectory of decline of these abilities as this has not been extensively researched. An initial literature review (Chapter 2) evaluated how these abilities have previously been examined in cognitively healthy and pathological impaired older adults.

A cross-sectional behavioural study (Chapter 3) conducted between young and older adults where each EF was assessed with a pair of tasks, showed age-associated decline in some measures. Results further demonstrated that inhibition, shifting, and updating declined at a comparable high rate, whereas DT declined independently at a lower rate. A following correlation analysis (Chapter 4) between task pair measures of each EF in both age groups, found a significant positive correlation in DT in the older adults. Confirmatory factor analysis (Chapter 4) of these task measures revealed the older adults showed a better common EF factor loading than the young adults. Furthermore, correlation loading analysis between the EFs showed a weakly correlated four-factor model in the young adults, and three- and two-factor models in the older adults, indicating age-related structural change of EFs due to dedifferentiation (Koen & Rugg, 2019; La Fleur et al., 2018).

Lastly, a voxel-based morphometry study (Chapter 6), using secondary imaging data from the OASIS-3 database (LaMontagne et al., 2019) of participants ranging from cognitive healthy to advance Alzheimer's disease, identified substantial atrophy in the medial temporal lobes but not in the prefrontal cortex, the region primarily associated with EF processing. Nevertheless, atrophy in midbrain structures which are important for EF processing seemed to be associated with performance in the EF tasks employed.

The findings of this thesis illustrate that cognitive ageing is not a unitary process, therefore, further research into how the trajectory of the four EFs differs in neuropathological conditions would aid in understanding cognitive impairment greatly.

Key words: Executive functions, cognitive abilities, cognitive ageing, cognitive decline, confirmatory factor analysis, dual-task, inhibition, shifting, WM updating.

Declaration

I hereby declare that this thesis has not been, and will not be submitted, in whole or in part to another University for the award of any other degree.

Related publication:

Idowu, M., Parton, A., & Szameitat, A. (2020). Investigating early changes in cognitive ability in the cognitively healthy and early-stage cognitively impaired older adult populations. *Alzheimer's & Dementia, 16, e037384.* (Poster abstract.)

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Glossary of Abbreviations

ACC	Anterior Cingulate Cortex
AD	Alzheimer's disease
ADL	Activities of Daily Living scale
ANOVA	Analysis of variance
APA	American Psychiatric Association
ApoE	Apolipoprotein E
APP	β-Amyloid Precursor Protein
BA	Brodmann area
BDS	Backward digit recall span task
CAT12	Computational Anatomy Toolbox - 12
CDR	Clinical Dementia Rating scale
CE	Central Executive
CFA	Confirmatory factor analysis
CH	Cognitively Healthy
DLPFC	Dorsolateral prefrontal cortex
DMPLC	Dorsomedial prefrontal cortex
DSM-IV	Diagnostic and Statistical Manual IV
DT	Dual-task
EF	Executive Function
FDG PET	8-Fluorodeoxyglucose Positron Emission Tomography
fMRI	Functional Magnetic Resonance Imaging
FTD	Frontotemporal dementia
GAS	Geriatric Anxiety Scale
GDS	Geriatric Depression Scale
GM	Gray matter
IADL	Instrumental Activities of Daily Living scale
ICD-11	International Classification of Diseases - 11
LBD	Lewy body disease
LTM	Long-term memory

MCI	Mild cognitive impairment
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
MRI	Magnetic Resonance Imaging
ms	Millisecond
MTL	Medial temporal lobe
NFT	Neurofibrillary tau tangle
NINCDS – ADRDA	National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association
OFC	Orbitofrontal Cortex
PD	Parkinson's disease
PFC	Prefrontal cortex
PIS	Participant Information Sheet
PRP	Psychological refractory period paradigm
PSEN1	Presenilin 1
PSEN2	Presenilin 2
R1	Response 1
R2	Response 2
RT	Response time
s	Second
S1	Stimuli 1
S2	Stimuli 2
SD	Standard deviation
SE	Standard error
SOA	Stimulus onset asynchrony
SPM	Statistical Parametric Mapping
SPSS	Statistical Package for the Social Sciences
ST	Single-task
STM	Short-term memory
TEA	Test for everyday attention
TMT	Trail making test

VaD	Vascular dementia
VBM	Voxel-based morphometry
VLPFC	Ventrolateral Prefrontal Cortex
VMPLC	Ventromedial Prefrontal Cortex
WHM	White matter
WM	Working Memory

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Chapter 1, Introduction

1.1 Introduction

Non-pathological cognitive ageing, or age-associated cognitive decline, is an important area of research. Cognitive abilities refer to mental processes that regulate and control our cognition, of which language, memory, and executive functions (EFs) are considered subsets. Studying the gradual decline and/or preservation of such processes allows for a better understanding of the trajectories of ageing and its differentiation from pathological cognitive impairment (Craik & Salthouse, 2008; Petersen et al., 1997; Salthouse, 2005, 2012; Salthouse et al., 1989; Salthouse & Meinz, 1995). Moreover, not all cognitive abilities are affected by ageing or decline at the same rate in older adults as compared with younger adults, due to individual variability (Craik, Eftekhari, et al., 2018). Similarly, in some older adults, the rate of cognitive decline can be substantially greater than expected, and these individuals may develop mild cognitive impairment (MCI), or a form of dementia (Riddle, 2007).

Accordingly, with a progressively ageing population, there is an urgent need to distinguish between cognitive abilities that have an increased or decreased susceptibility to normal ageing in order to aid in the early detection, monitoring, and potential treatment of pathological cognitive impairment, i.e. dementia. In the United Nations World Population Ageing 2019 report, there was estimated to be approximately 143 million individuals aged 80 years and older globally, which is expected to triple to 426 million by 2050. Additionally, data from the World Population Prospects: the 2019 Revision stated the number of individuals aged 65 years and older is projected to increase from one in eleven in 2019 (9%) to one in six (16%) by 2050 (United Nations, 2020).

Normal ageing supports the maintenance of cognitive ability, which is of great importance for preserving independence in older life (World Health Organisation, 2020). In the early to mid-twenties, cognitive abilities are thought to be at their optimum, before gradually declining with advanced age (Nissim et al., 2017; O'Shea et al., 2016). Thus, age-associated impairments in reasoning, processing speed, and particularly memory (Craik & Salthouse, 2008; Steinberg et al., 2013; Tromp et al., 2015), may start to arise at around 50 years of age

(Goh & Park, 2009; Hedden & Gabrieli, 2004). However, life experiences such as education, travelling and employment, may compensate for such deteriorations (Grady, 2012). Nevertheless, the transition to pathological cognitive impairment, particularly MCI and subsequently dementia, is not fully understood.

MCI is regarded as a precursor for all dementias, i.e. an intermediate stage between healthy cognition and pathological decline (Gauthier et al., 2006; Mufson et al., 2012). Approximately 5-20% of individuals aged 65 and over are living with MCI, with an annual average rate of 10-17% progressing to Alzheimer's disease (AD), the commonest type of dementia (Alzheimer's Society, 2015; Association Alzheimer's, 2017; Reinvang et al., 2012). Dementia is a group of progressive neurodegenerative disorders affecting approximately 850,000 individuals in the United Kingdom and 50 million globally, which is predicted to increase to 152 million by 2050. AD is estimated to affect 1 in 14 individuals aged 65 and over, increasing to 1 in 6 in individuals aged 80 and over. Although AD is usually associated with older age, approximately 1 in 20 incidences (i.e. 5%) are from individuals aged between 40 to 65. Hence, it is a major public health issue as there is currently no cure (Association Alzheimer's, 2017; National Health Service, 2021).

This study aimed to investigate how EFs differ as a consequence of cognitive ageing and pathological impairment. Assessment was focused on four functions commonly utilised in everyday life, dual-tasking, inhibition, shifting and updating (Alvarez & Emory, 2006; Baddeley, 2012; Miyake, Friedman, et al., 2000; Suchy, 2009). The aim was to better understand the nature and rate of their decline in order to gain further knowledge in the area and possibly limit public health burden in the future.

This introductory chapter will present an overview on cognition, its functional neuroanatomical correlates, and an overview of the four cognitive abilities relevant to this thesis. A discussion of age-associated cognitive decline and how it differs from cognitive impairment, including a description on how neuropathological changes in MCI and AD correlate with reduced cognitive abilities will also be presented. The chapter will conclude with an outline of the aims of the thesis.

1.2 Cognition and Cognitive Ability

Cognition refers to our ability to think, the mental process used in acquiring knowledge, such as attention, memory, perception, reasoning, and problem-solving. It is contingent on control from the frontal lobes, specifically the prefrontal cortex (PFC) with interaction from other brain regions, including the hippocampus within the temporal lobe (Craik & Salthouse, 2008; Garcia-Alvarez et al., 2019; Riggall & Postle, 2012). A summary of these processes and their associate brain regions can be viewed in Figure 1.1. and Table 1.1.

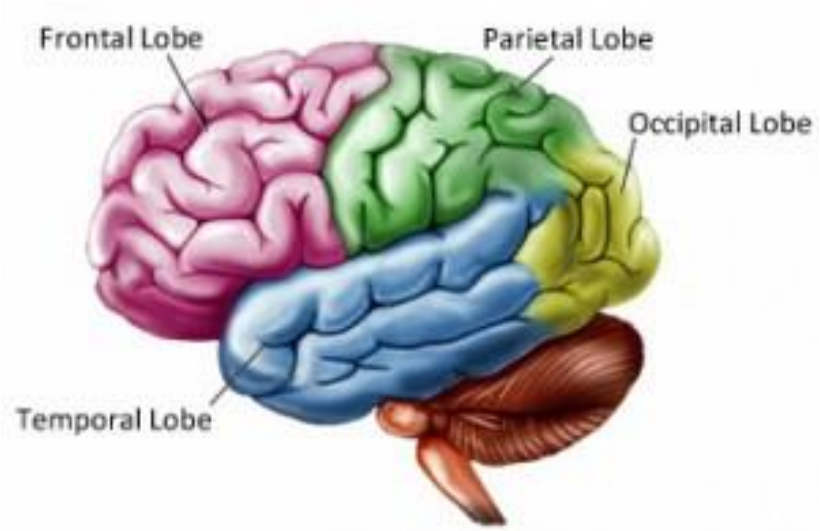


Figure 1.1. Lobes of the Human Brain (*The Northern Brain Injury Association*).

Cognitive ability is the mental capacity to perform tasks of various complexities including planning, abstract thinking, complex idea comprehension, memory, and learning from practice. These are key competencies that are required to meet the challenges of everyday life, such as in employment, education, training, and societal expectations. Issues in any of these areas can greatly affect an individual's ability to live a fulfilling life, and depending on the region of the brain affected, may be an indicator of a neurodegenerative condition affecting cognition. Thus, when decline in cognitive ability is witnessed it frequently reflects a decline in one or more EF (Craik & Salthouse, 2008; Engle et al., 1999; Urbanowitsch et al., 2015; Wongupparaj et al., 2015). These functions will now be discussed in detail in the following section.

Table 1.1. Cognitive functions of the Brain Lobes. This table presents the main cognitive functions associated to their brain region.

Brain Lobes	**Cognitive Function**
Frontal	Decision-making, thinking, planning, problem solving, emotions, behavioural control
Temporal	Memory processing (long-term), facial recognition, emotion, auditory processing, language comprehension, speech, vision
Parietal	Knowledge of numbers, object classification, perception, spelling, visuospatial processing
Occipital	Vision, spatial and visual processing, colour identification

1.3 Executive Functions: An Overview

EFs are traditionally conceptualised as a set of high-level cognitive processes implicated in the control and regulation of lower-level cognitive functions of goal-directed and future-oriented behaviours. Originally thought of as a single homogenous entity, further research determined EFs to be also considered as a heterogeneous group of functions. Homogenous, in that they have an underlying common factor ('unity') but also different ('diversity') (Miyake, Friedman, et al., 2000). Subsequently, several EFs have been identified, including abstract reasoning, attention, decision-making, dual-tasking, interference control, response inhibition, mental shifting, problem solving, and working memory (WM) updating, which are all vital for living a successful life (Alvarez & Emory, 2006; Baddeley, 1996, 2012; Collette & Linden, 2002; Friedman & Miyake, 2017; Lezak et al., 2012; Miyake, Friedman, et al., 2000; S. E. Price et al., 2010; Suchy, 2009). Miyake, Friedman, et al (2000) proposed the most fundamental EFs to be dual-tasking, response inhibition, mental shifting, and WM updating (Baddeley, 2012; Baddeley & Hitch, 1974; Miyake, Friedman, et al., 2000; Salthouse, 2005). Thus, this thesis aims to investigate the rate of deterioration of these four EFs as a consequence of healthy ageing. Such knowledge would be important in optimising assessments, diagnosis, and potential training and/or rehabilitation efforts in individuals living with cognitive impairments. The concept of WM and one of its models will now be discussed.

1.3.1 The Central Executive Model of Working Memory

The central executive (CE) model, proposed by Baddeley & Hitch (1974) and inspired by Norman and Shallice's Supervisory Attention System model (SAS) (Norman & Shallice, 1986), is one of the most influential models of WM. The SAS is described to comprise of two basic control systems to determine how activities are executed. The first is a lower-level system referred to as the 'contention scheduling system', which involves routine, overlearned and automatic behaviours. The second is a higher-level system termed the 'supervisory attention system', which involves the flexible modulation of the lower-level activities. Such modulations may involve the activation or inhibition of lower-level behaviours to allow for adaptation to non-routine or novel situations.

The CE model consisted of three systems, the central executive system (CES), and its two slave components, the phonological loop (PL) and the visuospatial sketchpad (VSSP). The CES, also known as the supervisory system, controls, coordinates, regulates, and integrates the influx of new information into the slave systems and the exchange between systems. In addition, it determines which system, the PL or VSSP, is recruited for the required information, and the allocation of cognitive resources to handle the integration and suppression of mental processes. Its key functions include selective attention, inhibition, shifting between tasks, and the updating of WM. Thus, the CES can be interpreted as a general controlling centre, akin to the SAS (Postle, 2017). The PL facilitates the storage of auditory information for language comprehension. It comprises two components, the phonological store, which is associated with speech perception, acting as an inner ear to hold verbal information for approximately 1 to 2 seconds, and the articulatory rehearsal component or loop, which prevents the rapid decay of memory traces by refreshing them through rehearsal of the internal voice. The VSSP, the inner eye, assists in the encoding and storage of two systems, the visual, for colour and shape information, and the spatial, for spatial and movement information. The fourth component, the episodic buffer, was added in 2000 (Baddeley, 2000). It is referred to as the third slave system and acts as a temporary storage unit capable of linking information from the PL and VSSP with long-term memory (LTM), therefore integrating all the information into a single episodic perception (Baddeley, 1996, 2000; Baddeley & Hitch, 1974). Figure 1.2 illustrates the entire CES model.

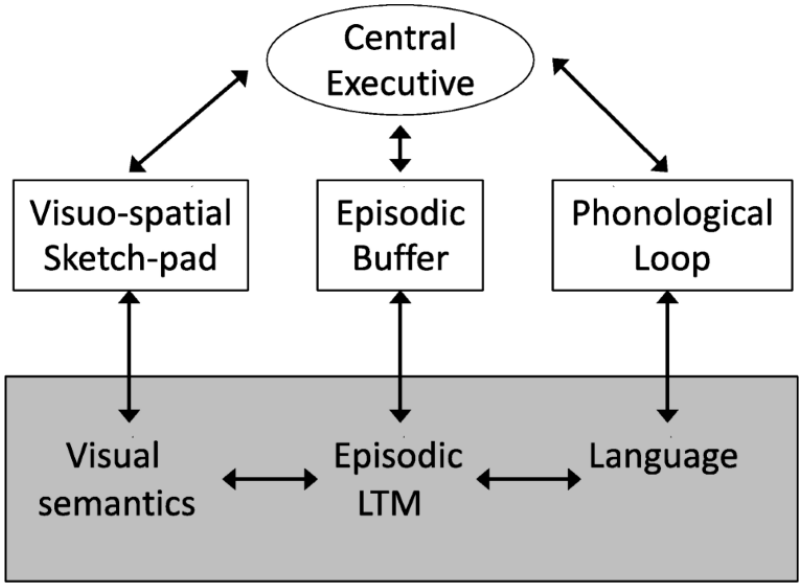


Figure 1.2. The Baddeley and Hitch Model of Working Memory (WM). The CES is presented with its three slave systems: the VSSP, PL and episodic buffer (Baddeley, 1996, 2000).

1.3.2 Executive Functions and the Prefrontal Cortex

Neuroanatomically, EFs are associated with several cortical, subcortical, and cerebellar areas of the brain. The PFC (anterior part of the frontal lobe) is primarily implicated and recognised as its controlling centre (Hunter & Sparrow, 2012), and according to the Baddeley and Hitch model of WM, it harbours the CES (Baddeley & Hitch, 1974). Thus, damage to this region, as observed in clinical cases of individuals with frontal lesions results in deficits in WM performance, which is evident by a Baddeley et al (1991) longitudinal study assessing individuals living with AD. These participants were especially impaired in performing a dual-task (DT) paradigm (the concurrent performance of two tasks), whilst single-task (ST) performance was maintained. Thus, the PFC neural networks are of great importance to EF performance and will be discussed in more detail in Chapter 5.

Structurally, the PFC can be divided into dorsolateral (DLPFC), dorsomedial (DMPLC), ventrolateral (VLPFC), ventromedial (VMPFC), and orbitofrontal (OFC) (Carlén, 2017; Funahashi & Andreau, 2013; Sarter et al., 2001) regions as shown in Figure 1.3. There is also a medial structure adjacent to the PFC known as the anterior cingulate cortex (ACC) (Alexander et al., 1986; Carlén, 2017; Christoff & Gabrieli, 2000; Reinvang et al., 2012).

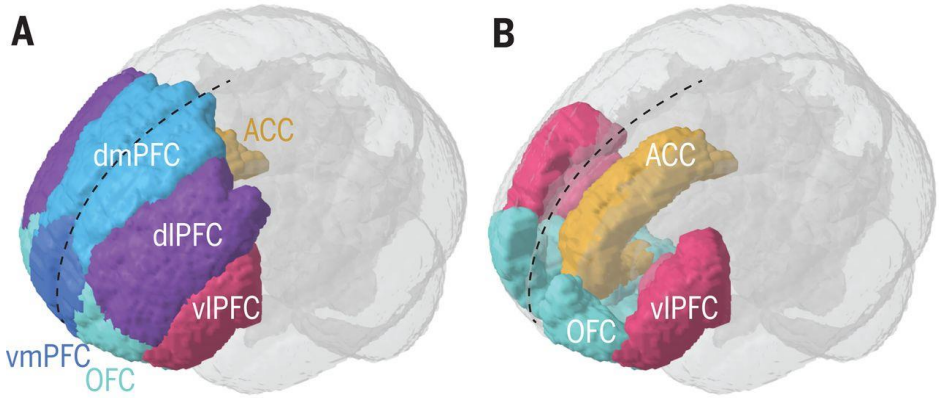


Figure 1.3. The Prefrontal Cortex and the Anterior Cingulate Cortex (ACC). The subregions of the PFC: the DLPFC, DMPLC, VLPFC, VMPFC, and OFC are shown, along with the ACC. Both views, A and B, represent the front-side view of the brain, with the dashed black line denoting the sagittal midline (Carlén, 2017).

The DLPFC can further be divided into smaller cytoarchitectonic regions referred to as a Brodmann's area (BA), encompassing BAs 8, 9 and 46. DMPLC consists of BA8 as well as BA9, however in literature it is typically included as part of the DLPFC (Carlén, 2017). It plays a central role in the executive control of EFs due to its many neural connections with the rest of the brain. It is typically associated with WM, attention and particularly in the monitoring and manipulating of cognitive processes (Curtis & D'Esposito, 2003; Rebecca, 2003; Suchy, 2009). Furthermore, through lesion studies, it has been found that the left DLPFC is required for manipulating information in WM whereas the right DLPFC deals with goal-directed behaviour and adaptive decision-making (Barbey et al., 2013; Postle, 2017).

The OFC (BA10 and 14) can be divided into three subregions, the ventral (vOFC), lateral (lOFC), and medial OFC (mOFC). It is associated with decision-making, emotional processing, pleasure, judgment, learning, and personality. Specifically, the vOFC is associated with reward and fear, the lOFC with stimulus-outcome associations and behavior processing, and the mOFC with stimulus-reward associations and behavior reinforcement (Bechara et al., 2000; Carlén, 2017; Rolls, 2019; Rolls & Grabenhorst, 2008; Rudebeck & Rich, 2018; Stalnaker et al., 2015).

The VLPFC (BAs 44, 45 and 12/47) sometimes referred as the inferior frontal gyrus (IFG) or inferior prefrontal cortex (IPC), is associated with the control and retrieval of processes from the posterior cortex and shifting processes (Barbey et al., 2013; Carlén, 2017; Konishi, Nakajima, Uchida, Kameyama, et al., 1998; Wise, 1999). In particular, the right region, for

cognitive control, goal-appropriate response selection in WM, and inhibitory mechanisms in WM, specifically for resolving interference from previous events (Aron et al., 2014; Konishi et al., 1999; Levy & Wagner, 2011; Nozari et al., 2016; Nozari & Thompson-Schill, 2015; Rebecca, 2003). Whilst the left region, Broca's area (BAs 44 and 45), is associated with language production, especially linguistic motor control, planning, syntax sequencing, and phonological processing (Teffer & Semendeferi, 2012; Wager & Smith, 2003).

The VMPLC (BAs 11, 12/47, and 13) is involved in the regulation and utilisation of emotional information for decision-making, i.e. emotional intelligence, as well as in planning and social conduct (Carlén, 2017; D'Argembeau, 2013; Lezak et al., 2012).

The ACC (BAs 24, 25, 32, and 33) has been described by many researchers as an important brain region in executive functioning and implicated in empathy, impulse control (e.g. performance monitoring and error detection), emotion, and decision-making (Carlén, 2017; Collette & Linden, 2002; Glisky, 2007). The dorsal ACC (dACC) is associated with cognitive factors through its connections with the PFC, parietal cortex, the motor system, and the frontal eye fields. The ventral ACC (vACC) is concerned with emotional factors, such as assessing emotional salience and motivational information (Bush et al., 2000).

The prefrontal-executive theory proposed by Dempster & Vegas (1992) and validated by West (1996) suggests that local structural and functional changes in the PFC areas, as observed during ageing and in neurodegenerative conditions, results in specific declines in EFs. This is thought to result in widespread cognitive deficits, observed mainly through task performance. Such performance change is elaborated upon in Chapter 5. The Scaffolding Theory of Ageing and Cognition (STAC), initially proposed in 2009 and updated in 2014 (Park & Reuter-Lorenz, 2009; Reuter-Lorenz & Park, 2014), also describes how ageing affects cognitive ability. It states the level of cognitive function a person exhibits is due to a combination of negative indices including neural degradation and functional decline, and positive processes, termed "compensatory scaffolding" to amend or offset these adverse effects. Such compensatory processes include the recruitment of supplementary neural networks to provide additional support to the ageing brain for preservation of cognitive function, and the influence of genetics, health, experience, and lifestyle on cognition.

To conclude, EFs control and regulate our cognition, primarily from the PFC, which can be subdivided into the DLPFC, DMPLC, OFC, VLPFC, VMPLC, and ACC. These regions work individually or in cooperation with one another and/or other brain regions to process appropriate input signals in order to produce a cognitive process. However, as a consequence of ageing and pathological conditions, changes in the PFC structure may result in modification of EFs and thus cognitive ability.

There has been considerable research regarding the identification of which EFs are fundamental to our daily lives. The consensus is that dual-tasking, response inhibition, (mental) shifting and (WM) updating are critical (Miyake et al., 2000). These are discussed in more detail in the following section.

1.4 The Four Fundamental Executive Functions

1.4.1 Dual-tasking

Dual-tasking is the simultaneous performance of two tasks (Baddeley, 1996; Della Sala et al., 1995b; Miyake, Friedman, et al., 2000). This has been implicated in the process of divided attention (Salo et al., 2015) which will be elaborated in the attention section 1.5.1. It is sometimes confused with task switching, i.e. shifting. However, the difference is that divided attention involves the simultaneous performance of two tasks, such as driving and using a mobile phone (Szameitat et al., 2015), in comparison to alternating (or shifting) between two or more tasks. This is essentially performing two tasks as single-tasks, such as going back and forth between reading an email and a text message on your phone (Monsell, 2003; Strobach et al., 2018; Worringer et al., 2019).

Various types of tasks are considered for DT assessment, but this discussion and overall research will be limited to DT ability in cognitive paper-and-pen and computer-based tasks, i.e. primary testing of mental skills not of motor function. These types of tests include the alphanumeric equation task and visual detection task (Clément et al., 2013; Compton & Logan, 1991; Logan, 1988), Brown Peterson task (J. Brown, 1958; Peterson & Peterson, 1959), test of everyday attention (TEA) DT telephone search subtest (Robertson et al., 1994), tracking and digit recall test (Baddeley et al., 1986), and the psychological refractory period (PRP) paradigm (Telford, 1931; Welford, 1952). These tasks are elaborated upon in Appendix 1. DT ability is typically assessed by comparing the difference in performance

during ST to performance during DT conditions. This is referred to as the DT cost, and quantified using the formula, “DT performance - ST performance”.

A number of studies (Collette & Linden, 2002; D’Esposito et al., 2000; Goldman-Rakic, 1995; Salmon et al., 1996; Wise, 1999) have identified the PFC as the control centre for DT performance. The precise region(s) activated within is thought to be dependent on the specific DT paradigm employed as well as the age of the participant (Hartley et al., 1999; Riby et al., 2004). It has been primarily associated with the DLPFC, with the ACC recruited as task difficulty increases (Collette, Olivier, et al., 2005; D’Esposito et al., 2000; D’Esposito & Postle, 2015; Hartley et al., 2011; Shi et al., 2014; Szameitat et al., 2002).

1.4.2 Inhibition

Inhibition can be defined in several ways, such as cognitive inhibition in reference to the inhibition of memory and thoughts. For the purposes of this thesis, the focus will be on response inhibition, defined as intended inhibition of prepotent responses or suppression of dominant responses. Effectively, the process by which automated, previously prepared response are suppressed (Bender et al., 2016; Diamond, 2013; Miyake, Friedman, et al., 2000; Salthouse et al., 2003).

It is commonly examined with the utilisation of interference paradigms which compares performance during congruent (non-inhibition) and incongruent (inhibition) conditions. Such tasks include the delay of gratification (Mischel et al., 1972), negative priming (Tipper, 1985), go/no-go (Newman & Kosson, 1986), stop-signal task (Logan et al., 2014), Hayling sentence completion task (HSCT) (Burgess & Shallice, 1997), Stroop task (Stroop, 1935), antisaccade task (Hallett, 1978), Simon task (Simon, 1969), and the flanker task (Eriksen & Eriken, 1974). Most of these are described in detail in Appendix 1.

The right VLPFC is said to be implicated during the incongruent condition (Aron et al., 2014; Aron, Robbins, et al., 2004; Bender et al., 2016; Blasi et al., 2006; Diamond, 2013; J. E. Fisk & Sharp, 2004; Konishi et al., 1999; Stuss & Alexander, 2000). Furthermore, the complexity of the processes involved in inhibition can require the involvement of other cortical areas such as the parietal cortex and the basal ganglia depending on the task need (Collette & Linden, 2002; Kok, 1999; A. Sebastian et al., 2013).

1.4.3 Shifting

Mental set shifting or switching, also referred to as attention switching, task switching or cognitive flexibility, is the process of moving or shifting attention between multiple tasks or operations (Diamond, 2013; J. E. Fisk & Sharp, 2004; Miyake, Friedman, et al., 2000; Schnitzspahn et al., 2013). It requires the alternation of performance between two similar tasks, i.e. the detachment from an irrelevant task set with the subsequent participation of a more relevant task set, important in decision-making situations (Diamond, 2013). Neuropsychological tasks utilised in its assessment include the design fluency task (Harter et al., 1999; Jones-Gotman & Milner, 1977), more-odd shifting task (Salthouse et al., 1998), task switching paradigm (G. Wylie & Allport, 2000), intra-extra dimensional set shifting (Saunders & Summers, 2010; Scheggia et al., 2014; Summers & Saunders, 2012), trail making test (TMT) (Reitan, 1992; Reitan & Wolfson, 1986) and the Wisconsin card sorting test (WCST) (Berg, 1948; Nelson, 1976). Please see Appendix 1 for more detail about the tasks. Participants are usually required to perform two task conditions separately, a repetition, i.e. completion of the same task repeatedly, and shifting, i.e. a mixed condition where two different tasks are randomly assigned for completion, so a participant must shift between task requirements. Shifting ability is quantified by the performance difference between the two conditions, referred to as the shifting/switching cost (G. Wylie & Allport, 2000) and calculated using the formula “Shifting performance – Repetition performance”.

Neuroanatomically, it is primarily associated with VLPFC for both repetition and shifting conditions, along with the dACC, parietal lobe and the occipital lobe (Brass & Cramon, 2004; Braver et al., 2003; Collette & Linden, 2002; Fellows & Farah, 2003; Chobok Kim, Johnson, et al., 2012; Kimberg et al., 2000; J. H. Kramer et al., 2007; Monsell, 2003; Worringer et al., 2019).

1.4.4 Updating

WM updating is defined as the constant revision of information in short-term memory (STM, the capacity to retain information for a short period of time), and of monitoring WM, i.e. the process of assessing ongoing functions and detecting errors (D’Esposito & Postle, 2015; Engle et al., 1999; Miyake, Friedman, et al., 2000). It continuously modifies the content of STM to accommodate new information, operating beyond simply maintaining task-relevant

information but by processing and manipulating the new content into WM (Lehto, 1996; Miyake, Friedman, et al., 2000; Morris & Jones, 1990; Salthouse et al., 2003). This is an important factor in accomplishing planned tasks in an ever-changing environment.

Common tasks utilised in its assessment include the alpha span task (Craik, Bialystok, et al., 2018), backward digit recall span (BDS) (Egeland, 2015; P. T. Griffin & Heffernan, 1983; Saklofske & Schoenberg, 2011; Wechsler, 2012), letter number sequencing (LNS) (Egeland, 2015; Mielicki et al., 2018; Saklofske & Schoenberg, 2011; Wechsler, 2012) and the n-back test (Jaeggi et al., 2010; Kirchner, 1958), all of which are described in Appendix 1. Its ability is assessed by quantifying the participants' performance across increasing memory load, which normally declines as load increases.

The DLPFC is known to be the central region for the updating process, though the medial prefrontal cortex (mPFC) including the DMPLC, VMPLC, dACC, are implicated as well. Further, the non-PFC regions, the basal ganglia, thalamus, and posterior parietal cortex (PPC) are also recruited in its process. More specifically, maintenance of WM is said to be dependent on the DLPFC, mPFC, and PPC, collectively known as the fronto-parietal network (FPN), whereas updating is believed to be reliant on the basal ganglia, and thalamus (Collette, Olivier, et al., 2005; Collette & Linden, 2002; D'Ardenne et al., 2012; D'Esposito et al., 1999; D'Esposito & Postle, 2015; Nir-Cohen et al., 2019; Nyberg & Eriksson, 2016; Postle, 2017; Roth & Courtney, 2007; Salmon et al., 1996; Stuss & Alexander, 2000; Stuss & Levine, 2002; Wager & Smith, 2003).

The brain structures and networks involved with these EFs are discussed in more detail in Chapter 5.

To summarise, this section reviewed the PFC regions and neuropsychology tasks primarily associated with the EFs dual-tasking, inhibition, shifting and updating. This is essential for understanding how cognitive processes occur and for establishing a foundation to investigate their behavioural and neural activity in various populations, for instance in healthy ageing and pathological populations. Hence, the subsequent two sections will be a summary of how healthy cognitive ageing and cognitive impairment affects EFs.

1.5 Cognitive Ageing

EF abilities vary across an individuals' life with improvement during childhood and adolescence before a gradual decline starting in the early thirties as a result of the brain starting to deteriorate (Buckner, 2004; Cheng, 2016; de Frias et al., 2006; J. E. Fisk & Sharp, 2004; Johnson et al., 2010; Kirova et al., 2015; Lamar et al., 2004; MacPherson et al., 2002; Meng & D'Arcy, 2012; Salthouse et al., 2003; Salthouse, 2012; Verhaeghen & Cerella, 2002). In addition, epidemiological studies have demonstrated that individual differences in age-associated brain changes, and its associated cognitive decline, including pathological impairment, may be attributed to lifetime experiences, e.g. educational and occupational attainment, leisure activities in later life, and genetics (Brayne et al., 2010; Cadar et al., 2016; Friedman et al., 2008; Hale et al., 2011; Meng & D'Arcy, 2012; Russell et al., 2019). Decline can be exacerbated by the occurrence of psychiatric conditions such as depression and the presentation of a cardiovascular condition such as diabetes, hypercholesterolemia, or hypertension (Cheng, 2016; Facal et al., 2014; Meng & D'Arcy, 2012; Urbanowitsch et al., 2015). Consequently, the concept of cognitive reserve, which refers to differences in the resilience of individuals to neuropathological changes has been introduced. The consensus is that individuals with increased education attainment, better occupation, and lifestyle tend to have higher cognitive reserve and thus maintain their cognitive abilities for longer and perform better in tasks (Barulli et al., 2013; Dubois et al., 2016; Kaufman et al., 2016). This may be possibly due to increase of these individuals' mental capacity to compensate for neurological damaged areas. Thus, encouraging more efficient neural processing through the recruitment of alternative brain networks, i.e. plasticity (Goh & Park, 2009). In persons with a genetic predisposition to developing cognitive impairment, it seems to delay the onset of dementia or create a stabilisation at the mild intermediate stage, i.e. MCI (Soldan, 2018).

Additionally, a portion of individuals maintain a constant level of their abilities throughout their life and as such perform comparably with younger individuals, these persons are labelled as super agers (Cadar, 2018; Glisky, 2007; Zanto & Gazzaley, 2019). Moreover, crystallised abilities or crystallised intelligence, i.e. skills attributed to general knowledge and vocabulary, are maintained with ageing, and can even improve, since they are formed through the accumulation of information created from an individual's life experience. As a

result, older adults have the tendency to be superior in tasks utilising these abilities such as the National Adult Reading test (NART) (Nelson, 1982), but not fluid abilities or intelligence, i.e. cognitive ability involved in the processing of unique information, which undergoes age-associated decline (Deary et al., 2009; Fjell et al., 2014; Grady & Craik, 2000; Harada et al., 2013; Park & Reuter-Lorenz, 2009; Reuter-Lorenz & Park, 2010; Salthouse, 2003a, 2009). Consequently, as a result of ageing and individual differences, variation in cognitive decline across populations exist, such as between the low and higher educated, young and old, and healthy and non-healthy individuals. Thus, in order to attain a thorough understanding of changes in EFs and cognitive decline, and the rate of deterioration of individual EFs across adulthood and various populations, this research will explore these factors in cognitively healthy (CH) young and older adults in Chapter 3, and the neuropathological impaired populations in Chapter 6.

The following paragraphs will describe the commonest cognitive functions investigated in age-associated cognitive decline, starting with an overview of generic processes before addressing specific EFs.

1.5.1 Attention

Attentional control (also known as controlled attention, executive attention, focused attention, or WM capacity) refers to the ability to keep focus and to maintain concentration over long periods of time. More specifically, the cognitive process that coordinates and directs our attention to a specific incident or task, so as to suppress our attention from unwanted distractors (Coubard et al., 2011; Gyurkovics et al., 2018; Wasylyshyn et al., 2011). Its decline in the healthy older adult population is predominantly observed in the completion of complex WM tasks (Bélanger et al., 2010; Braver & West, 2008; Coubard et al., 2011; Engle, 2002; Engle & Kane, 2004; Fountain-Zaragoza et al., 2018; Kane et al., 2001; Milham et al., 2002; Sylvain-Roy et al., 2015; Tsang, 2013). However, ageing does not seem to affect the completion of simple tasks (Langner & Eickhoff, 2013). Furthermore, the executive attention framework (Engle, 2002; Engle & Kane, 2004) suggests that older individuals are less efficient in their maintenance of this control when active tasks are experienced in difficult settings with high task-interference. This can cause problems in the planning and execution of many complex tasks, as these individuals may be unable to focus

on task requirements. This is of particular importance in tasks requiring vigilance, such as when monitoring an area for a randomly occurring signal (Bier et al., 2017; Hasher & Zacks, 1988; Rubinstein et al., 2001; Sylvain-Roy et al., 2015).

Attention can be described as the allocation of limited cognitive processing resources. Its sub-components, alternating attention, divided attention, and selective attention are especially important (Cadar, 2018; D'Esposito & Postle, 2015; Glisky, 2007). Alternating attention is the ability to shift the focus of attention and move between tasks, i.e. mental flexibility, and is utilised during shifting performances (see section 1.4.3). Decline in shifting capability amongst CH older adults has been reported by a number researchers, where performance deficits were apparent by increases in processing rate and increased errors made (Adólfsdóttir et al., 2017; Harada et al., 2013; McNab et al., 2015; Salthouse & Meinz, 1995; Verhaeghen & Cerella, 2002; Wasylyshyn et al., 2011).

Divided attention is recruited during dual- and multi-tasking conditions (Baddeley et al., 1991; Naveh-Benjamin et al., 2005; Tsang, 2013; Verhaeghen & Cerella, 2002). Several researchers have demonstrated age effects in DT ability (Belleville et al., 1998; Della Sala et al., 2010; Fraser & Bherer, 2013; Hartley & Maquestiaux, 2007; Hein & Schubert, 2004; Liebherr et al., 2016; Logie et al., 2004; Naveh-Benjamin et al., 2005; Salthouse et al., 2003; Salthouse & Meinz, 1995; Verhaeghen et al., 2003). CH older adults are seen as capable at completing DTs, but at a slower completion rate and with the production of a greater amount of performance errors than their younger counterparts. This suggests older individuals find it more difficult to divide their attention, and affectively allocate resources to more than one task (Baddeley et al., 1986; Hartley et al., 1999; Inasaridze et al., 2009; Logie et al., 2004; MacPherson et al., 2007; Salthouse et al., 2003).

The capacity to maintain a behavioural or cognitive set during distracting or competing stimuli requires selective attention (Cabeza et al., 2009; Glisky, 2007), which is used in the suppression of prepotent responses, i.e. inhibition (Miyake, Friedman, et al., 2000). Tasks employed to assess this ability include the Stroop task (Scarpina & Tagini, 2017; Stroop, 1935) where older adults have been observed to have slower response times (RTs) and increased errors in both the congruent and incongruent conditions of the task (Graf et al., 1995; Uttl & Graf, 1997). The inhibition deficit theory (Hasher & Zacks, 1988), states the

process of inhibition weakens through ageing due to a reduction of inhibitory resources. Specifically, individuals cannot remove irrelevant information effectively which restricts the retrieval of task-relevant information. This is evident by the larger interference rates usually observed in the older population when compared with younger adults (Lustig et al., 2007).

In line with this theory, the strategy-deficit hypothesis (Bailey et al., 2009) states that in combination with such cognitive processing deficiencies, ineffective or deficient use of strategies in older adults leads to additional age-related performance deficits. Specifically, they have difficulty producing and using appropriate strategies to encode information that may be required for task completion.

However, although decline is observed in these attentional resources and thus the EFs associated with them, the degree of its deterioration in comparison to other EFs is unclear. It seems the effects of ageing on inhibition is stronger than that on shifting and dual-tasking but possibly not as much as updating. However, due to the lack of studies which directly assess this relationship, it is currently unknown and will thus be explored in this thesis.

1.5.2 Memory

Memory issues are one of the first complaints of ageing individuals (Broadbent et al., 2004; Burke & Barnes, 2006). It can be grouped into STM, WM and LTM. STM and WM are associated with the PFC but the major difference between them is that STM is generally not affected by cognitive ageing. Most older adults are able to retain approximately 7 ± 2 digits in their memory for short periods, but experience difficulties in WM, for instance when having to recall digits in reverse order (Diamond, 2013; Glisky, 2007). Salthouse et al (1989) reported that their older adult participants showed significant deficits when performing memory tasks involving active manipulation, reorganisation, and WM updating. Importantly, these are all skills required for daily living including decision-making, planning of goal-directed behaviours, and problem-solving. Age-related decrements in WM updating is associated with increased activity in the superior PFC (specifically the DLPFC) (De Beni & Palladino, 2004; El Haj, Larøi, et al., 2015; J. E. Fisk & Sharp, 2004). The left PFC is said to be involved more with verbal tasks and the right side with visuospatial tasks, i.e. the PL and the VSSP in Baddeley's WM model (Baddeley & Hitch, 1974; Collette, Linden, et al., 1999).

LTM can be subdivided into procedural (primarily associated with the cerebellum) and declarative (mainly associated with the hippocampus) (Visser et al., 1999). Declarative memory can be divided into semantic memory (general or crystallised knowledge) (Binder & Desai, 2011) and episodic memory (memory of autobiographical events) (Greene et al., 1995). Of these memory types, procedural memory with priming, and semantic memory are usually well maintained in advanced age (Glisky, 2007; Grady, 2012) but not episodic memory (Clarys et al., 2009; Leyhe et al., 2009; Naveh-Benjamin et al., 2003; Radvansky & Radvansky, 2018; Tromp et al., 2015). Ward & Shanks (2018) have argued that procedural memory may be affected by ageing but to a much lesser degree than episodic memory. Interestingly, older adults may even perform better than their younger counterparts on tasks involving semantic memory (Azuma et al., 2013; Craik & Salthouse, 2008; Rentz et al., 2010). Nevertheless, it has been suggested that the decline in episodic memory, and possibly all age-related memory decline, may be due to i) reduced inhibitory control, ii) deterioration of systems required for information processing, iii) failure in the utilisation of appropriate encoding/retrieval strategies, and/or iv) decrease in the encoding of memory so older individuals rely more on retrieval cues in order to access the relevant information from memory stores (Craik & Salthouse, 2008; Naveh-Benjamin et al., 2003).

Declarative memory is known to involve the basal ganglia, cerebellum and limbic system within the brain (Campbell et al., 2012; Ward & Shanks, 2018). Semantic memory activates neural pathways in the temporal, inferior parietal lobes and the dorsomedial and inferior PFC, and priming in the anterior cortex, including the PFC (Ferraro et al., 1993; Schmidtke, 2002). Episodic memory, associated with the medial temporal lobe (MTL), which includes the parahippocampal cortical areas and the hippocampus, is most vulnerable to age-associated decline (Buckner, 2004; Cabeza et al., 2009; Convit et al., 2000; Nyberg et al., 2012; Radvansky & Radvansky, 2018; Salthouse et al., 2003; Squire et al., 2004; Tromp et al., 2015; Visser et al., 1999). This is a region, presented in Figure 1.4, that has been shown to be susceptible to an increased rate of atrophy in MCI and dementia leading to profound memory issues (Buckner, 2004; Convit et al., 2000; Dhikav et al., 2014; Jhoo et al., 2010; Visser et al., 1999).

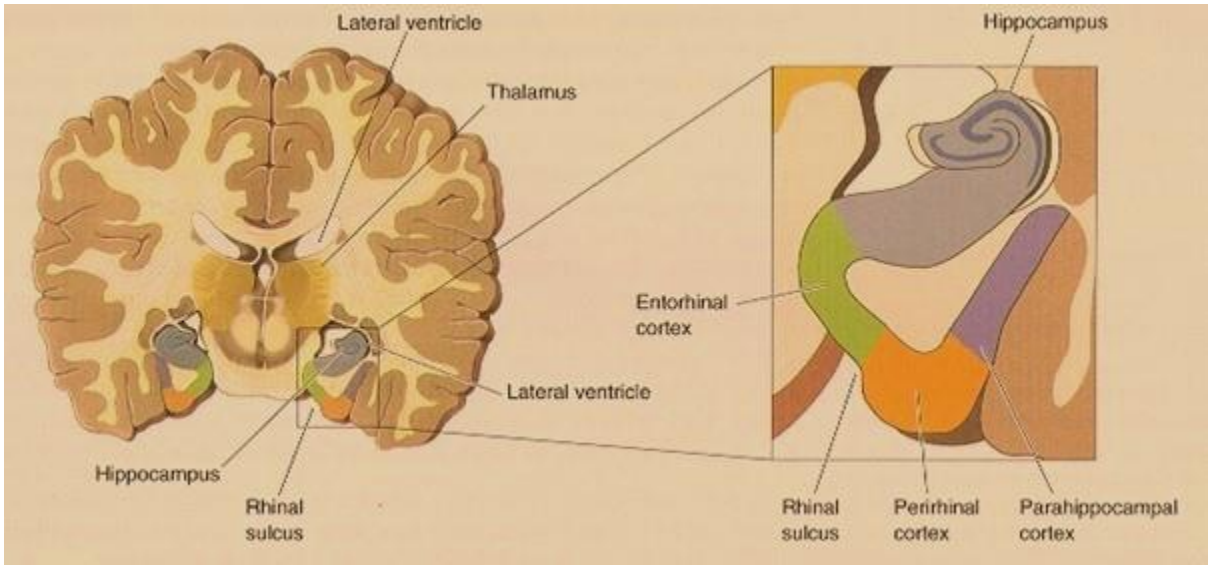


Figure 1.4. The Medial Temporal Lobe. This structure, particularly the hippocampus, is involved in the formation and storage of declarative LTM (*The Stroke Network*).

Another type of memory called prospective memory (Einstein & McDaniel, 1990), i.e. the ability to plan, retain, and retrieve information for future events, may decline in some individuals. Prospective memory tasks activate neurons in the hippocampus, the parietal, superior temporal cortices and the PFC (Boxberger et al., 2011; Lemaitre et al., 2012). It has been observed that the simultaneous deterioration in gray matter (GM) and white matter (WHM) integrity of these regions manifests behaviourally in its decline. However, performance deficits are dependent on the amount of atrophy in the brain and thus may not decline in all older individuals (Cabeza et al., 2009; Gazzaley et al., 2007; Harada et al., 2013; D. B. Howieson, 2015; Kirova et al., 2015; Logie & Maylor, 2009; Salthouse, 2012; Salthouse et al., 2003). Lastly, associative memory, the ability to correlate information and events in memory, has been linked to both episodic and prospective memories and shown to decline with age (T. Chen & Naveh-Benjamin, 2012; De Brigard et al., 2020; Old & Naveh-Benjamin, 2008; Salthouse, 1995; Schnitzspahn et al., 2013).

1.5.3 Processing Speed

Age-related declines in mental function have been attributed to the reduction of processing speed of cognitive processes, i.e. the ability to rapidly process information in order to perform tasks efficiently in a limited timeframe (Albinet et al., 2012; Bashore et al., 1989; Bier et al., 2017; Christensen, 2001; Deary et al., 2009; Frischkorn et al., 2019; Glisky, 2007;

Salthouse, 2019; Wecker et al., 2000). The degree of slowing appears dependent on the complexity of the task requirement, nature of the task, and the individual variability (Cerella, 1985; Gick et al., 1988; Salthouse, 1976, 1996). For instance, Baddeley's word length effect suggests that individuals are able to maintain in STM what they can covertly articulate within 2 seconds (Baddeley et al., 1975). However, if processing speed is reduced then the amount that can be articulated in 2 seconds is also reduced, and so is the amount of information memorised. Hence, age-associated deficits in WM span results from reduced activation and subvocal rehearsal of information (Baddeley, 2012; Salthouse, 1992, 1994). Furthermore, older individuals have been shown to be approximately 1.5 times slower than their younger peers in RTs (Maquestiaux, 2016). However, this slowness is traded for accuracy as this population tend to make sure they perform correctly (Salthouse, 1979). Also, it has been reported that age-related variance in span performance in several tasks was minimised when processing speed was factored out (Salthouse & Babcock, 1991).

Similarly, Salthouse' (1996) processing-speed theory proposes that age-associated deficits in cognitive functioning are due to the reduction in the speed of processing operations resulting in difficulties in the storage of information. First, processing is slowed because required actions cannot be successfully implemented, i.e. encoded, and stored within an adequate timeframe (limited time). Second, performance is affected as early processed information may not be available once information processing is complete as the information is removed before it can be rehearsed or retrieved from storage (simultaneity) (Salthouse, 1996).

Moreover, neuropsychological test performance is frequently measured in terms of RTs which can result in bias since this metric alone does not account for the speed-accuracy tradeoff. It is understood that RTs are longer as cognitive processing requirements increase (due to increased operations or task complexity), and RTs become shorter when processing becomes more automated and less reliant on perceptual processing speed (Bashore et al., 1989; Wecker et al., 2000). However, overall slowing in RTs confounds on the specific deficits in the cognitive function being assessed and so needs to be controlled for and removed when assessing EFs (Albinet et al., 2012; Bock et al., 2019).

Solutions have included the utilisation of Brinley plots (A. D. Fisk & Fisher, 1994; Myerson et al., 2003; Perfect, 1994), eliminating the speed factor (J. E. Fisk & Sharp, 2004; J. E. Fisk &

Warr, 1996), or employing tasks that rely on accuracy only, such as the digit span tasks (Conway et al., 2005; Wechsler, 2012). Alternatively, through statistical analysis of EF data, such as the utilisation of 'relative' measures like DT costs (M. Anderson et al., 2011) or task-shifting costs (G. Wylie & Allport, 2000), where the performance of two task conditions are compared and so any overall differences can be discounted. This can be accomplished by using a 2x2 analysis of variance (ANOVA) for group comparisons (e.g. young and older adult) and task condition (e.g. ST and DT). The general slowness in the older adults should present as an additive effect in task performances, as the two task conditions are affected similarly, although ST is usually performed faster than DT. Therefore, significance in RT will be observed for the more complex condition (DT) in the main group effect. Likewise, in assessing shifting, the shift task is usually performed slower than the repetition task, which will be more pronounced in the older adults than with the young adults, resulting in a significant interaction.

Structurally, processing speed is reliant on the WHM integrity of the brain, mainly within the left frontal, parietal and temporal regions (Albinet et al., 2012; Ballesteros et al., 2013; Godefroy et al., 2010; Harada et al., 2013; Kievit et al., 2014; Petersen et al., 1997; Turken et al., 2008). These regions are generally affected by the ageing process.

Thus, as part of this thesis, a voxel-based morphometry (VBM) study examining the neuroanatomical differences between CH older adults, and those living with MCI and AD will be presented in Chapter 6.

To summarise, ageing causes changes to our cognitive abilities. The main consequences of this on our cognition include subtle memory problems (Craik & Salthouse, 2008; Godefroy et al., 2010; D. B. Howieson, 2015; Radvansky & Radvansky, 2018; Verhaeghen & Cerella, 2002), reduced attentional abilities (Cabeza et al., 2009; Glisky, 2007), and decline in processing speed (Albinet et al., 2012). Of particular importance is its effect on alternate, divided, and selective attention, which corresponds to the EFs shifting, dual-tasking, and inhibition, respectively. However, the relative patterns of decline across these different functions are not well understood. This will be investigated in Chapter 3 in CH young and older adult populations.

1.6 Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD)

Impairment in EFs, also called executive dysfunction, can be caused by many diseases, conditions, and brain injuries. However, this thesis will focus on dementia (Fjell et al., 2014; Rabinovici et al., 2015), specifically, MCI and AD ("2020 Alzheimer's Disease Facts and Figures," 2020; Alzheimer's Society, 2015; Association Alzheimer's, 2017). Studies examining EFs have shown task performance deficits to be an early indicator of the onset of MCI and AD (Bayard et al., 2011; Bélanger et al., 2010). However, the degree and rate of deterioration of different EF components as the conditions progress is less understood, though it is clear that there is greater decline than observed with healthy older individuals (Marsico et al., 2014; Tromp et al., 2015).

MCI sufferers are described as having "*objective or subjective evidence of cognitive impairment but no significant functional impairment to meet criteria for dementia*" (Rosenberg et al., 2011, page 3). Accordingly, the National Institute on Ageing - Alzheimer's Association recommends that the following criteria be met for its diagnosis, *"1. Concern regarding a change in cognition, 2. Impairment in one or more cognitive domains, 3. Preservation of independence in functional abilities and 4. Not demented"* (Petersen et al., 2014, page 4). Several subtypes of MCI have now been identified, and can be classified as single or multi domains i.e. impairment in one or more EF (del Carmen Díaz-Mardomingo et al., 2017; Gauthier et al., 2006; Petersen et al., 1997, 1999; Reinvang et al., 2012; Rosenberg et al., 2011).

The most commonly reported type of MCI is amnestic MCI (aMCI), where memory impairment is the primary symptom. Other MCI subtypes include non-amnestic (attentional) MCI (naMCI) and MCI with executive dysfunction. However, MCI is commonly treated as a single condition, since neuropsychological testing cannot confidently distinguish between the types (Petersen et al., 1999, 2014; Reinvang et al., 2012). It is important to note that not all individuals living with MCI transition to a form of dementia (Emrani et al., 2018; Pandya et al., 2016), but as stated earlier, these individuals cannot be predicted (Rosenberg et al., 2011).

The risk factors for developing any of these MCI subtypes is the same (Loftus, 2017) which includes low educational level, hypertension, occurrence of depression and consumption of

some medications, specifically those with anticholinergic properties (Alzheimer's Society, 2015; Peraita et al., 2015). Furthermore, the diagnosis of a specific subtype can determine what type of dementia an individual may ultimately develop, e.g. aMCI sufferers are usually predisposed to developing AD (Rosenberg et al., 2011). Thus, the progression of naMCI and other MCI types, such as MCI with executive dysfunction (i.e. impairment in reasoning, judgment, problem solving) with no memory impairment, is not as definite. It may be heterogeneous, resulting in an array of dementias, including frontotemporal dementia (FTD), Lewy body disease (LBD), vascular dementia (VaD), or Parkinson's disease (PD) ("2020 Alzheimer's Disease Facts and Figures," 2020; Mufson et al., 2012; Reinvang et al., 2012; Sorbi et al., 2012).

AD is an irreversible progressive neurodegenerative disorder that is the commonest form of dementia affecting adults worldwide (NIA, 2020; Ulep et al., 2017; WHO, 2020). Currently, diagnosis is based on criteria set by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA), which includes neuropsychological, pathological and biomarker analysis (Jack et al., 2010, 2013). However, due to the nature of the condition, it is emphasised that it is for "probable AD" and confirmation of the condition cannot be made until post-mortem pathological examination. Although, the presence of genes predisposed to developing AD, i.e. the beta-amyloid precursor protein (APP), Presenilin 1 (PSEN1), and Presenilin 2 (PSEN2) allows for a more accurate diagnosis (Macpherson et al., 2015; Shao et al., 2017). Also, the presence of risk factors similar to that of MCI, including suffering from type 2 diabetes or a vascular condition such as hypertension, obesity, smoking tobacco, living a sedentary lifestyle, and having an occurrence of a head injury, all increase the probability of its development ("2020 Alzheimer's Disease Facts and Figures," 2020; Scheltens et al., 2016; Ulep et al., 2017).

AD contributes to approximately 60-70% of all new dementia cases ("2020 Alzheimer's Disease Facts and Figures," 2020). Women have been observed to possess an increased risk of developing the condition for reasons currently unknown. Some theories include the fact that 1) women usually live longer (i.e. survival bias), 2) women may lack the cognitive reserve demonstrated to protect from cognitive decline, and 3) the decreased level of oestrogen following the onset of menopause may be a possible contributing factor ("2020

Alzheimer's Disease Facts and Figures," 2020; Cheng, 2016; Hua et al., 2010; Meng & D'Arcy, 2012; Niu et al., 2017; Russell et al., 2019; Sundermann et al., 2020).

1.6.1 Neuropathology

Amnestic MCI is marked by atrophy within the limbic system, specifically of the MTL, the region containing the hippocampus (CA fields, dentate gyrus, and subicular complex), adjoining the perirhinal, entorhinal and parahippocampal cortices. Structural magnetic resonance imaging (sMRI) has revealed the WHM volume of the parahippocampal cortices is greatly reduced in MCI when compared to a normal age-matched non-AD control brain. Glucose hypo-metabolism within the hippocampus has also been observed (Albert et al., 2011; Gauthier et al., 2006; Kelley & Petersen, 2007; Mufson et al., 2012; Petersen et al., 1999, 2014). These areas are important in declarative memory, where the rate of MTL atrophy seems to correlate with the extent of declarative memory dysfunction. This relationship is thought to reflect decreased neural activation important for memory encoding within these regions (Leyhe et al., 2009; Mufson et al., 2012). Atrophy in AD sufferers extends this trajectory and progresses into other brain regions, starting with the frontal and parietal cortices. Although atrophy of the basal ganglia may also be observed in MCI sufferers (Mufson et al., 2012).

In AD sufferers, atrophy of the fronto-medial thalamic network causes a reduction in cortical thickness or decrease in GM density and seems to be associated with cognitive decline (Jacobs et al., 2013). Atrophy of the entorhinal cortex, parahippocampal, precuneus of the superior parietal lobe, subgenual cingulate cortex and orbitofrontal cortex (an area important for decision-making) has been observed to correlate with performance on the mini-mental state examination (MMSE) (Creavin et al., 2016; Folstein et al., 1975). Deterioration of the ACC and accompanying motor cortices has been linked to increased apathy, while atrophy of the left temporal and parietal cortices, with communication problems, including language production and comprehension (Ewers et al., 2011; J. Kim et al., 2017).

Damage to the WHM tracts (pathways linking the GM regions), particularly in the PFC is also observed in AD sufferers. One of the most important of these pathways is the cholinergic network. Impairment tracts has been reported to increase frontal dysfunction as it contains

overlapping cell groups of the basal forebrain, hippocampus, olfactory bulb, and amygdala. These cell groups are implicated in networks responsible for attention, memory, and emotion, cognitive impairment is witnessed (Ray et al., 2015; Stahl et al., 2007) and correlate with AD severity (Ballard et al., 2002; Brickman et al., 2008; Grambaite et al., 2011; Gunning-Dixon et al., 2009).

In addition, neurofibrillary tangles (NFT) which are abnormal accumulations of hyperphosphorylated forms of the protein tau inside neurons in GM, are also observed in both these conditions, as well as in healthy individuals (Jack et al., 2011). However, in MCI and AD, it is seen in higher proportion in the brain. In MCI, it is largely found within the amygdala, entorhinal cortex (EC), subiculum, the inferior parietal cortex (IPC), and the olfactory cortex, though its presence is not associated with any cognitive changes (Gauthier et al., 2006; Jack et al., 2005; Mielke & Kessler, 2006; Mufson et al., 2012). In AD it is more widespread, gradually spreading to the entire brain. Its distribution and density is based on the Braak NFT staging scheme, where early brain alterations are observed in the MTL, predominantly in the hippocampus, amygdala, and EC, before dispersing to the neocortex, resulting in atrophy of the frontal and parietal cortices (Convit et al., 2000; Jack et al., 2010, 2013; C. Wang et al., 2012). These lesions or biomarkers, can be viewed ante-mortem using 8-fluorodeoxyglucose positron emission tomography (FDG PET) otherwise histological examination is utilised post-mortem (Bauer et al., 2018; Kumari et al., 2002). Its accumulation is more associated with neuronal loss, particularly synaptic loss and synaptic dysfunction, which parallels the progression of cognitive decline (Ingelsson et al., 2004; Serrano-Pozo et al., 2011; Spires-Jones & Hyman, 2015).

In MCI and AD, there is also the presence and increased accumulation of the interrelated histological lesion Aβ (senile or amyloid) plaque deposits in brain matter but these can also be found in healthy individuals (Jack et al., 2010; Kirova et al., 2015; Lim et al., 2014, 2015; Pegueroles et al., 2017; Villemagne et al., 2013). Two isoforms exist, Aβ40 and Aβ42, where some plaques contain only Aβ42 and others contain both usually with an increased percentage of Aβ42. The amount of plaques present in MCI brains seems to fall between the levels found in CH older individuals and AD sufferers, and increases as AD advances (Gu & Guo, 2013). However, its occurrence does not seem to affect neuropsychological impairments and dementia severity (Schroeter et al., 2009; Serrano-Pozo et al., 2011).

Figure 1.5 displays how the accumulation of the brain atrophy, neural damage, tau filled NFT, and Aβ plaque results in the trajectory from a CH brain to MCI to AD, and its association with the onset of memory impairment and clinical presentation.

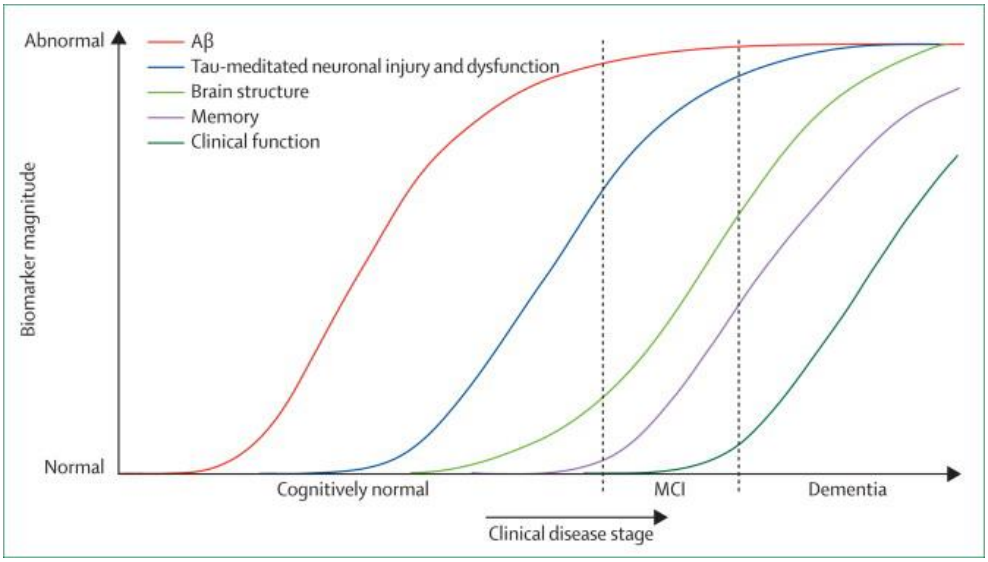


Figure 1.5. Trajectory of cognitive, clinical, and neurological markers from normal ageing to dementia. The Alzheimer's pathological cascade presents how the accumulation of neuropathological changes in the brain result in MCI and dementia (Jack et al., 2010).

1.6.2 Executive Dysfunction

These pathological changes manifest as impairments in an individuals' cognitive abilities, increasing in severity from MCI to severe AD (Baddeley et al., 1986, 2001; Belleville et al., 2014; S. T. Chen et al., 1998; Y. Chen et al., 2017; Collette, Van Der Linden, et al., 1999; Coubard et al., 2011; Greene et al., 1995; Leyhe et al., 2009; Spaan, 2016; Stopford et al., 2012; Swanberg et al., 2004). For example, the commonest feature detected in MCI, primarily in aMCI, is decline in episodic memory. While this is also a common feature of cognitive ageing, the level of decline is more pronounced in MCI and even greater in AD (where loss of function is progressive). Semantic memory is also severely affected in AD (El Haj, Antoine, Nandrino, et al., 2015; Greene et al., 1995; Leyhe et al., 2009; R. J. Perry et al., 2000; Tromp et al., 2015). To distinguish between the conditions, free recall testing is normally applied where poorer performance usually correlates with the deterioration of episodic memory (Petersen et al., 2014).

Impairments in other cognitive domains in MCI are less severe than those observed in AD. More explicitly, performance impairments in MCI lies at an intermediate level between CH

adults and AD. Deficits in the non-memory cognitive domains, namely attention and EFs have also been reported, especially in naMCI and multi-domain MCI ("2020 Alzheimer's Disease Facts and Figures," 2020; Aurtenetxe et al., 2016; Baddeley et al., 2001; S. T. Chen et al., 1998; De Toledo-Morrell et al., 2006; Kelley & Petersen, 2007; Kirova et al., 2015; R. J. Perry et al., 2000; R. J. Perry & Hodges, 1999; Reinvang et al., 2012; Scheltens et al., 2016; Toledo et al., 2015).

As discussed in section 1.5.1, an important factor for the completion of tasks is the possession of an adequate level of attentional control for the elimination of interference and distraction. There is evidence that MCI and AD have attentional impairment especially in tasks involving the control of divided attention, inhibition, task-switching, and WM (Aurtenetxe et al., 2016). In the testing of divided attention, individuals living with MCI and AD show a larger DT decrement than is observed in normal ageing. The ability may be maintained in mild MCI (Lonie et al., 2009; Nordlund et al., 2005; R. J. Perry et al., 2000; Silveri et al., 2007) but not in chronic sufferers, in line with the onset of AD when this ability has disappeared (Baddeley et al., 1991; Kaschel et al., 2009; Saunders & Summers, 2010). In addition, individuals with MCI tend to produce slightly more performance errors and have longer task completion times than in normal ageing (Belleville et al., 2007; Clément et al., 2013; Foley et al., 2011; Johns et al., 2012; Lopez et al., 2006; Makizako et al., 2013; S. E. Price et al., 2010).

Another prominent deficit observed is in inhibition as demonstrated with its assessment with the Stroop task. Performance deficits have been reported for both MCI and AD participants but AD populations show greater impairments (Ahn et al., 2011; Amieva, Phillips, et al., 2004; Bélanger et al., 2010; Bélanger & Belleville, 2009; Borella et al., 2017; Borgo et al., 2003; Chapman et al., 2010; N.-C. Chen et al., 2013; El Haj, Antoine, & Kapogiannis, 2015; El Haj, Larøi, et al., 2015; Gagnon & Belleville, 2011; Garcia-Alvarez et al., 2019; Grönholm-Nyman et al., 2010; Huang et al., 2017; Johns et al., 2012; J. H. Kramer et al., 2006; Lopez et al., 2006; Matías-Guiu et al., 2018; Nordlund et al., 2005; R. J. Perry et al., 2000; Puente et al., 2014; Sung et al., 2012; Tse et al., 2010; B. Yuan et al., 2016; Zheng et al., 2012). However, Belleville et al (2007) did not observe any inhibitory deficits with their MCI participants which may be due to a milder form of the condition or an increased proportion of aMCI in their MCI participant group.

Decline in shifting ability has been described in both groups (Ishizaki et al., 2013; Pa et al., 2010; Saunders & Summers, 2010; Summers & Saunders, 2012). In particular, deficits in the performance of the trail making test (TMT) in MCI and AD participants has been reported in several studies (Aurtenetxe et al., 2016; Chapman et al., 2010; Garcia-Alvarez et al., 2019; Grönholm-Nyman et al., 2010; Matías-Guiu et al., 2018; Nordlund et al., 2005; Pa et al., 2010; Peters et al., 2014; S. E. Price et al., 2010; Schmitter-Edgecombe & Sanders, 2009; Silveri et al., 2007; Smits et al., 2015; Tse et al., 2010; B. Yuan et al., 2016). However, Lopez et al (2006) failed to observe this is their MCI participants.

As mentioned earlier, memory decline is a prominent symptom of MCI and AD. Similarly, WM updating is also affected (Baddeley et al., 1991; Borgo et al., 2003; Facal et al., 2014; Huntley & Howard, 2010; Kirova et al., 2015) and routinely tested using a recall test. However, instead of testing with the straightforward recall task, updating requires a more challenging form of the test. Hence, the popular BDS is frequently employed, as participants are required to recall a sequence of numbers in reverse order. Deficits have been observed in both conditions by numerous researchers (Ahn et al., 2011; Aurtenetxe et al., 2016; Emrani et al., 2018; Garcia-Alvarez et al., 2019; Grönholm-Nyman et al., 2010; Kessels et al., 2011, 2015; Lopez et al., 2006; Matías-Guiu et al., 2018; Smits et al., 2015; Tse et al., 2010). Although others have found no significant performance difference with CH individuals (Bisiacchi et al., 2008; N.-C. Chen et al., 2013; Doi et al., 2013; J. H. Kramer et al., 2006; Liao et al., 2017; Mandzia et al., 2009).

In the late stages of AD, verbal communication is negatively affected and complete loss of LTM, including procedural memory is witnessed. Thus, neuropsychological tests assessing several subdomains in areas including memory, EFs and communication, are frequently administered in clinical and research settings to assess the level of overall cognition in these individuals. Such tests include MMSE (Folstein et al., 1975), Montreal cognitive assessment (MoCA) (Nasreddine et al., 2005), and clinical dementia rating (CDR) scale (C. P. Hughes et al., 1982).

To conclude, executive dysfunction is exhibited in individuals living with MCI and AD as a result of neuropathological changes. These include GM atrophy, decreased WHM integrity, and the presence of NFT throughout the brain but particularly in the limbic system within the MTLs in aMCI and early-stage AD, before spreading to the PFC and parietal lobes in

advance AD. The dysfunction can range from mild symptoms in MCI individuals to severe in advanced AD, based on the level of damage present, through the administration of neuropsychological assessments. Hence, the final study in this thesis, presented in Chapter 6, will explore the relationship between the neuroanatomy of CH older adults, and those living with MCI and AD, their cognitive status, and performance on a range of neuropsychological tests.

1.7 Study Overview

1.7.1 Study Aims and Hypothesis

The aim of this thesis was to investigate four EF abilities in CH young and older adults, and in older individuals living with MCI and early-stage AD through a cross-sectional study, to better understand the nature and trajectory of their deterioration. Due to the COVID-19 pandemic, the behavioural assessment of the MCI and AD populations and a functional MRI study could not be completed. Hence, only the CH young and older adults were assessed in dual-tasking, inhibition, shifting and updating ability.

The primary objective was to characterise the trajectory of these EFs in the populations, to test whether they declined at the same rate. The second objective was to determine the sensitivity of the standard EF tasks used for each of the EFs assessed as two were utilised per EF. A clearer understanding of the degree of EF impairment for the four EFs in these groups will be made. It was proposed that the older adults will perform poorer than their younger counterparts.

In addition, a VBM study examining the neuroanatomical difference between CH older adults and age-matched individuals living with MCI and various stages of AD will be presented.

1.7.2 Thesis Structure

Chapter 2 provides a literature review of studies and tasks and their attributes in researching EFs in CH and neuropathological impaired populations. Chapter 3 presents the behavioural studies, the investigation of the four EF abilities, dual-task, inhibition, shifting, and updating, in CH young adults, aged 18 to 33 years, and CH older adults, 60 years and older, with the utilisation of two tasks per EF. This was to ensure a true comparison in

cognitive ability was made. In addition to the eight EF tasks, a variety of neuropsychological tasks, tests, and surveys were utilised in the studies. Consequently, each participant underwent three assessment sessions. Through these studies, the trajectory of decline of the four EFs was completed.

A supplementary chapter presents the performance of only the young adults with these EFs to observe how sensitive the individual tasks were in their ability to detect EF decline, and the similarity of the output measures.

Chapter 4 investigated how much the two tasks employed to assess each EF correlated in their output data. For example, was the performance outputs of the updating task pair similar? Also the EF structure loading of the task measures were investigated with confirmatory factor analysis (CFA). Data from Chapter 3 was used to accomplish this.

In Chapter 5, another literature review of studies on the neuroimaging of EFs in the CH and neuropathological impaired populations was conducted. This provided a foundation into understanding the neural activity of the brain and how it alters with normal healthy ageing and with neuropathological impairment.

Subsequently, the final study described in Chapter 6, experiment 3, describes my utilisation of the OASIS-3 secondary imaging datasets to examine the neuroanatomical changes in the brains from CH to more severe AD. (As I was unable to complete my planned neuroimaging study assessing CH young and older adults, and MCI and AD participants on one of the EF task pair used in the behavioural study for each of the four EFs.)

Chapter 7 offers a final discussion of the findings of the behavioural and neuroimaging studies, and their importance in the assessment of cognitive impairment including limitations of the studies and possible directions for future research. I end the chapter with a final conclusion of the overall research.

Chapter 2, The Assessment of Executive Function Abilities - A Literature Review

2.1. Introduction

Decline in executive functions (EFs) is a prominent feature of cognitive ageing and neuropathological cognitive impairment, such as dementia (Cadar, 2018; Deary et al., 2009; Mortamais et al., 2017). Of particular interest are the four EF domains dual-tasking (DT), inhibition, shifting and updating, which have been argued to be fundamental for the accomplishment of tasks essential for everyday living (Miyake, Friedman, et al., 2000). The successful implementation of these cognitive abilities is associated with an individual's level of independence, as well as their capacity to understand and coordinate their thoughts effectively. Neuroanatomical changes in the brain resulting in performance impairments in one, or more, of these EF domains have been reported by numerous studies e.g. Espinosa et al, (2009) and de Faria et al, (2015). Specifically, they have been reported in cognitively healthy (CH) older individuals, and in those living with mild cognitive impairment (MCI) and/or dementia, specifically Alzheimer's disease (AD) (Albinet et al., 2012; Belleville et al., 1998; Clément et al., 2013; Guarino et al., 2020; Johns et al., 2012; Rabi et al., 2020; S. A. Wylie et al., 2007). This has been accomplished with the utilisation of an array of tasks validated for use in the diagnosis of executive dysfunction, although it should be noted that there are no standard instruments for measuring executive dysfunction in any study population.

EFs are heterogenous and multifaceted in nature (Norman & Shallice, 1986). Tasks employed in their assessment are normally dependent on additional skills, such as language, visuospatial skill, or speed processing. To deal with such issues, EF tasks normally employ two or more conditions (e.g. congruent and incongruent or repetition and shifting) that require similar supplementary skills but ideally differ only in the demand required by the specific EF. Therefore, to alleviate the effects of supplementary skills, the difference in performance between task conditions, i.e. task cost, is calculated. Hence, any deficits in these basic-level skills should not affect the specific EF, provided the skills are not so severe and prevent task performance. Nevertheless, not all studies calculate cost measures, so a true representation of EF decline may not be observed, as any dysfunction reported may

have occurred in one, or more, of the supplementary skills, or possibly a different EF entirely due to overlapping EF requirement, not actually being examined.

This latter issue of a task requiring multiple EF abilities relates to the purity of a task (Lezak et al., 2012). Although EF tasks have typically been created to assess a specific EF ability, sometimes they require the contribution of overlapping EF abilities to effectively perform that task. Thus, making interpretation of results difficult due to the complex mixture of cognitive processes. An example of such a task is the random number generation task (Baddeley, 1998), which requires the implementation of inhibition and updating ability for its successful completion (a brief description of this and all the EF tasks discussed in this chapter can be found in Appendix 1). Similarly, the Behavioural Assessment of the Dysexecutive Syndrome rule shift cards task (Wilson et al., 1996) requires the application of inhibition and shifting. Unlike supplementary skills, it is unknown if performance deficits found are caused by decline in either of the two involved EFs (inhibition and shifting, in this example) or a combination of both.

Another aspect of consideration is that performance in a task is not necessarily predictive of performance in another task measuring the same EF (Burda et al., 2017). Currently, there is no clear consensus amongst researchers on how best to measure EFs, thus a variety of tasks have been employed across various participant groups (Miyake, Emerson, et al., 2000). Although a preferred task may not be sensitive enough in assessing decline of that ability. Similarly, even with the use of the same task, different types of stimuli, and modifications to the task demand have further increased the heterogeneity of tasks across studies. Thus, a primary aim of this review was task factors, including task demand, task sensitivity, task stimuli, and the outcome measures employed by researchers, particularly in those that employed multiple tasks on the same group of participants.

The studies reviewed were those primarily assessing DT, inhibition, shifting, and updating in CH older adults, and in those living with MCI and AD published between 2000 and 2019, as it was felt these most recent studies would be more relevant to the current review. A second aim was to determine the EF tasks most frequently employed for each EF to aid in the selection of tasks (a pair per EF) for use in the behavioural studies of young and older adults, presented in Chapter 3. Consideration was focussed on the ease of administration to various

age groups and clinical conditions, task duration, and method of application, as well as participant group characteristics.

2.2. Methods

A literature search of English language journal articles published between 2000 and 2019 was conducted in PubMed/Medline, PsycINFO, Embase, Web of Science and Google Scholar databases. The search was based on a combination of key terms 'Alzheimer's disease (AD), age-associated cognitive decline, cognitive decline, cognitive ageing/aging, cognitive impairment, dementia, dual-/multi-task or tasking, executive dysfunction, executive function(s), inhibition, mild cognitive impairment (MCI), older adult, shifting, switching, working memory, working memory updating and updating'. For example, 'cognitive ageing and DT'. The articles were then screened for their suitability before being included in the review. Eligibility included studies with CH older adult participants or those with a diagnosis of MCI or AD, with the employment a control group, i.e. comparing CH older adults with their younger counterparts, or MCI and/or AD groups with CH groups.

Studies were excluded if 1) they did not use the mini-mental state examination (MMSE) test (Folstein et al., 1975) during the screening session to measure cognitive status, 2) in the case of DT, assessed non-cognitive DT ability, i.e. motor function involving walking or standing, 3) article was a review, and 4) in the pathological cognitively impaired studies, MCI and AD was not a primary diagnosis of the participants, i.e. secondary to another condition.

2.3. Characterisation of participants

2.3.1 Cognitive Status

Determining the global cognitive status of participants is important, particularly when dealing with middle-aged and older individuals, due to cognitive ageing. This review focused on the employment of the MMSE (Folstein et al., 1975) or modified forms, i.e. 3MSE (E.L. & Chui, 1987; T. N. Tombaugh et al., 1996), during the screening process of participants prior to EF assessment.

There were a number of studies that do not screen their so-called 'cognitive healthy middle- and/or older aged' participants, thus it is unknown whether these participants were indeed CH. This was evident in a study reported by Ebert & Anderson (2009) who determined a

proportion of their CH older adult participants met the criteria for amnestic MCI (aMCI) following psychometric testing. Therefore, studies that do not confirm the cognitive status of their control group may have mistakenly included individuals with pathological cognitive impairments.

Furthermore, when considering dementia, the Alzheimer's disease assessment scale-cognitive subscale (ADAS-Cog) (Rosen et al., 1984), clinical dementia rating scale (CDR) (C. P. Hughes et al., 1982), MoCA (Nasreddine et al., 2005) and Mattis dementia rating scale (DRS) (Mattis, 1976), are also frequently used, and have been considered to be more sensitive in rating the cognitive status of memory impaired individuals (Balsis et al., 2015; Perneczky et al., 2006; Pinto et al., 2019). Thus, a participant who is categorised as CH with the MMSE might not be considered the same with one of these other cognitive tests.

Therefore, in this review, studies were only considered which assessed the cognitive status with the MMSE or modified forms in all investigated groups, including the older adult CH control groups.

2.3.2 Physical Health

While not important to this review, the level of physical health of participants in the examination of EFs should also be considered. This attribute was assessed by Hillman et al (2006) and Boucard et al (2012) in addition to age effects of EF ability. In both cases, the more active of the groups performed better than their sedentary counterparts.

Thus, it is important to note the physical health and not just the educational and cognitive health of a study population when comparing results from studies assessing the same type of cognitive domain. Such characteristics may greatly affect results.

2.4. The Assessment of Executive Function Abilities

2.4.1 Dual-tasking

DT is the simultaneous performance of two tasks (MacPherson, 2018), which occurs in many day-to-day situations.

Between the years of 2000 and 2019, nine studies were reviewed to have compared this ability between CH young and older adults, 10 studies researching MCI and 10 studies researching AD (two of which compared both MCI and AD), see Table 2.1.

Table 2.1. Assessing Cognitive Dual-Task capacity in Cognitive Ageing, and MCI and AD sufferers. Studies are arranged by publication year under each heading.

Study	Participants	MMSE (Mean/SD)	Task/Test	Deficit
Cognitive Ageing studies				
McCabe & Hartman (2003)	CHOA 48 CHYA 48	29.4 (0.7) NA	DT word span task	Yes NA
Bherer et al (2006)	CHOA 7M 5F CHYA 5M 7F	MM 56 (UNK) NA	Auditory discrimination and visual identification task	Yes NA
Maquestiaux et al (2010)	CHOA 3M 9F CHYA 10M 10F	29.2 (1.0) NA	PRP Paradigm	Yes NA
Strobach et al (2012a)	CHOA 5M 5F CHYA 5M 5F	29.8 (0.4) NA	PRP Paradigm	Yes NA
Strobach et al (2012b)	CHOA 5M 5F CHYA 5M 5F	29.8 (0.4) NA	PRP Paradigm	Yes NA
Laguë-Beauvais et al (2015)	CHOA 6M 13F CHYA 7M 9F	28.26 (0.93) NA	Colour and Letter dual-task (PRP Paradigm)	Yes NA
Ren et al (2017)	CHOA 20 CHYA 20	UNK UNK	Audiovisual temporal asynchrony integration task (PRP Paradigm)	Yes NA
Ren et al (2018)	CHOA 15 CHYA 15	UNK UNK	Audiovisual temporal asynchrony integration task (PRP Paradigm)	Yes NA
B. Wang et al (2018)	CHOA 25 CHYA 27	> 24 > 24	Audiovisual temporal asynchrony integration task (PRP Paradigm)	Yes NA
MCI and AD studies				
Perry & Hodges (2000)	aMCI 12 CHOA 20	26.2 (1.6) 29.0 (1.0)	Della Sala DT	No NA
Perry et al (2000)	mAD 14 miAD 13 CHOA 30	20.4 (2.0) 26.08 (1.6) 29.4 (0.8)	Della Sala DT	Yes No NA
Baddeley et al (2001) – Experiment 4	AD 26M 10F CHOA 18M 18F CHOY 10M 26F	19.94 (1.78) UNK NA	Visual search and auditory detection DT	Yes Yes NA
Calderon et al (2001)	AD 6M 3F	21.4 (2.2)	Della Sala DT	Yes

	CHOA 7M 10F (DLB 8M 2F)	28.8 (1.0) [20.0 (3.1)]		NA Yes
Logie et al (2004) – Experiment 1	AD 4M 4F CHOA 4M 4F CHOY 4M 4F	21.1 (2.3) 28.9 (1.3) NA	Baddeley's digit recall and tracking	Yes No NA
MacPherson et al (2004)	AD 12 CHOA 12 CHOY 12	22.0 (2.0) UNK NA	Della Sala DT	Yes Yes NA
Dannhauser et al (2005)	aMCI 5M 5F CHOA 4M 10F	24.5 (1.5) 28.3 (1.6)	Visual and auditory processing paradigm	Yes NA
Nordlund et al (2005)	MCI 35 CHOA 112	28.5 (1.5) 29.3 (1.1)	Baddeley's digit recall and tracking DT	No NA
Lopez et al (2006)	mixMCI 13M 15F aMCI 6M 4F CHOA 142M 232F	3MSE 88.2 (7.3) 92.6 (6.2) 96.0 (12.3)	Baddeley's digit recall and tracking DT	Yes No NA
Sebastian et al (2006)	AD 8M 19F CHOA 7M 20F CHOY 3M 27F	20.37 (2.20) 27.56 (2.12) NA	Della Sala DT	Yes No NA
MacPherson et al (2007)	AD 5M 10F CHOA 10M 10F CHOY 10M 10F	22.1 (1.8) UNK NA	Baddeley's digit recall and tracking DT	Yes No NA
Silveri et al (2007)	mixMCI 8 naMCI 12 aMCI 13 CHOA 21	26.00 (1.41) 27.00 (2.67) 26.54 (1.98) 29.05 (0.97)	Test for Everyday Attention DT	Yes No No NA
Kaschel et al (2009)	AD 12M 10F CHOA 9M 15F (D 21M 22F)	21.5 (3.3) 28.5 (1.3) [29.1 (0.8)]	Baddeley's digit recall and tracking DT	Yes NA (No)
Lonie et al (2009)	mAD 3M 7F aMCI 16M 17F CHOA 8M 13F (D 3M 14F)	25.0 (2.3) 28.4 (1.6) 29.1 (0.7) [28.6 (1.5)]	Baddeley's digit recall and tracking DT	No No NA (No)
Price et al (2010)	aMCI 8M 25F CHOA 9M 24F	27.4 (1.4) 29.0 (0.9)	Test for Everyday Attention DT	No NA
Foley et al (2011)	AD 23M 27F MCI 18M 31F CHOA 22M 28F	19.32 (4.14) 27.04 (1.74) UNK	Della Sala DT	Yes No NA
Clément et al (2013)	LMCI 5M 7F HMCI 5M 7F CHOA 6M 8F	27.00 (1.81) 28.92 (1.68) 29.29 (1.14)	Alphanumeric equation task and visual detection DT	Yes Yes NA
Foley et al (2013)	AD 23M 27F CHOA 22M 28F	19.32 (4.14) NA	Digit recall and tracking DT	Yes NA
Makizako et al (2013)	aMCI 21M 15F CHOA 26M 36F	27.1 (1.8) 27.0 (2.0)	Visual stimuli and cognitive test DT	Yes NA

3MSE - modified Mini-Mental State Examination, a - amnestic, AD - Alzheimer's disease, CHOA - Cognitively healthy older adult, CHYA - Cognitively healthy young adult, HMCI - high cognition MCI, LMCI - low cognition MCI, MCI - Mild Cognitive Impairment, m - mild, mi - minimal, mix – mixed, mo - moderate, MM - modified extended Mini-Mental State Examination, NA - non applicable, UNK – unknown.

DT abilities was most frequently assessed between young and older adults with the psychological refractory period (PRP) paradigm, or a variant, observed in 78% of the studies reviewed. Where performance deficits in the older group was reported in all the studies. Whereas the Della Sala DT (Della Sala et al., 1995a) was most commonly employed in 30% of the studies involving MCI participants, and 40% of AD participants studies, with one study assessing both groups (Foley et al., 2011). No DT deficits were reported with the MCI participants except for one study with two MCI groups, where the mild MCI group showed deficits but not the minimal (the less severe) MCI group (R. J. Perry et al., 2000). The (Baddeley) digit recall and tracking DT (Baddeley et al., 1986; Foley et al., 2013) was also used in 40% of AD participants. Deficits with this group was observed in all the studies that used the Della Sala DT, and in all the digit and tracking DT studies except for one (Lonie et al., 2009).

2.4.2 Inhibition

The EF inhibition is defined as the suppression of prepotent thoughts and actions (Miyake, Friedman, et al., 2000).

Thirty-five studies were found to have assessed inhibitory control between young and older adults, 46 studies assessing MCI participants, and 39 studies assessing AD participants, see Table 2.2.

Table 2.2. Assessing Inhibition ability in Cognitive Ageing, and MCI and AD sufferers

Study	**Participants**	**MMSE (Mean/SD)**	**Task/Test**	**Deficit**
Cognitive Ageing studies				
Nielson et al (2002)	CHOA 4M 4F CHYOA 1M 8F CHMA 3M 4F CHYA 6M 4F	> 26 > 26 > 26 NA	Go/No-Go	Yes No No NA
Langenecker & Nielson (2003)	CHOA 3M 8F CHYA 4M 7F	> 26 > 26	Go/No-Go	No NA
Nielson et al (2004)	CHOA 6M 8F	28.6 (1.5)	Go/No-Go	Yes

	CHYA 8M 6F	NA		NA
Langenecker et al (2004)	CHOA 5M 8F CHYA 6M 7F	28.4 (1.56) NA	Stroop	Yes NA
Bherer et al (2006)	CHOA 7M 5F CHYA 5M 7F	MM 56 (UNK) NA	Stroop	Yes NA
Keightley et al (2006)	CHOA 30 CHYA 30	28.8 (0.9) 29.7 (0.5)	Stroop	Yes NA
Jennings et al (2007)	CHOA 35M 28F CHYA 25M 35F	29.21 (SE 0.12) NA	Flanker (Attentional network task)	Yes NA
Langenecker et al (2007)	CHOA 11 CHYA 11	29.4 (0.8) 29.3 (0.7)	Go/No-Go	Yes NA
Andrés et al (2008) – Experiment 1	CHOA 30 CHYA 30	28.46 (1.13) NA	Stroop	Yes NA
Andrés et al (2008) – Experiment 1	CHOA 30 CHYA 30	28.46 (1.13) NA	Negative Priming	No NA
Andrés et al (2008) – Experiment 2	CHOA 43 CHYA 45	29.1 (1.3) NA	Stop-signal	Yes NA
Andrés et al (2008) – Experiment 2	CHOA 43 CHYA 45	29.1 (1.3) NA	Negative Priming	No NA
Damoiseaux et al (2008)	CHOA 9M 13F CHYA 5M 5F	28.73 (1.4) 29.50 (0.5)	Stroop	Yes NA
Clarys et al (2009)	CHOA 44 CHYA 44	> 27 NA	Stroop	Yes NA
Gamboz et al (2009)	CHOA 40 CHYA 40	29.5 (0.8) NA	Stop-signal	Yes NA
Kubo-Kawai & Kawai (2010)	CHOA 9M 6F CHYA 6M 12F	≥ 24 NA	Simon	Yes NA
Kubo-Kawai & Kawai (2010)	CHOA 9M 6F CHYA 6M 12F	≥ 24 NA	Simon (Go/no-go version)	No NA
Maquestiaux et al (2010)	CHOA 3M 9F CHYA 10M 10F	29.2 (1.0) UNK	Modified Stroop	Yes NA
Morrone et al (2010)	CHOA 12M 18F CHYA 10M 20F	29.5 (0.62) NA	Hayling	Yes NA
Morrone et al (2010)	CHOA 12M 18F CHYA 10M 20F	29.5 (0.62) NA	Stroop	Yes NA
Vallesi et al (2010)	CHOA 9M 11F CHYA 8M 12F	28.5 (UNK) NA	Letter-Number Go/No-Go	Yes NA
Vallesi et al (2010)	CHOA 9M 11F CHYA 8M 12F	28.5 (UNK) NA	Number Go/No-Go	Yes NA
Albinet et al (2012)	CHOA 17M 22F CHYA 11M 17F	28.4 (1.4) NA	Stroop	Yes NA
Albinet et al (2012)	CHOA 17M 22F CHYA 11M 17F	28.4 (1.4) NA	Stop-signal	Yes NA

Albinet et al (2012)	CHOA 17M 22F CHYA 11M 17F	28.4 (1.4) NA	Random Number Generation, Adjacency	Yes NA
Boucard et al (2012)	acCHOA 7M 8F seCHOA 7M 8F acCHYOA 7M 8F seCHYOA 7M 8F acCHYA 15M 17F seCHYA 15M 16F	29.2 (0.8) 28.9 (1.0) 29.1 (0.8) 29.1 (1.0) NA NA	Random Number Generation, Adjacency	Yes Yes Yes Yes NA NA
Boucard et al (2012)	acCHOA 7M 8F seCHOA 7M 8F acCHYOA 7M 8F seCHYOA 7M 8F acCHYA 15M 17F seCHYA 15M 16F	29.2 (0.8) 28.9 (1.0) 29.1 (0.8) 29.1 (1.0) NA NA	Simon	Yes Yes Yes Yes NA NA
Boucard et al (2012)	acCHOA 7M 8F seCHOA 7M 8F acCHYOA 7M 8F seCHYOA 7M 8F acCHYA 15M 17F seCHYA 15M 16F	29.2 (0.8) 28.9 (1.0) 29.1 (0.8) 29.1 (1.0) NA NA	Stroop	Yes Yes Yes Yes NA NA
Endrass et al (2012)	CHOA 11M 11F CHYA 10M 11F	29.1 (0.9) NA	Modified Flanker	Yes NA
Hsieh et al (2012)	CHOA 9M 7F CHYA 6M 10F	29.56 (0.63) 29.69 (0.70)	Flanker (PRO-bias)	No NA
Hsieh et al (2012)	CHOA 9M 7F CHYA 6M 10F	29.06 (0.93) 29.63 (0.62)	Flanker (non-bias)	No NA
Hsieh et al (2012)	CHOA 9M 7F CHYA 6M 10F	29.19 (0.83) 29.63 (0.50)	Flanker (ANTI - bias)	No NA
Kawai et al (2012)	CHOA 13M 2F CHYA 8M 5F	27.7 (UNK) NA	Flanker	No NA
Kawai et al (2012)	CHOA 13M 2F CHYA 8M 5F	27.7 (UNK) NA	Simon	Yes NA
Mayas et al (2012)	CHOA 7M 11F CHYA 7M 11F	29.44 (0.70) 29.44 (0.70)	Stroop	Yes NA
Mayas et al (2012)	CHOA 7M 11F CHYA 7M 11F	29.44 (0.70) 29.44 (0.70)	Negative Priming	Yes NA
Wang & Su (2013)	CHOA 16M 16F CHOM 21M 21F CHYA 16M 16F	> 27 > 27 > 27	Hayling - Part B	Yes Yes NA
Wang & Su (2013)	CHOA 7M 11F CHOM 7M 11F CHYA 7M 11F	> 27 > 27 > 27	Stroop	Yes No NA
Aisenberg et al (2014) – Experiment 1	CHOA 15 CHYA 15	29.3 (UNK) NA	Simon	Yes NA

Amer & Hasher (2014)	CHOA 9M 23F CHYA 12M 22F	29.09 (1.06) NA	Stroop	Yes NA
Pettigrew & Martin (2014)	CHOA 60 CHYA 102	28.8 (1.1) NA	Flanker	Yes NA
Pettigrew & Martin (2014)	CHOA 60 CHYA 102	28.8 (1.1) NA	Stroop	Yes NA
Pettigrew & Martin (2014)	CHOA 60 CHYA 102	28.8 (1.1) NA	Nonverbal Stroop task	Yes NA
Pettigrew & Martin (2014)	CHOA 60 CHYA 102	28.8 (1.1) NA	Picture-word interference	No NA
Tournier et al (2014)	CHOA 31 CHYA 30	28.93 (1.06) NA	Hayling	Yes NA
Aisenberg et al (2015) – Experiment 1	CHOA 51 CHYA 45	> 27 NA	Simon	Yes NA
Laguë-Beauvais et al (2015)	CHOA 6M 13F CHYA 7M 9F	28.26 (0.93) NA	Stroop	Yes NA
Sylvain-Roy et al (2015)	CHOA 28M 46F CHYA 33M 42F	29.0 (1.1) NA	Antisaccade	Yes NA
Sylvain-Roy et al (2015)	CHOA 28M 46F CHYA 33M 42F	29.0 (1.1) NA	Modified Stroop	Yes NA
Coxon et al (2016)	CHOA 9M 11F CHYA 9M 11F	≥ 27 ≥ 29	Stop-signal	Yes NA
Hsieh et al (2016)	CHOA 7M 9F CHYA 7M 9F	27.19 (0.73) 28.19 (1.01)	20% Go/80% No-Go (small demand)	Yes NA
Hsieh et al (2016)	CHOA 8M 8F CHYA 8M 8F	26.69 (1.10) 28.50 (0.71)	50% Go/50% No-Go (equal demand)	Yes NA
Hsieh et al (2016)	CHOA 7M 9F CHYA 7M 9F	27.06 (1.14) 28.63 (0.60)	80% Go/20% No-Go (high demand)	Yes NA
Crawford et al (2017)	CHOA 15 CHYA 16	UNK NA	Antisaccade	Yes NA
Crawford et al (2017)	CHOA 15 CHYA 16	UNK NA	Memory-guided Antisaccade	Yes NA
Crawford et al (2017)	CHOA 15 CHYA 16	UNK NA	Go/No-Go Antisaccade	Yes NA
Dupart et al (2018)	CHOA 7M 31F CHYA 8M 30F	28.97 (1.35) NA	Emotional Hayling	Yes NA
Waring et al (2019)	CHOA 17M 19F CHYA 24M 20F	29.17 (1.06) NA	Emotional Go/No-Go	Yes NA
Waring et al (2019)	CHOA 17M 19F CHYA 24M 20F	29.17 (1.06) NA	Colour word interference	Yes NA
MCI and AD studies				
Perry & Hodges (2000)	AD 12 CHOA 20	26.2 (1.6) 29.0 (1.0)	Stroop	Yes NA

Perry et al (2000)	mAD 14 miAD 13 CHOA 30	20.4 (2.0) 26.08 (1.6) 29.4 (0.8)	Stroop	Yes Yes NA
Calderon et al (2001)	AD 6M 3F CHOA 7M 10F (DLB 8M 2F)	21.4 (2.2) 28.8 (1.0) [20.0 (3.1)]	Stroop	Yes NA (NA)
Collette et al (2002)	AD 4M 22F CHOA 4M 22F	19.3 (4.2) UNK	Go/No-Go	Yes NA
Collette et al (2002)	AD 4M 22F CHOA 4M 22F	19.3 (4.2) UNK	Hayling	Yes NA
Collette et al (2002)	AD 4M 22F CHOA 4M 22F	19.3 (4.2) UNK	Stroop	Yes NA
Dwolatzky et al (2003)	mAD 13M 16F MCI 17M 13F CHOA 13M 26F	24.17 (3.25) 27.63 (1.54) 29.03 (1.11)	Go/No-Go	Yes Yes NA
Dwolatzky et al (2003)	mAD 13M 16F MCI 17M 13F CHOA 13M 26F	24.17 (3.25) 27.63 (1.54) 29.03 (1.11)	Stroop	NA Yes NA
Amieva et al (2004)	revAD 6M 16F revCHOA 6M 16F intAD 5M 17F intCHOA 5M 17F	21.4 (2.4) 27.5 (1.7) 21.1 (3.0) 27.9 (1.7)	Modified Stroop	Yes NA Yes NA
Crawford et al (2005)	mAD 13M 5F CHOA 8M 10F CHOY 8M 9F	20.9 (4.3) 29.2 (1.1) NA	Antisaccade	Yes Yes NA
Crawford et al (2005)	mAD 13M 5F CHOA 8M 10F CHOY 8M 9F	UNK > 27 NA	Go/No-Go	Yes Yes NA
Nordlund et al (2005)	MCI 35 CHOA 112	28.5 (1.5) 29.3 (1.1)	Picture Stroop	Yes NA
Nordlund et al (2005)	MCI 35 CHOA 112	28.5 (1.5) 29.3 (1.1)	Victoria Stroop	No NA
Belleville et al (2006)	AD 4M 8F CHOA 4M 8F CHOY 6M 6F	22.9 (2.0) 28.2 (1.1) NA	Hayling	Yes Yes NA
Belleville et al (2006)	AD 4M 8F CHOA 4M 8F CHOY 6M 6F	22.9 (2.0) 28.2 (1.1) NA	Stroop	Yes Yes NA
Duong et al (2006)	AD 39 MCI 61 CHOA 60	29.12 (0.97) 27.20 (2.25) 22.08 (3.76)	Picture Stroop	Yes Yes NA
Duong et al (2006)	AD 39 MCI 61 CHOA 60	29.12 (0.97) 27.20 (2.25) 22.08 (3.76)	Victoria - Stroop	Yes No NA
Kramer et al (2006)	AD 33 aMCI 22 CHOA 35	25.2 (1.3) 28.5 (1.5) 29.5 (0.8)	Stroop	Yes Yes NA

Lopez et al (2006)	mixMCI 13M 15F aMCI 6M 4F CHOA 142M 232F	3MSE 88.2 (7.3) 92.6 (6.2) 96.0 (12.3)	Stroop	Yes No NA
Belleville et al (2007)	AD 19 CHOA 29 in total MCI 28 CHOA 29 in total	24.65 (3.60) 28.74 (0.93) 28.36 (1.98) 28.88 (0.99)	Hayling	Yes NA No NA
Belleville et al (2007)	AD 19 CHOA 29 in total MCI 28 CHOA 29 in total	24.65 (3.60) 28.74 (0.93) 28.36 (1.98) 28.88 (0.99)	Victoria - Stroop	Yes NA No NA
Traykov et al (2007)	MCI 16M 4F CHOA 14M 6F	28.95 (1.1) 29.5 (0.5)	Stroop	Yes NA
Zamarian, Semenza, et al (2007)	AD 6M 9F CHOA 7M 13F MCI 11M 7F CHOA 5M 15F	21.3 (2.2) 29.1 (0.8) 27.0 (1.4) 28.8 (0.8)	Math Stroop	Yes NA Yes NA
Zamarian, Semenza, et al (2007)	AD 6M 9F CHOA 7M 13F MCI 11M 7F CHOA 5M 15F	21.3 (2.2) 29.1 (0.8) 27.0 (1.4) 28.8 (0.8)	Colour word interference	Yes NA Yes NA
Zhang et al (2007)	MCI 32 CHOA 32	27.4 (2.0) 28.7 (1.8)	Go/No-Go	No NA
Zhang et al (2007)	MCI 32 CHOA 32	27.4 (2.0) 28.7 (1.8)	Negative Priming	No NA
Zhang et al (2007)	MCI 32 CHOA 32	27.4 (2.0) 28.7 (1.8)	Stroop	No NA
Belleville et al (2008)	AD 6M 7F CHOA M 11F MCI 8M 12F CHOA M 15F	24.85 (4.0) 28.69 (0.8) 28.15 (2.1) 28.9 (0.9)	Stroop - Victoria	Yes NA No NA
Bisiacchi et al (2008) – Experiment 2	AD 8M 12F aMCI 6M 8F CHOA 5M 9F	20.79 (1.92) 25.71 (1.59) 27.80 (1.57)	Hayling	Yes No NA
Kaufmann et al (2008)	MCI 6 CHOA 9	24.8 (1.2) 29.0 (1.2)	Numerical Stroop	Yes NA
Bélanger & Belleville (2009)	AD 8 MCI 18 CHOA 16 CHYA 20	23.5 (4.0) 27.3 (1.8) 29.2 (0.9) NA	Hayling	Yes Yes Yes NA
Bélanger & Belleville (2009)	AD 8 MCI 18 CHOA 16 CHYA 20	23.5 (4.0) 27.3 (1.8) 29.2 (0.9) NA	Stroop	No No NA NA
Brambati et al (2009)	mMCI 18 5M 5F aMCI-MD 3M 11F	22.5 (2.3) 26.5 (1.8)	Stroop - Victoria	Yes Yes

	aMCI-SD 5M 6F CHOA 5M 8F	28.5 (1.0) 29.1 (1.2)		No NA
C. Li et al (2009)	AD 5M 5F MCI 5M 4F CHOA 4M 5F	16.7 (2.6) 26.4 (4.2) 28.8 (0.9)	Stroop	Yes Yes NA
Zhou & Jia (2009)	MCI/AD 12M 18F MCI/SVD 36M 20F CHOA 45M 35F	26.2 (1.1) 26.7 (2.2) 28.8 (1.1)	Stroop	Yes Yes NA
Bélanger et al (2010)	AD 11 MCI 20 CHOA 20 CHYA 20	23.4 (3.7) 27.4 (2.1) 28.8 (1.4) NA	Stroop	Yes Yes Yes NA
Grönholm-Nyman et al (2010)	AD 3M 6F MCI 6M 7F CHOA 3M 9F	25.3 (3.2) 27.5 (1.5) 29.1 (0.7)	Stroop	Yes Yes NA
Hutchison et al (2010)	AD (mild) 21M 17F CHOA 24M 39F	28.22 (UNK) 29.19 (UNK)	Stroop	Yes NA
Luks et al (2010)	AD 4M 2F MCI 6M 3F CHOA 12M 10F (CBD 1M 1F FTD 8M 3F PNFA 1M 1F PSP 1M 2F SD 6M 4F)	27.0 (0.8) 29.0 (1.0) 29.0 (0.7) [28.0 (0.0) 27.0 (2.9) 27.0 (0.0) 27.0 (4.2) 24.0 (5.8)]	Flanker	Yes No NA (Yes Yes No Yes Yes)
McGuinness et al (2010)	AD 28 CHOA 75 (VaD 46)	> 12 ≥ 28 (≥ 12)	Stroop	Yes NA (Yes)
Pa et al (2010)	AD 6M 4F MCI 30M 27F CHOA 20M 20F (ALS 5M 1F CBD 4M 8F FTD 17M 4F SD 9M 5F)	26.0 (3.1) 28.4 (1.5) 29.8 (0.5) [29.2 (2.0) 27.3 (2.0) 26.1 (4.4) 23.5 (6.2)]	Colour word interference	Yes Yes NA (No Yes Yes Yes)
S. E. Price et al (2010)	aMCI 8M 25F CHOA 9M 24F	27.4 (1.4) 29.0 (0.9)	Colour word interference	No NA
Sinai et al (2010)	MCI-able 6M 10F MCI-cue 3M 2F MCI-unable 2M 4F CHOA 5M 12F	28.40 (0.4) 26.20 (0.8) 25.17 (0.8) 28.6 (0.4)	Stroop - Victoria	No No No NA
Tse et al (2010)	AD 74 CHOA 246 CHYA 32	26.58 (2.78) 28.99 (1.36) NA	Stroop	Yes Yes NA

Tse et al (2010)	AD 74 CHOA 246 CHYA 32	26.58 (2.78) 28.99 (1.36) NA	Simon	Yes Yes NA
Ahn et al (2011)	AD 52M 118F aMCI 47M 52F CHOA 56M 86F	19.3 (5.0) 26.2 (2.5) 28.7 (1.5)	Go/No-Go	Yes Yes NA
Ahn et al (2011)	AD 52M 118F aMCI 47M 52F CHOA 56M 86F	19.3 (5.0) 26.2 (2.5) 28.7 (1.5)	Stroop	Yes Yes NA
Gagnon & Belleville (2011)	AD 16 aMCI 13 and md aMCI 7 CHOA 20	23.94 (2.29) 27.95 (1.50) 28.80 (1.06)	Stroop - Victoria	Yes No NA
C. Li et al (2011)	AD 3M 3F CHOA 3M 5F (VaD 4M 2F)	20.4 (UNK) 28.7 (UNK) [20.4 (UNK)]	Stroop	Yes NA (Yes)
Apostolova et al (2012)	AD 16M 27F MCI 22M 11F CHOA 25M 21F	22.2 (4.9) 27.8 (2.3) 29.5 (0.6)	Stroop	Yes Yes NA
Guerdoux et al (2012) – Experiment 2	AD 7M 10F aMCI 10M 7F CHOA 11M 6F	24.0 (1.9) 27.5 (1.6) 28.4 (1.3)	Stroop - Victoria	Yes No NA
Johns et al (2012)	aMCI 18M 22F CHOA 13M 19F	28.1 (1.4) 28.9 (1.1)	Stroop	Yes NA
Johns et al (2012)	MCI 18M 22F CHOA 13M 19F	28.1 (1.4) 28.9 (1.1)	Hayling	Yes NA
Zheng et al (2012)	aMCI 14M 20F CHOA 18M 18F	28.3 (1.5) 29.5 (0.7)	Stroop	No NA
Zheng et al (2012)	aMCI 14M 20F CHOA 18M 18F	28.3 (1.5) 29.5 (0.7)	Stop-signal	Yes NA
Sung et al (2012)	MCI 16 CHOA 16	[1]24.87 (3.40) [1]26.45 (2.11)	Go/No-Go	No NA
Sung et al (2012)	MCI 16 CHOA 16	[1]24.87 (3.40) [1]26.45 (2.11)	Stroop	Yes NA
Chen et al (2013)	AD 88M 38F aMCI 82M 38F CHOA 68M 32F	20.2 (3.6) 26.6 (1.4) 28.4 (1.7)	Stroop	Yes Yes NA
Crawford et al (2013)	AD 18 CHOA 18 CHYA 17 (PD 25)	20.9 (4.3) 29.2 (1.1) UNK [28.8 (1.2)]	Antisaccade	Yes NA No (No)
Stricker et al (2013)	MCI 13M 19F CHOA 30M 51F	27.45 (1.95) 28.05 (1.68)	Stroop	Yes NA
Cid-Fernández et al (2014)	aMCI 14M 16F CHOA 22M 41F	25.9 (2.4) 28.2 (1.5)	Go/No-Go	Yes NA
Peltsch et al (2014)	AD 22M 50F	27.0 (2.0)	Antisaccade	Yes

	aMCI 10M 12F CHOA 9M 15F	27.0 (2.0) 29.0 (1.0)		Yes NA
Peltsch et al (2014)	AD 22M 50F aMCI 10M 12F CHOA 9M 15F	27.0 (2.0) 27.0 (2.0) 29.0 (1.0)	Stroop	Yes Yes NA
Pereiro et al (2014)	md aMCI 31 sd aMCI 31 CHOA 41	23.87 (1.78) 27.54 (1.47) 28.58 (1.35)	Simon	Yes Yes NA
Puente et al (2014)	MCI 7M 10F CHOA10M 16F	25.9 (2.4) 28.0 (2.0)	Stroop	Yes NA
Zheng et al (2014)	aMCI 16M 34F CHOA 19M 29F	27.9 (1.5) 29.5 (0.7)	Stop-signal	Yes NA
El Haj, Larøi, et al (2015)	AD 8M 23F CHOA 10M 23F	21.68 (1.87) 28.00 (1.52)	Stroop	Yes NA
El Haj, Antoine, & Kapogiannis (2015)	AD 8M 16F CHOA 9M 17F	21.83 (1.52) 28.31 (1.28)	Stroop	Yes NA
B. Y. Li et al (2016)	MCI 15M 9F CHOA 14M 8F	26.41 (2.12) 28.95 (0.95)	Stroop	No NA
Mudar et al (2016)	aMCI 9M 16F CHOA 9M 16F	28.4 (1.3) 28.6 (0.5)	Go/No-Go	Yes NA
Yuan et al (2016)	aMCI 57M 62F CHOA 42M 37F	26.21 (2.69) 28.21 (1.46)	Stroop	Yes NA
Borella et al (2017)	MCI 6M 9F CHOA 7M 11F	27.40 (1.45) 29.50 (0.62)	Stroop	Yes NA
Huang et al (2017)	AD 11M 20F CHOA 17M 14F	21.2 (3.2) 27.0 (1.2)	Stroop	Yes NA
Martyr et al (2017)	AD 18M 12F CHOA 22M 32F (PD 15M 18F)	23.10 (2.87) 28.78 (1.00) [29.39 (1.12)]	Hayling	Yes NA (Yes)
Borsa et al (2018)	aMCI 5M 2F CHOA 5M 2F	27.14 (2.11) 28.42 (1.81)	Flanker (Attentional network task)	Yes NA
Matías-Guiu et al (2018)	AD 7M 12F CHOA 9M 10F (bvFTD 9M 10F ALS 8M 11F)	24.26 (4.33) 29.16 (1.21) [24.00 (4.79) 28.00 (1.63)]	Hayling	Yes NA (Yes No)
Matías-Guiu et al (2018)	AD 7M 12F CHOA 9M 10F (bvFTD 9M 10F ALS 8M 11F)	24.26 (4.33) 29.16 (1.21) [24.00 (4.79) 28.00 (1.63)]	Stroop	Yes NA (Yes No)
Cervera-Crespo et al (2019)	moAD 8M 8F mAD 7M 8F CHOA 8M 8F	22.46 (1.06) 23.81 (0.91) 28.66 (2.49)	Hayling	Yes Yes NA
Garcia-Alvarez et al (2019)	AD 27M 30F MCI 27M 21F CHOA 49M 75F	21.21 (4.28) 25.96 (2.03) 28.49 (1.40)	Stroop	UNK Yes NA

Ferreira et al (2019)	moAD 11 mAD 22 CHOA 56 (D 19)	19.00 (UNK) 22.50 (UNK) 29.00 (UNK) [29.00 (UNK)]	Stroop	Yes Yes NA No

[1]Korean MMSE, ac - active, ALS - amyotrophic lateral sclerosis, bv - behavioural variant, CBD - cortical basal degeneration, FTD - frontotemporal dementia, int - performed the Interference task first, MCI/SVD - cerebral small vessel disease originated, MCI/AD - AD originated, md - multi-domain, p - Progressors, rev - performed the reverse task first, rMCI - reverted back to CH, sd - single-domain, se - sedentary, SD - semantic dementia, SE - Standard Error, sMCI - stayed as MCI, VaD - Vascular dementia.

Between young and older adults, the Stroop task (Stroop, 1935), or a modified version such as the nonverbal Stroop (Pettigrew & Martin, 2014), was employed 17 times across 16 studies. Pettigrew & Martin (2014) used a picture-word interference task (Lupker, 1979; Schriefers et al., 1990) as well. Inhibition deficits were reported in all. A similar task, the colour-word interference task (Delis et al., 2001) was utilised in one study (Waring et al., 2019) and also showed performance deficits.

The Stroop task, including other versions such as the Victoria (Spreen & Strauss, 1998), picture (Duong et al., 2006; Nordlund et al., 2005), math (Zamarian, Semenza, et al., 2007), and numerical (Kaufmann et al., 2008), was also observed to be the primary task used in the pathological cognitive impaired studies. It was employed in 34 studies involving MCI participants, and 33 studies with AD participants. 18 of these assessed both participant groups. Inhibitory deficits was reported in 62% (21) of the MCI participant studies, though two studies (Brambati et al., 2009; Lopez et al., 2006) with multiple MCI subtypes also reported finding no deficits with other MCI types assessed. All but one study (Bélanger & Belleville, 2009) reported deficits with the AD participants, however two did not assess their participants (Dwolatzky et al., 2003; Garcia-Alvarez et al., 2019).

2.4.3 Shifting

Shifting, also referred to as switching, is the ability to effectively move back and forth between two tasks (Miyake, Friedman, et al., 2000).

24 studies were reviewed comparing performance of this ability between CH young and older adults, 42 studies in older individuals living with MCI, and in 35 studies with AD participants, see Table 2.3.

Table 2.3. Assessing Shifting ability in Cognitive Ageing, and MCI and AD sufferers

Study	Participants	MMSE (Mean/SD)	Task/Test	Deficit
Cognitive Ageing studies				
Hartman et al (2001) – Experiment 1	CHOA 31M 45F CHYA 31M 54F	> 24 NA	WCST	Yes NA
Hartman et al (2001) – Experiment 2	CHOA 22M 26F CHYA 19M 29F	29.2 (0.9) NA	Modified WCST	Yes NA
Souchay & Isingrini (2004)	CHOA M F CHYA M F	28.65 (1.43) NA	WCST	Yes NA
Rhodes & Kelley (2005)	CHOA 50 CHYA 50	> 27 > 27	TMT	Yes NA
Rhodes & Kelley (2005)	CHOA 50 CHYA 50	> 27 > 27	WCST	Yes NA
Bherer et al (2006)	CHOA 7M 5F CHYA 5M 7F	MM 56 (UNK) NA	TMT Part B	Yes NA
Chee et al (2006) – Experiment 1	CHOA 6M 11F CHYA 7M 13F	28.7 (1.05) 29.4 (0.92)	TMT Part B	Yes NA
Hillman et al (2006)	acCHOA 17 seCHOA 15 acCHYA 18 seCHYA 16	27.8 (0.4) 29.1 (0.3) 28.9 (0.3) 29.2 (0.3)	Task Switching paradigm	Yes Yes NA NA
Keightley et al (2006)	CHOA 30 CHYA 30	28.8 (0.9) 29.7 (0.5)	TMT	No NA
Damoiseaux et al (2008)	CHOA 9M 13F CHYA 5M 5F	28.73 (1.4) 29.50 (0.5)	TMT	No NA
Skinner & Fernandes (2008)	CHOA 30 CHYA 30	28.73 (1.26) NA	TMT	Yes NA
Clarys et al (2009)	CHOA 44 CHYA 44	> 27 NA	Number-Letter	Yes NA
Clarys et al (2009)	CHOA 44 CHYA 44	> 27 NA	WCST	Yes NA
Gamboz et al (2009)	CHOA 40 CHYA 40	29.5 (0.8) NA	Number-Letter	Yes NA
Gamboz et al (2009)	CHOA 40 CHYA 40	29.5 (0.8) NA	WCST	Yes NA
Taconnat et al (2009)	CHOA 15M 47F CHYA 36M 26F	> 27 NA	WCST	Yes NA
Gold et al (2010)	CHOA 10 M 10F CHYA 10 M 10F	> 28 NA	Number-Letter	Yes NA
Maquestiaux et al (2010)	CHOA 3M 9F CHYA 10M 10F	29.2 (1.0) UNK	TMT	No NA
Albinet et al (2012)	CHOA 17M 22F CHYA 11M 17F	28.4 (1.4) NA	Dimension-Switching	Yes NA

Albinet et al (2012)	CHOA 17M 22F CHYA 11M 17F	28.4 (1.4) NA	S-R compatibility switching task	Yes NA
Albinet et al (2012)	CHOA 17M 22F CHYA 11M 17F	28.4 (1.4) NA	WSCT	Yes NA
Boucard et al (2012)	acCHOA 7M 8F seCHOA 7M 8F acCHYOA 7M 8F seCHOYA 7M 8F acCHYA 15M 17F seCHYA 15M 16F	29.2 (0.8) 28.9 (1.0) 29.1 (0.8) 29.1 (1.0) NA NA	Dimension-Switching	Yes Yes Yes Yes NA NA
Boucard et al (2012)	acCHOA 7M 8F seCHOA 7M 8F acCHYOA 7M 8F seCHOYA 7M 8F acCHYA 15M 17F seCHYA 15M 16F	29.2 (0.8) 28.9 (1.0) 29.1 (0.8) 29.1 (1.0) NA NA	(Digit) Number–Letter	Yes Yes Yes Yes NA NA
Boucard et al (2012)	acCHOA 7M 8F seCHOA 7M 8F acCHYOA 7M 8F seCHYOA 7M 8F acCHYA 15M 17F seCHYA 15M 16F	29.2 (0.8) 28.9 (1.0) 29.1 (0.8) 29.1 (1.0) NA NA	Plus–Minus	No No No No NA NA
Laguë-Beauvais et al (2013)	CHOA 3M 16F CHYA 8M 13F	29.00 (1.15) NA	TMT	Yes NA
Wang & Su (2013)	CHOA 16M 16F CHOM 21M 21F CHYA 16M 16F	> 27 > 27 > 27	WCST	Yes Yes NA
Müller et al (2014)	CHOA 8M 12F CHYA 8M 12F	29.25 (0.97) NA	TMT	Yes NA
Tournier et al (2014)	CHOA 31 CHYA 30	28.93 (1.06) NA	TMT	Yes NA
Laguë-Beauvais et al (2015)	CHOA 6M 13F CHYA 7M 9F	28.26 (0.93) NA	TMT	Yes NA
Sylvain-Roy et al (2015)	CHOA 28M 46F CHYA 33M 42F	29.0 (1.1) NA	Left–right shifting	Yes NA
Sylvain-Roy et al (2015)	CHOA 28M 46F CHYA 33M 42F	29.0 (1.1) NA	Number–Letter	Yes NA
Sylvain-Roy et al (2015)	CHOA 28M 46F CHYA 33M 42F	29.0 (1.1) NA	Plus–Minus	No NA
Waring et al (2019)	CHOA 17M 19F CHYA 24M 20F	29.17 (1.06) NA	TMT	Yes NA
MCI and AD studies				
Perry et al (2000)	mAD 14 miAD 13 CHOA 30	20.4 (2.0) 26.08 (1.6) 29.4 (0.8)	MCST	Yes No NA

Perry et al (2000)	mAD 14 miAD 13 CHOA 30	20.4 (2.0) 26.08 (1.6) 29.4 (0.8)	Visual Elevator	Yes No NA
Calderon et al (2001)	AD 6M 3F CHOA 7M 10F (DLB 8M 2F)	21.4 (2.2) 28.8 (1.0) [20.0 (3.1)]	MCST	Yes NA (Yes)
Traykov et al (2002)	AD 6M 3F CHOA 7M 10F (VaD 8M 2F)	23.2 (2.4) 29.2 (0.6) [23.9 (2.0)]	MCST	Yes NA (Yes)
Traykov et al (2002)	AD 6M 3F CHOA 7M 10F (VaD 8M 2F)	23.2 (2.4) 29.2 (0.6) [23.9 (2.0)]	TMT Part B	Yes NA (Yes)
Nagahama et al (2003)	AD 54 MCI 17 CHOA 22	20.8 (3.3) 26.4 (2.0) 29.1 (0.8)	MCST	Yes Yes NA
Nordlund et al (2005)	MCI 35 CHOA 112	28.5 (1.5) 29.3 (1.1)	MCST	No NA
Nordlund et al (2005)	MCI 35 CHOA 112	28.5 (1.5) 29.3 (1.1)	TMT Part B	Yes NA
Baudic et al (2006)	mAD 6M 12F vmAD 3M 15F CHOA 3M 14F	29.1 (0.6) 25.6 (1.0) 21.2 (1.2)	MCST	Yes Yes NA
Baudic et al (2006)	mAD 6M 12F vmAD 3M 15F CHOA 3M 14F	29.1 (0.6) 25.6 (1.0) 21.2 (1.2)	TMT Part B	Yes Yes NA
Kramer et al (2006)	AD 33 aMCI 22 CHOA 35	25.2 (1.3) 28.5 (1.5) 29.5 (0.8)	Modified TMT	Yes Yes NA
Loewenstein et al (2006)	mAD 6M 12F MCI/AD 3M 15F MCI/Vas 3M 15F CHOA 3M 14F	22.9 (2.8) 25.54 (2.1) 27.1 (1.9) 27.7 (1.6)	TMT Part B	Yes Yes No NA
Lopez et al (2006)	mixMCI 13M 15F aMCI 6M 4F CHOA 142M 232F	3MSE 88.2 (7.3) 92.6 (6.2) 96.0 (12.3)	TMT Part B	Yes Yes NA
Kramer et al (2007)	AD 16 CHOA 36 (FTD 30 SD 19)	22.8 (4.1) 29.6 (0.6) [25.6 (3.7) 24.1 (4.6)]	Design Fluency	Yes NA (Yes No)
Silveri et al (2007)	mixMCI 8 naMCI 12 aMCI 13 CHOA 21	26.00 (1.41) 27.00 (2.67) 26.54 (1.98) 29.05 (0.97)	TMT Part B	Yes No No NA
Silveri et al (2007)	mixMCI 8 naMCI 12	26.00 (1.41) 27.00 (2.67)	Visual Elevator	Yes No

	aMCI 13 CHOA 21	26.54 (1.98) 29.05 (0.97)		Yes NA
Silveri et al (2007)	mixMCI 8 naMCI 12 aMCI 13 CHOA 21	26.00 (1.41) 27.00 (2.67) 26.54 (1.98) 29.05 (0.97)	WCST	Yes No No NA
Traykov et al (2007)	MCI 16M 4F CHOA 14M 6F	28.95 (1.1) 29.5 (0.5)	MCST	Yes NA
Traykov et al (2007)	MCI 16M 4F CHOA 14M 6F	28.95 (1.1) 29.5 (0.5)	TMT Part B	No NA
Zamarian, Semenza, et al (2007)	AD 6M 9F CHOA 7M 13F MCI 11M 7F CHOA 5M 15F	21.3 (2.2) 29.1 (0.8) 27.0 (1.4) 28.8 (0.8)	TMT Part B	NA NA Yes NA
Zamarian, Stadelmann, et al (2007)	MCI 11M 7F CHOA 7M 11F CHOY 8M 10F	26.9 (1.2) 29.8 (0 .4) NA	TMT Part B	Yes NA NA
Zhang et al (2007)	MCI 32 CHOA 32	27.4 (2.0) 28.7 (1.8)	TMT	Yes NA
Belleville et al (2008)	AD 6M 7F CHOA M 11F MCI 8M 12F CHOA M 15F	24.85 (4.0) 28.69 (0.8) 28.15 (2.1) 28.9 (0.9)	Task Switching paradigm	Yes NA Yes NA
Belleville et al (2008)	AD 6M 7F CHOA M 11F MCI 8M 12F CHOA M 15F	24.85 (4.0) 28.69 (0.8) 28.15 (2.1) 28.9 (0.9)	Spatial Shifting	Yes NA Yes NA
Borkowska et al (2009)	MCI 9M 21F CHOA 9M 21F (D 9M 21F)	25.3 (0.9) 29.5 (1.9) [29.1 (1.3)]	WCST	Yes NA (Yes)
Ebert & Anderson (2009)	aMCI 15 CHOA 44 CHYA 27	28.4 (1.8) 29.3 (1.0) NA	TMT	No NA NA
Espinosa et al (2009)	AD 12M 38F MCI 28M 22F CHOA 13M 37F	21.94 (2.58) 26.06 (2.68) 28.38 (1.68)	Rule Shift Cards	Yes Yes NA
Lonie et al (2009)	AD 3M 7F aMCI 16M 17F CHOA 8M 13F (D 3M 14F)	25.0 (2.3) 28.4 (1.6) 29.1 (0.7) [28.6 (1.5)]	TMT	Yes Yes NA (Yes)
Mandzia et al (2009)	MCI 7M 7F CHOA 7M 7F	27.7 (1.1) 28.6 (1.1)	WCST	No NA
J. L. Price et al (2009)	AD 38 CHOA 59	28.1 (SE 0.4) 28.2 (SE 0.3)	TMT	No NA
Schmitter-Edgecombe & Sanders (2009)	MCI 12M 14F CHOA 12M 14F	27.38 (1.77) 28.85 (1.22)	Task Switching paradigm	Yes No

Schmitter-Edgecombe & Sanders (2009)	MCI 12M 14F CHOA 12M 14F	27.38 (1.77) 28.85 (1.22)	TMT Part B	Yes NA
Chang et al (2010)	MCI LEF 137M 58F MCI HEF 96M 67F CHOA 115M 107F	26.98 (1.68) 27.35 (1.75) 29.12 (0.99)	TMT Part B	Yes Yes NA
Grönholm-Nyman et al (2010)	AD 3M 6F MCI 6M 7F CHOA 3M 9F	25.3 (3.2) 27.5 (1.5) 29.1 (0.7)	TMT	Yes Yes NA
Hutchison et al (2010)	mAD 32 CHOA 64	28.22 (UNK) 29.19 (UNK)	TMT	Yes NA
McGuinness et al (2010)	AD 28 CHOA 75 (VaD 46)	> 28 ≥ 12 (≥ 12)	Colour Trails	Yes NA (Yes)
Pa et al (2010)	AD 6M 4F MCI 30M 27F CHOA 20M 20F (ALS 5M 1F CBD 4M 8F FTD 17M 4F SD 9M 5F)	26.0 (3.1) 28.4 (1.5) 29.8 (0.5) [29.2 (2.0) 27.3 (2.0) 26.1 (4.4) 23.5 (6.2)]	Design Fluency	Yes Yes NA (No Yes Yes Yes)
Pa et al (2010)	AD 6M 4F MCI 30M 27F CHOA 20M 20F ALS 5M 1F CBD 4M 8F FTD 17M 4F SD 9M 5F)	26.0 (3.1) 28.4 (1.5) 29.8 (0.5) [29.2 (2.0) 27.3 (2.0) 26.1 (4.4) 23.5 (6.2)]	TMT	Yes Yes NA (No Yes Yes Yes)
S. E. Price et al (2010)	aMCI 8M 25F CHOA 9M 24F	27.4 (1.4) 29.0 (0.9)	TMT	Yes NA
Sinai et al (2010)	MCI-able 6M 10F MCI-cue 3M 2F MCI-unable 2M 4F CHOA 5M 12F	28.4 (0.4) 26.2 (0.8) 25.17 (0.8) 28.6 (0.4)	Task Switching paradigm – separates MCI sufferers	No Yes and No Yes NA
Sinai et al (2010)	MCI-able 6M 10F MCI-cue 3M 2F MCI-unable 2M 4F CHOA 5M 12F	28.4 (0.4) 26.2 (0.8) 25.17 (0.8) 28.6 (0.4)	TMT	No Yes Yes NA
Tse et al (2010)	AD 74 CHOA 246 CHYA 32	26.58 (2.78) 28.99 (1.36) NA	Task Switching paradigm	Yes Yes NA
Tse et al (2010)	AD 74 CHOA 246 CHYA 32	26.58 (2.78) 28.99 (1.36) NA	TMT	Yes NA NA
P. J. Brown et al (2011)	AD 102M 91F aMCI 256M 138F CHOA 119M 110F	23.34 (2.06) 27.04 (1.78) 29.11 (1.00)	TMT	Yes Yes NA

Kessels et al (2011)	AD 10M 15F MCI 14M 11F CHOA 13M 12F	21.1 (2.3) 24.9 (2.9) 28.2 (1.5)	TMT	Yes Yes NA
Apostolova et al (2012)	AD 16M 27F aMCI 22M 11F CHOA 25M 21F	22.2 (4.9) 27.8 (2.3) 29.5 (0.6)	TMT	Yes Yes NA
Guerdoux et al (2012) – Experiment 2	AD 7M 10F aMCI 10M 7F CHOA 11M 6F	24.0 (1.9) 27.5 (1.6) 28.4 (1.3)	TMT	Yes No NA
Zheng et al (2012)	aMCI 14M 20F CHOA 18M 18F	28.3 (1.5) 29.5 (0.7)	More-odd shifting	Yes NA
Ballesteros et al (2013)	MCI 10M 10F CHOA 12M 8F CHYA 12M 8F	24.70 (1.03) 29.40 (0.68) 29.65 (0.49)	WCST	Yes Yes NA
Bastug et al (2013)	AD 30 aMCI 30 CHOA 25	[2]24.4 (UNK) [2]26 (UNK) [2]28 (UNK)	TMT	Yes Yes NA
Bastug et al (2013)	AD 30 aMCI 30 CHOA 25	[2]24.4 (UNK) [2]26 (UNK) [2]28 (UNK)	Oral TMT (OTMT)	Yes Yes NA
Chen et al (2013)	AD 88M 38F aMCI 82M 38F CHOA 68M 32F	20.2 (3.6) 26.6 (1.4) 28.4 (1.7)	Modified TMT Part B	Yes Yes NA
Chen et al (2013)	AD 88M 38F aMCI 82M 38F CHOA 68M 32F	20.2 (3.6) 26.6 (1.4) 28.4 (1.7)	Design Fluency	Yes Yes NA
Lee et al (2013)	AD 8M 23F CHOA 5M 26F	[1]16.16 (5.25) [1]25.58 (3.60)	TMT	Yes NA
Makizako et al (2013)	aMCI 21M 15F CHOA 26M 36F	27.1 (1.8) 27.0 (2.0)	TMT	No NA
Stricker et al (2013)	MCI 13M 19F CHOA 30M 51F	27.45 (1.95) 28.05 (1.68)	TMT	Yes NA
Stricker et al (2013)	MCI 13M 19F CHOA 30M 51F	27.45 (1.95) 28.05 (1.68)	WSCT	Yes NA
Guild et al (2014)	sd aMCI 2M 12F CHOA 22M 26F	28.14 (1.46) 28.88 (1.36)	TMT	No NA
Guild et al (2014)	sd aMCI 2M 12F CHOA 22M 26F	28.14 (1.46) 28.88 (1.36)	MSCT	No NA
Peltsch et al (2014)	AD 22M 50F aMCI 10M 12F CHOA 9M 15F	27.0 (2.0) 27.0 (2.0) 29.0 (1.0)	WSCT	Yes Yes NA
Peters et al (2014)	pMCI 8M 10F sMCI 9M 13F CHOA 6M 14F	27.2 (2.0) 28.1 (1.4) 29.6 (0.5)	TMT	No No NA
Puente et al (2014)	MCI 7M 10F CHOA 10M 16F	25.9 (2.4) 28.0 (2.0)	TMT	Yes NA

Zheng et al (2014)	aMCI 16M 34F CHOA 19M 29F	27.9 (1.5) 29.5 (0.7)	Alternating trail making (TMT Part B)	Yes NA
Zheng et al (2014)	aMCI 16M 34F CHOA 19M 29F	27.9 (1.5) 29.5 (0.7)	More-odd shifting	Yes NA
El Haj, Larøi, et al (2015)	AD 8M 23F CHOA 10M 23F	21.68 (1.87) 28.00 (1.52)	Plus–Minus	Yes NA
El Haj, Antoine, & Kapogiannis (2015)	AD 8M 16F CHOA 9M 17F	21.83 (1.52) 28.31 (1.28)	Plus–Minus	Yes NA
Huff et al (2015)	AD 104 CHOA 213 CHMA 208 CHYA 30	26.62 (3.12) 28.66 (1.41) 29.32 (1.04) NA	Task Switching paradigm	Yes Yes Yes NA
Smits et al (2015)	AD 101M 98F CHOA 49M 63F (VaD 6M 4F DLB 26M 0F bvFTD 14M 6F lvFTD 12M 3F)	22.0 (4.0) 28.0 (1.0) [25.0 (4.0) 23.0 (3.0) 26.0 (3.0) 24.0 (3.0)]	TMT	Yes NA (Yes Yes No No)
Aurtenetxe et al (2016)	MCI 11M 9F CHOA 8M 12F	28.3 (1.7) 29.4 (0.7)	TMT	No NA
Aurtenetxe et al (2016)	MCI 11M 9F CHOA 8M 12F	28.3 (1.7) 29.4 (0.7)	Rule shift cards	Yes NA
Mudar et al (2016)	aMCI 9M 16F CHOA 9M 16F	28.4 (1.3) 28.6 (0.5)	TMT	Yes NA
Redondo et al (2016)	AD 16M 6F CHOA 11M 12F (DB 12M 8F)	23.71 (4.25) 28.12 (1.61) [26.57 (1.95)]	WCST	Yes NA (Yes)
Yuan et al (2016)	aMCI 57M 62F CHOA 42M 37F	26.21 (2.69) 28.21 (1.46)	TMT	Yes NA
Huang et al (2017)	AD 11M 20F CHOA 17M 14F	21.2 (3.2) 27.0 (1.2)	Colour Trails B	Yes NA
Huang et al (2017)	AD 11M 20F CHOA 17M 14F	21.2 (3.2) 27.0 (1.2)	WCST	No NA
Matías-Guiu et al (2018)	AD 7M 12F CHOA 9M 10F (bvFTD 9M 10F ALS 8M 11F)	24.26 (4.33) 29.16 (1.21) [24.00 (4.79) 28.00 (1.63)]	TMT	Yes NA (Yes No)
Garcia-Alvarez et al (2019)	AD 27M 30F MCI 27M 21F CHOA 49M 75F	21.21 (4.28) 25.96 (2.03) 28.49 (1.40)	TMT	Yes Yes NA

[2] - median scores, CHMA - Cognitive healthy middle-aged adult, DB - Diabetic, DLB - dementia with Lewy bodies, HEF - higher executive function, LEF - lower executive function, lv - language variant, MCI/Vas - vascular originated, MCST - Modified card sorting test, TMT - Trail making test, VaD - vascular dementia, vm - very mild, WCST - Wisconsin card sorting test.

The trail making test (TMT) (Reitan, 1992; Reitan & Wolfson, 1986) was found to be the most common shifting task amongst the young and older adult studies, used 50% of the time. Shifting deficits was reported in 75% of these. Similarly, the TMT or a variant, i.e. oral TMT (Bastug et al., 2013), was observed frequently employed in the studies that recruited MCI participants, 67% (28) and 60% (21) with AD participants. 14 assessed both pathological participant groups with this task. Shifting deficits were observed in 52% (11) of these studies, though three studies (Loewenstein et al., 2006; Silveri et al., 2007; Sinai et al., 2010) had subtypes of MCI participants, reporting deficits in one or more of the other MCI groups but not in all. Only one of studies failed to find deficits with the AD participants, thus 95% reported performance deficits. One study however did not assess their AD participants (Zamarian, Semenza, et al., 2007).

2.4.4 Updating

Updating, defined as the continuous updating of content in WM, is examined by the completion of a task that requires the manipulation of WM (Miyake, Friedman, et al., 2000).

The updating of WM between young and older adults was reviewed in 32 studies, in 38 studies examining participants living with MCI, and in 32 studies assessing participants living with AD, see Table 2.4

Table 2.4. Assessing Updating ability in Cognitive Ageing, and MCI and AD sufferers

Study	**Participants**	**MMSE (Mean/SD)**	**Task/Test**	**Deficit**
Cognitive Ageing studies				
Clarys et al (2002)	CHVOA 28 CHOA 27 CHYOA 27	28.75 (0.89) 28.63 (0.97) NA	Alpha span	Yes Yes NA
Clarys et al (2002)	CHVOA 28 CHOA 27 CHYOA 27	28.75 (0.89) 28.63 (0.97) NA	Word backward span	Yes Yes NA
Salat et al (2002)	CHOA 15M 16F CHYA 10M 10F	28.6 (0.2) NA	N-back (3)	Yes NA
Gutchess et al (2005)	CHOA 7M 6F CHYA 7M 7F	28.62 (1.33) 29.29 (1.07)	BDS	Yes NA
Gutchess et al (2005)	CHOA 7M 6F CHYA 7M 7F	28.62 (1.33) 29.29 (1.07)	LNS	Yes NA
Rhodes & Kelley (2005)	CHOA 50 CHYA 50	> 27 > 27	Operation span	Yes NA
Bherer et al (2006)	CHOA 7M 5F	MM 56 (UNK)	BDS	No

	CHYA 5M 7F	NA		NA
Chee et al (2006) – Experiment 1	CHOA 6M 11F CHYA 7M 13F	28.7 (1.05) 29.4 (0.92)	BDS	Yes NA
Chee et al (2006) – Experiment 1	CHOA 6M 11F CHYA 7M 13F	28.7 (1.05) 29.4 (0.92)	Backward Spatial Span	Yes NA
Keightley et al (2006)	CHOA 30 CHYA 30	28.8 (0.9) 29.7 (0.5)	LNS	Yes NA
Isaacowitz et al (2006)	CHOA 23M 27F CHYOA 16M 19F	27.72 (1.93) 29.48 (1.06)	BDS	No NA
Damoiseaux et al (2008)	CHOA 9M 13F CHYA 5M 5F	28.73 (1.4) 29.50 (0.5)	BDS	No NA
McCabe & Hartman (2008) – Experiment 1	CHOA 36 CHYOA 36	29.1 (1.0) NA	N-back (2), verbal	Yes NA
McCabe & Hartman (2008) – Experiment 1	CHOA 36 CHYOA 36	29.1 (1.0) NA	N-back (3), verbal	Yes NA
McCabe & Hartman (2008) – Experiment 2	CHOA 36 CHYOA 36	29.2 (1.0) NA	N-back (2)	Yes NA
McCabe & Hartman (2008) – Experiment 2	CHOA 36 CHYOA 36	29.2 (1.0) NA	N-back (3)	Yes NA
Vaughan et al (2008) – Experiment 1	CHOA 58 CHYOA 54	> 27 NA	N-back (4)	Yes NA
Clarys et al (2009)	CHOA 44 CHYA 44	> 27 NA	N-back (2)	Yes NA
Daffner et al (2011)	CHOAh 6M/3F CHOAl 2M/7F CHYAh 5M/7F CHYAl 3M/8F	29.1 (0.9) 29.1 (0.9) NA NA	N-back (2)	Yes Yes Yes NA
Gamboz et al (2009)	CHOA 40 CHYA 40	29.5 (0.8) NA	Reading span	Yes NA
Rose et al (2009)	CHOA 9M 15F CHYA 7M 17F	28.2 (1.2) NA	LNS	Yes NA
Maquestiaux et al (2010)	CHOA 3M 9F CHYA 10M 10F	29.2 (1.0) UNK	LNS	Yes NA
Morrone et al (2010)	CHOA 12M 18F CHYA 10M 20F	29.5 (0.62) NA	LNS	No NA
Missonnier et al (2011)	CHOA 10M 22F CHYA 13M 19F	UNK UNK	N-back (3)	Yes NA
Nagel et al (2011)	CHOA 15M 15F CHYA 15M 15F	> 26 NA	N-back (3)	Yes NA
Albinet et al (2012)	CHOA 17M 22F CHYA 11M 17F	28.4 (1.4) NA	Random Number	No NA

			Generation, Redundancy	
Albinet et al (2012)	CHOA 17M 22F CHYA 11M 17F	28.4 (1.4) NA	Spatial running span task	Yes NA
Albinet et al (2012)	CHOA 17M 22F CHYA 11M 17F	28.4 (1.4) NA	Verbal running span task	Yes NA
Boucard et al (2012)	acCHOA 7M 8F seCHOA 7M 8F acCHYOA 7M 8F seCHYOA 7M 8F acCHYA 15M 17F seCHYA 15M 16F	29.2 (0.8) 28.9 (1.0) 29.1 (0.8) 29.1 (1.0) NA NA	N-back (2)	Yes Yes Yes Yes NA NA
Boucard et al (2012)	acCHOA 7M 8F seCHOA 7M 8F acCHYOA 7M 8F seCHYOA 7M 8F acCHYA 15M 17F seCHYA 15M 16F	29.2 (0.8) 28.9 (1.0) 29.1 (0.8) 29.1 (1.0) NA NA	Spatial Running Span	Yes Yes Yes Yes NA NA
Boucard et al (2012)	acCHOA 7M 8F seCHOA 7M 8F acCHYOA 7M 8F seCHYOA 7M 8F acCHYA 15M 17F seCHYA 15M 16F	29.2 (0.8) 28.9 (1.0) 29.1 (0.8) 29.1 (1.0) NA NA	Verbal Running Span	Yes Yes Yes Yes NA NA
Laguë-Beauvais et al (2013)	CHOA 3M 16F CHYA 8M 13F	29.00 (1.15) NA	LNS	No NA
Amer & Hasher (2014)	CHOA 9M 23F CHYA 11M 21F	29.19 (1.15) NA	N-back (1)	Yes NA
Ford et al (2014) – Experiment 1	CHOA 10M 22F CHYA 10M 22F	29.3 (0.13) NA	BDS	No NA
Ford et al (2014) – Experiment 2	CHOA 8M 24F CHYA 11M 21F	29.0 (0.20) NA	BDS	No NA
Pettigrew & Martin (2014)	CHOA 60 CHYA 102	28.8 (1.1) NA	BDS	Yes NA
Pettigrew & Martin (2014)	CHOA 60 CHYA 102	28.8 (1.1) NA	Operation span	Yes NA
Schroeder (2014)	CHOA 18M 24F CHYA 17M 25F	28.45 (1.48) 29.05 (1.50)	Alpha span	Yes NA
Schroeder (2014)	CHOA 18M 24F CHYA 17M 25F	28.45 (1.48) 29.05 (1.50)	BDS	No NA
Tournier et al (2014)	CHOA 31 CHYA 30	28.93 (1.06) NA	Operation Span	No NA
Laguë-Beauvais et al (2015)	CHOA 6M 13F CHYA 7M 9F	28.26 (0.93) NA	LNS	Yes NA
Sylvain-Roy et al (2015)	CHOA 28M 46F CHYA 33M 42F	29.0 (1.1) NA	Keep-track	Yes NA

Sylvain-Roy et al (2015)	CHOA 28M 46F CHYA 33M 42F	29.0 (1.1) NA	Letter updating	No NA
Sylvain-Roy et al (2015)	CHOA 28M 46F CHYA 33M 42F	29.0 (1.1) NA	Tone-monitoring	Yes NA
Sylvain-Roy et al (2015)	CHOA 28M 46F CHYA 33M 42F	29.0 (1.1) NA	Reading span	Yes NA
Berger et al (2017)	CHOA 7M 18F CHYA 8M 17F	29.20 (0.91) NA	N-back (1)	Yes NA
Berger et al (2017)	CHOA 7M 18F CHYA 8M 17F	29.20 (0.91) NA	N-back (2)	Yes NA
MCI and AD studies				
Perry & Hodges (2000)	AD 12 CHOA 20	26.2 (1.6) 29.0 (1.0)	BDS	No NA
Perry et al (2000)	mAD 14 miAD 13 CHOA 30	20.4 (2.0) 26.08 (1.6) 29.4 (0.8)	BDS	No No NA
Calderon et al (2001)	AD 6M 3F CHOA 7M 10F (DLB 8M 2F)	21.4 (2.2) 28.8 (1.0) [20.0 (3.1)]	BDS	Yes NA (Yes)
Belleville et al (2003)	AD 6M 17F CHOA 4M 19F CHOY 7M 8F	22.57 (UNK) UNK NA	Alphabet span	Yes No NA
Lambon Ralph et al (2003)	sevAD 8 moAD 8 mAD 22 MCI 17 CHOA UNK	6.9 (UNK) 14.9 (UNK) 21.4 (UNK) 26.9 (UNK) 28.7 (UNK)	BDS	Yes Yes Yes No NA
Grundman et al (2004)	moAD 83M 100F mAD 67M 55F MCI 417M 352F CHOA 43M 63F	19.9 (3.5) 23.3 (2.4) 27.3 (1.9) 29.1 (1.3)	BDS	UNK UNK No NA
Griffith et al (2006)	MCI 13M 36F CHOA 14M 35F	28.42 (1.64) 29.12 (1.22)	LNS	Yes NA
Kramer et al (2006)	AD 33 aMCI 22 CHOA 35	25.2 (1.3) 28.5 (1.5) 29.5 (0.8)	BDS	No No NA
Lopez et al (2006)	mixMCI 13M 15F aMCI 6M 4F CHOA 142M 232F	3MSE 88.2 (7.3) 92.6 (6.2) 96.0 (12.3)	BDS	Yes No NA
Belleville et al (2007)	AD 19 CHOA 29 in total MCI 28 CHOA 29 in total	24.65 (3.60) 28.74 (0.93) 28.36 (1.98) 28.88 (0.99)	Alphabet span	Yes NA Yes/No NA
Bisiacchi et al (2008) – Experiment 2	AD 8M 12F aMCI 6M 8F CHOA 5M 9F	20.79 (1.92) 25.71 (1.59) 27.80 (1.57)	BDS	Yes No NA

Bélanger & Belleville (2009)	AD 8 MCI 18 CHOA 16 CHYA 20	23.5 (4.0) 27.3 (1.8) 29.2 (0.9) NA	BDS	Yes Yes No NA
Borkowska et al (2009)	MCI 9M 21F CHOA 9M 21F (D 9M 21F)	25.3 (0.9) 29.5 (1.9) [29.1 (1.3)]	N-back (1)	Yes NA (Yes)
Mandzia et al (2009)	MCI 7M 7F CHOA 7M 7F	27.7 (1.1) 28.6 (1.1)	BDS	No NA
Schmitter-Edgecombe & Sanders (2009)	MCI 12M 14F CHOA 12M 14F	27.38 (1.77) 28.8 (1.22)	LNS	No NA
Zhou & Jia (2009)	MCI/AD 12M 18F MCI/SVD 36M 20F CHOA 45M 35F	26.2 (1.1) 26.7 (2.2) 28.8 (1.1)	BDS	No Yes NA
Chang et al (2010)	MCI LEF 137M 58F MCI HEF 96M 67F CHOA 115M 107F	26.98 (1.68) 27.35 (1.75) 29.12 (0.99)	BDS	Yes Yes NA
Grönholm-Nyman et al (2010)	AD 3M 6F MCI 6M 7F CHOA 3M 9F	25.3 (3.2) 27.5 (1.5) 29.1 (0.7)	BDS	Yes Yes NA
Hutchison et al (2010)	mAD 32 CHOA 64	28.22 (UNK) 29.19 (UNK)	BDS	Yes NA
Muangpaisan et al (2010)	MCI 12M 14F CHOA 12M 14F	26.5 (1.6) 28.1 (1.8)	BDS	Yes NA
Pa et al (2010)	AD 6M 4F MCI 30M 27F CHOA 20M 20F (ALS 5M 1F CBD 4M 8F FTD 17M 4F SD 9M 5F)	26.0 (3.1) 28.4 (1.5) 29.8 (0.5) [29.2 (2.0) 27.3 (2.0) 26.1 (4.4) 23.5 (6.2)]	BDS	Yes Yes NA (No Yes Yes Yes)
Sinai et al (2010)	MCI-able 6M 10F MCI-cue 3M 2F MCI-unable 2M 4F CHOA 5M 12F	28.4 (0.4) 26.2 (0.8) 25.17 (0.8) 28.6 (0.4)	LNS	No No No NA
Tse et al (2010)	AD 74 CHOA 246 CHYA 32	26.58 (2.78) 28.99 (1.36) NA	BDS	Yes NA NA
Ahn et al (2011)	AD 52M 118F aMCI 47M 52F CHOA 56M 86F	19.3 (5.0) 26.2 (2.5) 28.7 (1.5)	BDS	Yes Yes NA
Gagnon & Belleville (2011)	AD 16 aMCI 13 and md aMCI 7 CHOA 20	23.94 (2.29) 27.95 (1.50) 28.80 (1.06)	Operation Span	Yes No NA
Kessels et al (2011)	AD 10M 15F	21.1 (2.3)	BDS	Yes

	MCI 14M 11F CHOA 13M 12F	24.9 (2.9) 28.2 (1.5)		Yes NA
Kessels et al (2011)	AD 10M 15F MCI 14M 11F CHOA 13M 12F	21.1 (2.3) 24.9 (2.9) 28.2 (1.5)	LNS	Yes Yes NA
Apostolova et al (2012)	AD 16M 27F aMCI 22M 11F CHOA 25M 21F	22.2 (4.9) 27.8 (2.3) 29.5 (0.6)	BDS	Yes No NA
Guerdoux et al (2012) – Experiment 2	AD 7M 10F aMCI 10M 7F CHOA 11M 6F	24.0 (1.9) 27.5 (1.6) 28.4 (1.3)	BDS	Yes No NA
Johns et al (2012)	aMCI 18M 22F CHOA 13M 19F	28.1 (1.4) 28.9 (1.1)	LNS	Yes NA
Sung et al (2012)	MCI 16 CHOA 16	[1]24.87 (3.40) [1]26.45 (2.11)	BDS	Yes NA
Sung et al (2012)	MCI 16 CHOA 16	[1]24.87 (3.40) [1]26.45 (2.11)	Word backward span	Yes NA
Zheng et al (2012)	aMCI 14M 20F CHOA 18M 18F	28.3 (1.5) 29.5 (0.7)	Keep track	Yes NA
Zheng et al (2012)	aMCI 14M 20F CHOA 18M 18F	28.3 (1.5) 29.5 (0.7)	N-back (2)	Yes NA
Bastug et al (2013)	AD 30 aMCI 30 CHOA 25	[2]24.4 (UNK) [2]26 (UNK) [2]28 (UNK)	BDS	No No NA
Doi et al (2013)	LS aMCI 37 ES aMCI 34 CHOA 29	27.0 (1.9) 26.6 (1.9) 27.6 (2.0)	BDS	Yes No NA
Chen et al (2013)	AD 88M 38F aMCI 82M 38F CHOA 68M 32F	20.2 (3.6) 26.6 (1.4) 28.4 (1.7)	BDS	Yes No NA
Crawford et al (2013)	AD 18 CHOA 18 (PD 25)	20.9 (4.3) 29.2 (1.1) [28.8 (1.2)]	BDS	Yes NA (No)
Guild et al (2014)	sd aMCI 2M 12F CHOA 22M 26F	28.14 (1.46) 28.88 (1.36)	BDS	No NA
Zheng et al (2014)	aMCI 16M 34F CHOA 19M 29F	27.9 (1.5) 29.5 (0.7)	Keep track	Yes NA
El Haj, Larøi, et al (2015)	AD 8M 23F CHOA 10M 23F	21.68 (1.87) 28.00 (1.52)	N-back (2)	No NA
El Haj, Antoine, & Kapogiannis (2015)	AD 8M 16F CHOA 9M 17F	21.83 (1.52) 28.31 (1.28)	N-back (2)	Yes NA
Kessels et al (2015)	AD 6M 8F MCI 6M 5F CHOA 9M 16F	19.00 (3.3) 26.7 (1.0) 29.4 (0.8)	BDS	Yes Yes NA
Kessels et al (2015)	AD 6M 8F MCI 6M 5F	19.00 (3.3) 26.7 (1.0)	Backward Spatial Span	Yes No

	CHOA 9M 16F	29.4 (0.8)		NA
Smits et al (2015)	AD 101M 98F CHOA 49M 63F (VaD 6M 4F DLB 26M 0F bvFTD 14M 6F lvFTD 12M 3F)	22.0 (4.0) 28.0 (1.0) [25.0 (4.0) 23.0 (3.0) 26.0 (3.0) 24.0 (3.0)]	BDS	Yes NA (Yes Yes No No)
Aurtenetxe et al (2016)	MCI 11M 9F CHOA 8M 12F	28.3 (1.7) 29.4 (0.7)	BDS	Yes NA
Mudar et al (2016)	aMCI 9M 16F CHOA 9M 16F	28.4 (1.3) 28.6 (0.5)	BDS	No NA
Pitarque et al (2016)	AD 7M 23F aMCI 10M 20F CHOA 7M 23F CHYA 14M 28F	20.53 (0.67) 24.83 (0.82) 28.40 (0.28) NA	BDS	Yes Yes NA NA
Redondo et al (2016)	AD 16M 6F CHOA 11M 12F (DB 12M 8F)	23.71 (4.25) 28.12 (1.61) [26.57 (1.95)]	N-back (2)	Yes NA (No)
Redondo et al (2016)	AD 16M 6F CHOA 11M 12F (DB 12M 8F)	23.71 (4.25) 28.12 (1.61) [26.57 (1.95)]	N-back (3), verbal	Yes NA (Yes)
Liao et al (2017)	aMCI 28M 33F CHOA 27M 38F (D 20M 41F)	26.3 (2.8) 28.4 (1.4) [27.8 (1.6)]	BDS	No NA (No)
Emrani et al (2018)	aMCI 15 mixMCI 18 CHOA 33	26.73 (2.21) 26.44 (1.58) 27.69 (1.75)	BDS	Yes Yes NA
Matías-Guiu et al (2018)	AD 7M 12F CHOA 9M 10F (bvFTD 9M 10F ALS 8M 11F)	24.26 (4.33) 29.16 (1.21) [24.00 (4.79) 28.00 (1.63)]	BDS	No NA (No No)
Cervera-Crespo et al (2019)	moAD 8M 8F mAD 7M 8F CHOA 8M 8F	22.46 (1.06) 23.81 (0.91) 28.66 (2.49)	Alpha span	Yes Yes NA
Garcia-Alvarez et al (2019)	AD 27M 30F MCI 27M 21F CHOA 49M 75F	21.21 (4.28) 25.96 (2.03) 28.49 (1.40)	BDS	Yes Yes NA
Garcia-Alvarez et al (2019)	AD 27M 30F MCI 27M 21F CHOA 49M 75F	21.21 (4.28) 25.96 (2.03) 28.49 (1.40)	LNS	Yes Yes NA
Garcia-Alvarez et al (2019)	AD 27M 30F MCI 27M 21F CHOA 49M 75F	21.21 (4.28) 25.96 (2.03) 28.49 (1.40)	N-back (1)	Yes Yes NA
Ferreira et al (2019)	moAD 11 mAD 22 CHOA 56 (D 19)	19.00 (UNK) 22.50 (UNK) 29.00 (UNK) [29.00 (UNK)]	BDS	Yes Yes NA (Yes)

ES - early stage, h - high, LS - late stage, l - low, p - progressive, sev - severe, s - stable.

The n-back task (Jaeggi et al., 2010; Kirchner, 1958) was reviewed to be most frequently used to assess updating performance between young and older adults. Used 34% with various span lengths from 1- to 4-back, with 2-back being the commonest. Performance deficits were reported in all. While the backward digit span (BDS) task (Egeland, 2015; P. T. Griffin & Heffernan, 1983; Wechsler, 2012) was regularly employed in the examination of MCI participants, in 79% (32) of the studies, and AD participants, 78% (25) of the studies. 16 of which examined both of the latt
er participant groups. Updating deficits were reported in 56% (18) of these studies assessing MCI participants. Although two studies which subdivided their MCI participants reported deficits in one of the subtypes but not the other (Doi et al., 2013; Lopez et al., 2006; Zhou & Jia, 2009). Performance deficits were reported in 80% (20) of these AD participant studies. One study however, did not assess their AD groups (mild and moderate) with the BDS task, only their MCI participants (Grundman et al., 2004).

2.5. Tasks

While the tasks listed in the above sections were employed in their assessment of the specific EF, differences in their demand, sensitivity, outcome measure and stimuli were observed. This section will briefly discuss these factors.

2.5.1 Stimuli

The type of stimuli used in a task may affect the power in detecting differences, i.e. age effects, in the investigated EF ability.

With the employment of the backward *spatial* span (Wechsler, 1987), Kessels et al (2015) reported updating deficits only in their AD participants, but with the backward *digit* span they reported deficits in both the MCI and AD participants. This result was also reported during assessment with the forward spatial span (Wechsler, 1987) and forward digit span (Wechsler, 2012). Thus, the difference in findings on the same group of MCI participants can only be attributed to the stimulus difference, i.e. numerical versus spatial. It was concluded that the spatial test of WM load was limited and less vulnerable to subtle impairments.

Therefore, suggesting that the modality, type and/or nature of the stimuli used by a task may account for performance differences in research, and as such should be considered during task selection. Though, the overall task may further differ in other parameters as well.

2.5.2 Demand

The cognitive demand of a task which relates to the different cognitive processes and/or functions embedded may further contribute to how well a participant performs. In that a simple task may require a small number of cognitive processes, whereas complex tasks may require several. Though task demands may not be clearly defined, as a task that appears easy to perform may in fact be more difficulty than it seems and vice versa. Therefore, researchers may choose or modified tasks to reduce or increase performance difficulty in their participants.

An example of this is observed in the inhibition studies reviewed where several researchers used the Victoria version (Spreen & Strauss, 1998) of the Stroop task (Stroop, 1935) in the assessment of the pathological impaired. This is a briefer and seemingly easier task to perform than the traditional Stroop and was observed to produce no performance deficits in all the MCI participant groups that completed it. However, with the traditional Stroop, performance deficits were reported in the majority of the studies that assessed MCI participants. Thus, this may indicate variance in task performance due to demand.

Further, modified versions of the traditional task were also used by other researchers. This included Maquestiaux et al (2010) with the inclusion of a fourth task where participants shifted between identifying the colour of the ink and reading the word aloud, Sylvain-Roy et al (2015) where each of three standard task conditions was presented randomly, and a nonverbal computerised Stroop task by Pettigrew & Martin (2014) using the position and direction of an arrow as the stimuli, in the cognitive ageing studies. Whilst in the pathological studies, Amieva et al (2004) modified the task by having two Stroop types - an Interference and Reverse Stroop, Duong et al (2006) and Nordlund et al (2005) used pictures as a stimuli, Kaufmann et al (2008) employed a numerical Stroop, and Zamarian, Semenza, et al (2007) a math Stroop. Although the tasks were modified to change the task demand,

performance deficits were reported in all the CH older adults and cognitively impaired participants recruited in these studies.

Another example is the adapted stop-signal task Logan et al (1984) employed by Albinet et al (2012) where the stop signals were placed 20%, 40%, 60%, 80%, and 100% following the presentation of a visual stimulus. Gamboz et al (2009) also adapted this task (Williams et al., 1999). The presentation of the stop signal was based on a tracking system which involved the increase presentation frequency of the stop signal (harder to inhibit) or decrease (easier to inhibit) based upon the participant correctly stopping during the previous stop signal trial.

Additionally, to examine shifting ability in the cognitively impaired population numerous researchers used a simpler shortened modified version of the Wisconsin card sorting task (WSCT) (Berg, 1948; Nelson, 1976). Hartman et al (2001) simplified the task by utilising visual cues to remind the participant of the identity and outcome of the prior sort, resulting in a less demanding version. Thus, the demand of EF tasks may be revised for a desired outcome or to reduce the possibility of floor (too difficult) or ceiling (too easy) effects in the group being assessed.

In sum, the heterogeneity of task demands across studies could mean a fair comparison of the performance outcomes may not be made due to the different or additional cognitive processes required for their completion, particularly if task cost measures are not calculated.

2.5.3 Sensitivity

The sensitivity of tasks refers to how well its findings detects an effect based on the effect size[1] or statistical power[2] of the research conducted. Of the 183 studies reviewed, only a limited number reported these values, although they can be manually calculated by readers. Effect sizes were reported in sixty-five studies (Aisenberg et al., 2015; Albinet et al., 2012; Amer & Hasher, 2014; Audiffren et al., 2009; Aurtenetxe et al., 2016; Ballesteros et al., 2013; Bélanger et al., 2010; Bélanger & Belleville, 2009; Belleville et al., 2008; Bherer et al., 2006; Bisiacchi et al., 2008; Borella et al., 2017; Boucard et al., 2012; Cervera-Crespo et al., 2019;

[1] The strength of the relationship between two variables in a population.
[2] The probability of the null hypothesis being correctly rejected when it is false.

Y. L. Chang et al., 2010; Dupart et al., 2018; Ebert & Anderson, 2009; Emrani et al., 2018; Endrass et al., 2012; Ferreira et al., 2019; Ford et al., 2014; Gagnon & Belleville, 2011; Guerdoux et al., 2012; Guild et al., 2014; Hillman et al., 2006; Huang et al., 2017; Huff et al., 2015; Isaacowitz et al., 2006; Jaeggi et al., 2010; Johns et al., 2012; Kaschel et al., 2009; Kaufmann et al., 2008; Laguë-Beauvais et al., 2015; Laguë-Beauvais, Brunet, et al., 2013; Langenecker et al., 2004, 2007; Logie et al., 2004; Lopez et al., 2006; Martyr et al., 2017; J. McCabe & Hartman, 2003, 2008; Nagel et al., 2011; Nordlund et al., 2005; Pereiro et al., 2014; Pettigrew & Martin, 2014; S. E. Price et al., 2010; Puente et al., 2014; Redondo et al., 2016; Ren et al., 2018; Rhodes & Kelley, 2005; Rose et al., 2009; Schmitter-Edgecombe & Sanders, 2009; Schroeder, 2014; Sinai et al., 2010; Strobach et al., 2012b; Sung et al., 2012; Sylvain-Roy et al., 2015; Tournier et al., 2014; Tse et al., 2010; Vallesi et al., 2010; Vaughan et al., 2008; Z. Wang & Su, 2013; Waring et al., 2019; Zheng et al., 2012; Zhou & Jia, 2009), 36%, and statistical power calculated in three studies (Clarys et al., 2009; Strobach et al., 2012b; Waring et al., 2019), 2%, to determine a sufficient sample number.

Another important aspect of task sensitivity is the power of EF tasks in assessing their intended cognitive process. Several studies in this review were observed to have employed multiple tasks to assess the same EF on the same group of participants. A proportion reported converging results between two or more tasks, leading the reader to assume these tasks seem to measure the same process with the same power. These studies included for the ageing studies, Berger et al (2017), Chee et al (2006), Crawford et al (2017), Ford et al (2014), Gutchess et al (2005), Hsieh et al (2012) , Mayas et al (2012), McCabe & Hartman (2008), Rhodes & Kelley (2005), Vallesi et al (2010), and Waring et al (2019), and the pathological studies, Ahn et al (2011), Bastug et al (2013), Baudic et al (2006), Chen et al (2013), Clarys et al (2002), Collette et al (2002), Crawford et al (2005), Belleville et al (2007), Belleville et al (2008), Garcia-Alvarez et al (2019), Guild et al (2014), Johns et al (2012), Matías-Guiu et al (2018), Peltsch et al (2014), Perry et al (2000), Redondo et al (2016), Schmitter-Edgecombe & Sanders (2009), Sinai et al (2010), Stricker et al (2013), Traykov et al (2002), Tse et al (2010), Zhang et al (2007), and Zheng et al (2014).

However, and of particular interest were the studies that reported conflicting findings with two or more tasks. Observed in the ageing studies, Albinet et al (2012), Andrés et al (2008), Boucard et al (2012), Kawai et al (2012), Kessels et al (2011), Kessels et al (2015), Kubo-

Kawai & Kawai (2010), Pettigrew & Martin (2014), Schroeder (2014), Sylvain-Roy et al (2015), and Wang & Su (2013), and in the pathological impaired studies, Aurtenetxe et al (2016), Bélanger & Belleville (2009), Belleville et al (2007), Duong et al (2006), Dwolatzky et al (2003), Huang et al (2017), Nordlund et al (2005), Pa et al (2010), S. E. Price et al (2010), Silveri et al (2007), Sinai et al (2010), Sung et al (2012), Traykov et al (2007), Zheng et al (2012).

Two of these cognitive ageing studies, Albinet et al (2012) and Boucard et al (2012), both employed three tasks to assess each of their EF assessments. Albinet et al (2012) examined updating ability between CH young and older adults with the random number generation (Baddeley, 1998), spatial running span (Albinet et al., 2012; Boucard et al., 2012; Morris & Jones, 1990), and verbal running span tasks (Albinet et al., 2012; Boucard et al., 2012; Morris & Jones, 1990). Reporting no age effects with the random number generation only. Boucard et al (2012) assessed shifting ability between CH young, middle-aged, and older adults with the digit number-letter task (Rogers & Monsell, 1995), dimension-switching task (Albinet et al., 2012; Monsell & Mizon, 2006; Rogers & Monsell, 1995), and plus-minus task (Jersild, 1927; Miyake, Friedman, et al., 2000; Spector & Biederman, 1976). Finding no age effect with the plus-minus task in the middle-aged and older adult groups only. Thus, these findings may suggest that the tasks which did not detect significant decline of their intended EF ability were not sensitive enough as two of three tasks did.

Similarly, in the pathological impairment studies, Silveri et al (2007) assessed shifting ability with the part B of the TMT, visual elevator task (Robertson et al., 2001), and WCST on CH older adults, aMCI, non aMCI, and mixed MCI participants. Reporting performance deficits in the mixed MCI group with all the tasks but only in the aMCI group with the visual elevator task. This may indicate that the visual elevator task used an additional cognitive process which had declined in aMCI was not detected by the other two, highlighting the issue of task purity.

While systematic variation of tasks may also account for how well a task detects an affect. Such that easy tasks will probably not detect a decline, resulting in a ceiling effect. Whereas a hard task may detect a false effect, in that it is too hard to complete, causing a floor effect. For example, Pettigrew & Martin (2014) employed four tasks to assess inhibitory ability between young and older adults, the flanker task (Eriksen & Eriken, 1974), Stroop task, a

nonverbal Stroop task, and the picture-word interference task. Reporting no age effects with the picture-word interference task only, where a near ceiling effect seemed to have occurred in the accuracy performance, a 97.8% average was shown. The highest accuracy rate from all the tasks used. RT was marginal. Thus, it would seem that the picture-word interference task should not be employed when assessing inhibition for age effects, as these results suggest it is easy to complete. Nevertheless, this was the only study found to have employed this task between young and older adults, so this may not be true.

To conclude, these findings highlight the importance of carefully selecting tasks and strongly suggest that the application of more than one or two tasks in the assessment of an EF is advantageous to confidently assess an ability, as the absence of an effect on a specific task cannot be taken to indicate the cognitive domain is unimpaired. Although it is important to note that tasks assessing the same cognitive domain may report differently due to variations in their cognitive requirements.

2.5.4 Outcome measure

Many of the EF tasks employed by the studies reviewed compared performance between two task conditions, such as congruent versus incongruent, reporting the task cost, ratio, or some other measure. However, not all researchers use this type of relative cost measure, possibly because this was not their intended outcome measure. Instead, for instance some studies only reported findings from one half of a task, such as part B of the Hayling sentence completion test (HSCT) (Burgess & Shallice, 1997) or the TMT. Though this latter outcome measure assesses the intended EF ability of the mentioned tasks, it does not take into consideration the overlapping supplementary cognitive abilities used in both parts of the task which are eliminated by using the cost measure. For example, if participants spent longer completing part B, they may have also spend longer completing part A, suggesting no significant difference in the cost measure. Therefore, significance in part B of a task may be present between age groups but not in the cost measure. This is observed in the Damoiseaux et al (2008) study who reported the outcome measure for parts A and B of the TMT separately, indicating significance in both. However, comparable performance was reported in the ratio measure, TMT part B/TMT part A.

Therefore, one should be mindful when analysing and comparing study outcomes, as the reporting of age-related performance deficits is dependent on the outcome measure being employed.

2.6. Conclusion

The multitude of tasks utilised in these studies was evaluated, with a discussion on the factors which should be considered when examining EFs including stimuli, task demand, task sensitivity, outcome measure, as well as the number of tasks employed during EF assessment. Furthermore, the sample size is especially important, particularly when considering the power of a study, as is the participant group.

The tasks observed to be most frequently employed in the cognitive ageing studies reviewed for DT ability was the PRP paradigm, for inhibition ability the Stroop task, for shifting ability the TMT, and for updating the n-back task. In the cognitively impaired participant studies, DT was frequently evaluated with the (Baddeley's) digit recall and tracking, and Della Sala DT, inhibition ability with the Stroop task, shifting ability with the TMT, and updating with the BDS.

While the findings from the MCI and the AD studies are fascinating, they are not directly relevant to the current study, because an originally planned behavioural study on these participants was not successfully completed due to the restrictions on face-to-face research imposed by the COVID-19 lockdown.

Chapter 3, Executive Function Abilities in Cognitively Healthy Young and Older Adults, a Cross-Sectional and Trajectory of Decline Study

3.1 Introduction

Cognitive decline is a well-known concept of the healthy ageing process, which may adversely affect our cognitive abilities (Cabeza et al., 2009; Craik & Salthouse, 2008; Salthouse, 2009, 2012). It depends on many variables including diet, well-being, educational attainment, and physical health which contribute to the neural, psychophysiological, and anatomical process of ageing (Friedman et al., 2008; Haier et al., 2003; MacPherson et al., 2019). The commonest complaint amongst older adults is memory problems (N. D. Anderson & Craik, 2017; Gazzaley et al., 2007; Nyberg et al., 2012; Radvansky & Radvansky, 2018; Salthouse, 2003b; Tromp et al., 2015), as well as reduced mental speed (Bashore et al., 1989; Godefroy et al., 2010; Salthouse, 1976, 2019; Wecker et al., 2000) in comparison to their younger counterparts (Cabeza et al., 2005; Cadar, 2018; Deary et al., 2009; Grady, 2012; Hedden & Gabrieli, 2004).

Numerous executive function (EF) studies with cognitive healthy (CH) older adults have suggested many cognitive domains remain functional, although when compared to younger adults there are considerable differences in the performance of such tasks (Burda et al., 2017; de Frias et al., 2006; J. E. Fisk & Sharp, 2004; Reynolds & Horton Jr, 2008; Tucker-Drob & Salthouse, 2008; Wecker et al., 2000). Older individuals are more susceptible to the effects of distracting interference during the performance of cognitive tasks which is attributed to reduced attentional control (Borella et al., 2011; Burda et al., 2017; Coubard et al., 2011; Fountain-Zaragoza et al., 2018; Sylvain-Roy et al., 2015; Tsang, 2013).

A few hypotheses have been proposed to describe these age-associated differences. For example, the processing-speed theory was proposed by Salthouse (1996) to explain the generic slowing of cognitive processing. It suggested that the decline in processing speed results in cognitive functioning impairments due to the limited time mechanism and the simultaneity mechanism (see Chapter 1 for details). The limited time mechanism occurs because pertinent cognitive actions are performed at too slow a speed, so are not successfully completed in the available time. While the simultaneity mechanism is assumed

to operate as a result of a reduction in the amount of simultaneously available information required for the processing of higher-level processes due to the decrease in processing rate.

Another theory, the executive attention framework (Engle, 2002; Engle & Kane, 2004), states that older individuals cannot effectively maintain cognitive control with active tasks in difficult settings with high task interference. While the strategy-deficit hypothesis (Bailey et al., 2009) suggests that due to advanced age, older individuals are ineffective or deficient in their use of strategies for performing tasks, and the prefrontal-executive hypothesis by West (1996) associates the structural changes that occur in the prefrontal cortex (PFC) with age as the cause of EF decline. Thus, cognitive ageing can be viewed as a heterogeneous process. However, its transition to pathological impairment is not well understood so a better grasp of 'normal' cognitive ageing is required (Massaldjieva, 2018). Age-related decline in the EFs dual-tasking, inhibition, shifting and updating are of particular importance as they are frequently recruited in everyday activities and deemed to be the key EFs (Baddeley, 1996; Miyake, Friedman, et al., 2000). They will be discussed in the following paragraphs.

Dual-tasking, has been shown to have age-related impairment (Craik, 1977; Craik et al., 1996; Fraser & Bherer, 2013; Hartley et al., 1999; McDowd & Craik, 1988; Verhaeghen et al., 2003; Verhaeghen & Cerella, 2002; Wright, 1981). Older adults are reported to be able to complete such tasks but at a slower rate (Verhaeghen & Cerella, 2002). Typically, dual-tasking is assessed by the difference in response time (RT) and errors produced between the single-task (ST) and dual-task (DT) conditions, which is referred to as DT cost. Thus, several studies have described higher costs in older adults in comparison to younger individuals (Craik, 1977; Craik & Salthouse, 2008; Crossley & Hiscock, 1992; Hartley, 2001; Hartley et al., 1999; McDowd & Craik, 1988; Naveh-Benjamin et al., 2005; Salthouse et al., 1984; Verhaeghen et al., 2003; Wright, 1981). That is, the older individuals generally made much more errors and generated even longer RTs during the DT condition in comparison to the ST condition than younger individuals. This could be indicative of a reduction in processing resources as dual-tasking creates more competition for limited resources, such as attention, than ST situations. Bier et al (2017) and Sebastian & Mediavilla (2017) found that their older participants were incapable of controlling their attention, concluding it to be the significant factor for the age-related difference in DT cost. Other researchers have suggested that there

is no age-associated decline in dual-tasking (M. Anderson et al., 2011; Argiris et al., 2019; Logie et al., 2004). However, overwhelming evidence confirms that decline in (divided) attention is the prominent factor affecting older adults in completing DTs, although the effect seems moderate.

In terms of inhibition, older individuals seem to be less proficient at efficiently suppressing irrelevant thoughts and actions which is believed to be linked to decreased attentional control (Adólfsdóttir et al., 2017; Borella et al., 2008; Wecker et al., 2000; Zuber et al., 2019). This has been theorised as the inhibition-deficit hypothesis (Hasher & Zacks, 1988; Lustig et al., 2007), which implies that older individuals possess less inhibitory control than younger individuals and is the cause of age-associated deficits observed in several cognitive tasks, such as working memory (WM) (Hasher et al., 2008). However, a meta-analysis performed by Rey-Mermet & Gade (2018) suggested otherwise. Differences in inhibitory decline were observed with the utilisation of different tasks. For instance, no age-related deficit was reported with the Stroop, flanker, and local tasks, but were with the go/no-go and stop-signal tasks. While results were inconclusive for the Simon, global-local, and the positive and negative compatibility tasks. Due to these inconsistences, it is unclear whether older individuals are indeed less effective in inhibiting unwanted resources. However, it may be a mild occurrence in that only certain tasks are able to highlight the issue, or that "inhibition" is not one unitary concept but has different aspects, e.g. response inhibition vs perceptual inhibition, and that only some of those aspects are affected.

Similar to inhibition, it is unclear if the ability to maintain and coordinate two alternating task sets, i.e. shifting or switching, is affected by ageing. Verhaeghen & Cerella (2002) determined in their meta-analysis that it did not show a specific age-related deficit. A conclusion which was also reported by another researcher (Zuber et al., 2019). Nonetheless, in another meta-analysis by Wasylyshyn et al (2011) and a paper by Verhaeghen (2011), a deficit in shifting was reported for the global shift cost only, which is the difference in shift RTs from shift blocks and a repetition blocks. Local shift costs described as the differences in RTs between non-shift and shifting trials within mixed blocks were considered comparable for young and old. However, local shift costs are typically referred to as the better measure of shift costs, thus it can be concluded that no deficit was observed. Adólfsdóttir et al (2017) also reported shifting costs in their longitudinal study but they failed to indicate their type

and acknowledged that they did not analyse the error rate effects. As presented in Chapter 2, the task employed can affect the result observed, i.e. the level of impairment may differ. Wecker et al (2005) reported differences in the nature and size of age-related shifting decline with the use of three tasks, the trail making test (TMT), verbal fluency test and design fluency test, which require verbal and nonverbal cognitive shifting. Therefore, it is uncertain as to whether ageing does affect shifting and/or if the sensitivity of the task employed determines the level of questionable decline observed in this population.

The process of updating WM has been reported to undergo moderate decline with age (Zuber et al., 2019). With the use of a letter span task, Linden et al (1994) observed that with low memory load demands older participants were comparable to younger individuals in their performance. However, as the span list increased, older participants' updating capability decreased. A finding that was confirmed by Artuso et al (2017). In addition, a steady decline in WM ability has been observed from young to older adults in a study utilising backward span task (BDS) (Grégoire & Van der Linden, 1997). In line with this, De Beni & Palladino (2004) also reported older individuals had more difficulty in recalling spans. In regards to span tasks, it seems a decline in updating ability is attributed to an increase in intrusion errors, caused by a failure to eliminate previously activated irrelevant information in older adults (De Beni & Palladino, 2004; Palladino & De Beni, 1999). Age-related decline with the use of another updating task has also been observed. In a meta-analysis by Bopp & Verhaeghen (2018) assessing ageing with the use of the n-back task, it was seen that older individuals performed worse with longer lists, particularly over the 1-back condition of the task. Accordingly, these studies prove that updating is affected by the ageing process, in comparison to the other EFs discussed.

Having discussed these four EFs individually, it can be concluded that they all appear to be affected by the ageing process to a varying degree. However, it is unknown whether they are affected in the same way, or if some are more affected than others, which is of great importance to this research. Thus, the individual rate of decline of the four EFs due to healthy ageing will be explored.

In a confirmatory factor analysis (CFA) study by Miyake et al, (2000) that investigated the loadings of the 4 EFs, using task performance measures, on a generic EF factor, it was reported that inhibition, shifting and updating loaded similarly and thus may share an

underlaying factor, while DT loaded uniquely from the three. Nevertheless, this finding was demonstrated in young adults. In the older generations, the loading correlations have been found to differ (Bettcher et al., 2016; Bock et al., 2019; Glisky et al., 2020; Hedden & Yoon, 2006; Hull et al., 2008; Vaughan & Giovanello, 2010). In the Glisky et al, (2020) study, updating and inhibition were reported to load similarly, whereas shifting loaded on its own individual rate. The loadings were stronger with advance age, indicating an age effect. (DT was not assessed.) These finding suggest EFs decline at diverse rates, though some may possess comparable rates. Consequently, in this study, the influence of regular normal ageing on the cognitive decline of the four EFs was investigated.

CH young and older adults completed two separate tasks for each EF in a cross-sectional study. A repeated-measures design was conducted to allow a comparison between the four EF measures and the two age groups to determine how ageing affects the four EFs by comparing the performance outputs. This also allowed for analysis of rate of decline of the individual EFs.

It was theorised that this older population would perform less efficiently and present with an overall increase in error rates while demonstrating poorer RTs than the young adult group. Hence, higher RT and error rate costs would be observed. Furthermore, in the assessment of these four EFs, I propose that updating will be most affected by the ageing process based on the above discussion, followed by inhibition, then dual-tasking, and finally shifting.

3.2 Methods

3.2.1 Participants

A total of 32 (7M/25F) young adult participants were initially recruited into the study, three (2M/1F) withdrew after the first (screening) session and two (2F) after the second. The data of one female participant (aged 47) was withdrawn due to being an age outlier. The data for the two individuals who completed only two of the three sessions was used in the study Thus, 26 participants (5M/21F) were aged 18 to 33 years (mean of 21.18, SD 4.43) completed all study sessions.

For the older adults, one female (aged 53) was withdrawn as an age outlier, thus 25 older adult participants (11M/14F), aged 60 to 84 years (mean of 71.56, SD 6.63), where recruited into the study. There were no withdrawals.

All had normal or corrected to normal vision and hearing.

3.2.2 Procedure

The young adult participants were recruited through poster and online advertisement at Brunel University London, and the older adults through poster placement in the Brunel Older People's Reference Group (BORG) newsletter, in and around the campus of Brunel University. As well as through online advertisement at Brunel University London, by handing out of leaflets to the public, and word of mouth.

Individuals were provided with the participant information sheet (PIS) for their review prior to the first screening session. Once agreement to participate was confirmed, the participant completed the online study recruitment questionnaire to determine study participation suitability in their own time prior to any study session. Data collected included demographic information, level of education, profession, medical history of severe auditory or visual abnormalities, psychiatric, neurological, or systemic diseases which could cause cognitive impairments. In addition, severe physical disability, a history of epilepsy or other conditions that may cause uncontrolled movements or tremours were all considered exclusion criteria. Once accepted for participation, all individuals were invited to the screening visit.

Participants completed three sessions, screening and two EF visits, each lasting approximately 60 minutes in duration. With the older adults, most study visits took place at the participant's home. With the remaining participants, sessions were completed at Brunel University London's Uxbridge campus or at a local library or facility of the participant's choice. Once written informed consent was obtained all the screening assessments were completed. The participants completed the tests, the geriatric anxiety scale (GAS), geriatric depression scale (GDS) (Yesavage et al., 1983), activities of daily living scale (ADL) instrumental activities of daily living scale (IADL), and the spot-the-word test online via a Qualtrics link. As well as the Hopkins verbal learning test (HVLT) (Brandt, 1991) in person.

In the first EF session, the assessments were completed in the following order: test for everyday attention (TEA) DT telephone code search subtest, computerised task switching test, backward digit recall span (BDS)**,** and the Hayling sentence completion test (HSCT). In the second EF session, the assessments were completed in the following order: trail making test (TMT), computerised n-back, Stroop task, and the computerised psychological refractory period (PRP) paradigm task. All the computerised tasks except the BDS and Stroop task, included a practice run prior to beginning the actual study task. All assessments are described in detail below.

Participants completed the sessions in the same order as outlined above. However, due to computer issues, two older participants did not follow this order.

Following completion of all study sessions, all participants were presented with the study debrief form and compensated with either 12 course credits or a £20 Amazon voucher for the young adults, or a £21 Amazon voucher for the older adults, as compensation.

All study documents, including the PIS, study consent form and debrief sheet can be viewed in the Appendix (2, 3, and 4, respectively). This study was approved by Brunel University's Life Sciences Ethics Committee.

3.2.3 Screening Assessments

The following tests measured the cognitive function and premorbid intelligence level of the participants during the screening session (Session 1):

Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005)

The MoCA is a pen-and-paper screening instrument used to detect cognitive decline and takes approximately 10 minutes to administer. It consists of eight domains: visuospatial/executive function, naming, memory, attention, language, abstraction, delayed recall, and orientation. Participants were assessed in an interview type setting with an examiner (all assessments were conducted by Mojitola Idowu). Scores range from 0 to 30 and are based on accuracy performance. Scores greater than 25 suggest normal cognition, 20 to 25 mild cognitive impairment (MCI), 19 to 14 early-stage dementia, and below 14 indicate dementia.

Mini-Mental State Examination (MMSE) (Folstein et al., 1975)

The MMSE tool is a pen-and-paper screening instrument used to detect cognitive decline and takes approximately 10 minutes to administer. It is a simple test of cognitive function and is based on a total possible score of 30 points. It is divided into six domains: orientation, concentration, attention, verbal memory, naming, and visuospatial skills. A score of 28-30 suggest normal cognition, 25-27 MCI, 19-24 mild dementia, 10-18 moderate dementia, 0-9 indicates severe dementia.

Geriatric Anxiety Scale (GAS) (Segal et al., 2010)

The GAS is a self-report anxiety measure specifically developed for use with older adults and takes approximately 5-10 minutes to complete. It consists of 30 items of which 25 items represent three common domains of anxiety symptoms among older adults (cognitive, somatic, and affective) and the last 5 items represent common content areas of worry. There are approximately 8 to 9 items for each domain. Participants are required to indicate how often they have experienced each symptom within the last week and including the current day of the assessment using the 4-point Likert scale ranging from 0 (not at all) to 3 (all of the time). Higher scores indicate higher levels of anxiety. Scores are generated from the 25 items of the three common domains only, obtained by summing the point values assigned to each response. The additional 5 are for clinical use only. Thus, scores can range from 0 for no anxiety to 75 for severe anxiety. This test was completed online via a Qualtrics link.

Geriatric Depression Scale (GDS) (Yesavage et al., 1983)

The GDS is a self-report measure consisting of 30 yes/no response questions designed specifically for assessing depression in older adults. It takes approximately 5 – 10 minutes to complete. Scores are generated from the summation of the first 25 items, where responses are designated either a ‘0’ or ‘1’. Higher total scores indicate a higher level of depression. The remaining 5 items are for clinical use. The following cut-off points are used to determine depression level: 0-9 normal range; 10-19 declares mild depression; 20-30, moderate to severe depression. This test was completed online via a Qualtrics link.

Activities of daily living scale (ADL) (Lawton et al., 1969)

The ADL is a 6-item test assesses an individual's present level of functional ability on a series of basic activities performed daily required for independent living at home and/or in the community. These functions include personal, self-care, domestic and general home maintenance activities in and around the home. Scores are out of 6, with 6 representing the best level of independence. It takes approximately 2-5 minutes to complete. This test was completed online via a Qualtrics link.

Instrumental activities of daily living scale (IADL) (Lawton et al., 1969)

The IADL is an 8-item test that assesses slightly more complex skills not fundamental to life than the ADL, however aid in an individual's ability to live independently in a community. These skills include managing finances, handling transportation, shopping, preparing meals, using the telephone or other communication devices, managing medications, doing laundry, housework, and basic home maintenance. Scores are out of 8, with 8 representing the best level of ability. It takes approximately 2-5 minutes to complete. This test was completed online via a Qualtrics link.

Spot-the-word test (Baddeley et al., 1993)

This test is used to estimate premorbid intelligence which takes approximately 10 minutes to complete. It involves presenting the participants with pairs of items comprising one actual word and one non-word (e.g. *lentil* or *glotex*) and requiring the participant to identify the actual word. The participant's number of correctly identified true words was recorded out of a total of 60. This test was completed online via a Qualtrics link.

Hopkins Verbal Learning Test (HVLT) (Brandt, 1991)

The pen-and-paper HVLT is a brief measure of verbal memory which takes approximately 10 minutes to administer. In part A, the immediate recall section, participants are read a list of 12 words composed of four words from 3 semantic categories (e.g. 'precious stones - emerald'; 'human shelter - hotel'; 'animals - tiger') aloud and asked to recall as many as they can by the examiner. This is repeated three times. An average score is derived from the total of the 3 free recall trials ('Total recall'). Part B, delayed recall section, involved the recognition of words from part A, where a single list of 24 words was read aloud by the

examiner and participants were asked to identify which of these words were included in the original list of 12 by responding with ‘yes’ or ‘no’. This was performed once. Correctly identified words were recorded as true positives. The list also contained 6 distractors from the same semantic categories (related false positives or FP-related) and 6 unrelated distractors (unrelated false positives or FP-unrelated). The Discrimination index (true positives - false positives) was calculated.

3.2.4 Executive Function Assessments

Each EF was assessed with two individual tasks to examine the cognitive ability of the participants in dual-tasking, inhibition, shifting and updating.

3.2.4.1 Dual-Tasking

Pen-and-paper based modified test for everyday attention (TEA) DT telephone code search subtest (Robertson et al., 1994)

The TEA telephone search test assesses divided attention. Participants were required to undertake a visual search for several occurrences of a specific telephone area code with a corresponding symbol in a fictional telephone directory consisting of several telephone area codes with corresponding symbol combinations, as seen in Figure 3.1. At the same time, participants were additionally required to count the number of low tones they heard in a series of randomly mixed low and high tones played aloud by a computer or laptop in the background. They were given 2 minutes to complete this. The participant’s count of area code/symbol and low tone audio number were recorded. There were 17 target phone numbers in the list, and 10 low tones.

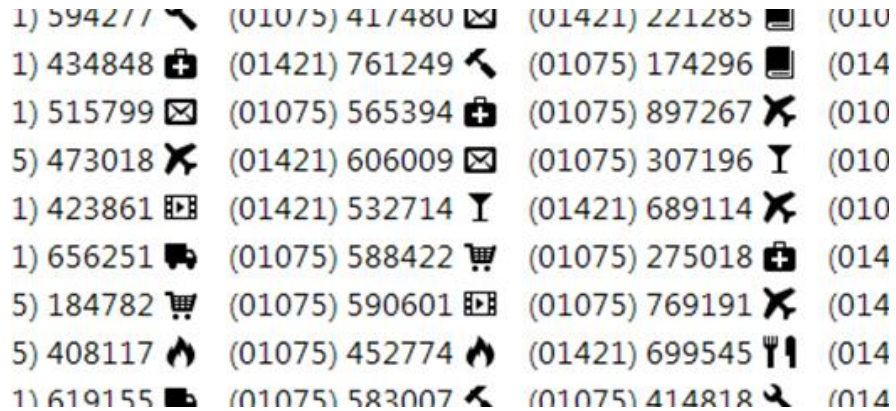


Figure 3.1. Test for everyday attention (TEA) telephone code search. This task involves participants search for a particular symbol/telephone area code combination from a list of various symbol/telephone area code combinations.

The older adult participants performed both tasks individually as ST prior to undertaking the DT condition. Hence, they counted a series of auditory tones being played in the background as a ST and searched for a specific area code with a corresponding symbol in a fictional telephone directory, as another ST. The correct auditory number was 4 and count was 7.

The accuracy rate of the responses was recorded. Please note, the value for participants who guessed greater than the actual number of auditory or code count was modified by subtracting the error rate, i.e. the overestimate, from the value guessed. For example, for 24, that was 24-17 = 7, then an (7/17 =) 41.18% error rate and (100-41.18=) 58.88% accuracy rate.

Psychological Refractory Period paradigm task (PRP) (Pashler, 1984)

The PRP task was ran in Presentation (version 18.1.06.09.15, www.neurobs.com). Participants were required to give two responses (R1 and R2) to two stimuli (S1 and S2), auditory and visual, separately as STs and concurrently as DTs in separate blocks. Each block was cued at the start, so participants were aware of which trial to perform.

Single-tasks

In the auditory, A, ST, participants were required to discriminate between high and low tones during 2 blocks of 25 trials. Each tone sequence was played on the background of a black computer screen for 300ms. The QWERTY keyboard 'Z' and 'X' keys represented 'low' and 'high' frequency tones, respectively. Similarly, in the visual, V, ST, participants are required to discriminate between the numerical values '1' or '2' during 2 blocks of 25 trials. The keys 'N' and 'M' represented '1' and '2', respectively. Each presentation occurs on a black computer screen for 300ms. In both cases, the participant was required to respond within 9000ms otherwise an error was recorded. The overall task duration was dependent on the response speed of the participant. Performance was assessed by the average RTs and error rates produced for each ST.

Dual-tasks

In the DT condition of the PRP task, participants were required to complete 2 blocks of 25 trials at two stimulus onset asynchrony (SOA), 0ms and 1000ms, as shown in Figure 3.2a, where the auditory stimulus, S1, was always presented before the visual stimulus, S2, as seen in Figure 3.2b.

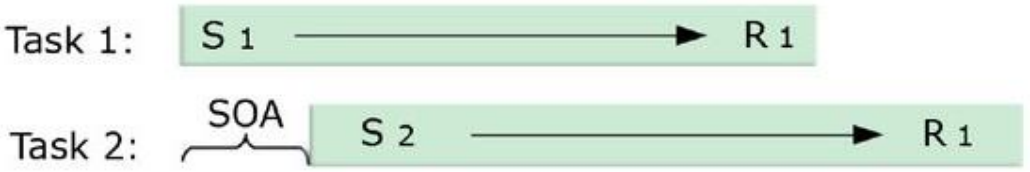


Figure 3.2a. The Stimulus Onset Asynchrony (SOA). Participants are required to perform two successively presented stimuli (S1 and S2) at different SOA with two different responses (R1 and R2). The SOA can be short, i.e. 0ms, or long, i.e. 1000ms (Aschersleben & Muesseler, 2008).

In both cases, participants were required to respond to the auditory stimulus first then the visual stimulus within a 9000ms otherwise an error is recorded. Each stimulus was presented on a black screen. The overall task duration was dependent on the response speed of the participant. Performance was assessed by the average response times (RTs) and error rates produced for each DT condition, i.e. SOA 0ms and SOA 1000ms. DT cost [DT minus ST performance] was also calculated for the RTs and error rates at SOA 0ms.

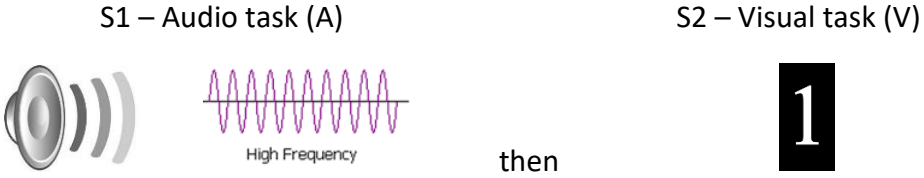


Figure 3.2b. The Psychological Refractory Period (PRP) paradigm task. In the task, two stimuli are presented during the DT condition, where the auditory stimulus is always presented first.

3.2.4.2 Inhibition

Stroop task (Golden, 1978)

The pen-and-paper Stroop task was administered to measure the participants susceptibility to Stroop interference, and took approximately 5 minutes to complete. This task consisted of three parts, each having 100 items organised in five columns of 20. Part 1, word reading (W), had the words **RED**, **GREEN**, and **BLUE** printed in black ink, randomly arranged. No word followed itself within a column. Part 2, colour naming (C), had items written as XXXX in

the colours green, blue, and red, i.e. **XXXX**, **XXXX** and **XXXX**, randomly arranged. No colour followed itself or matched the corresponding item. Part 3, naming of the incongruent colour of the ink of the word presented, colour-word (CW), consisted of the words in part 1 printed in the colour of the items in part 2 for all 100 items, i.e. **RED**, **GREEN**, or **BLUE**, randomly arranged. This section assessed the inhibition ability of the participant to inhibit the word presented as reading is an automated process whilst colour naming is not. Participants were given 45 seconds for each part and instructed to read the words, name the colours, and name the ink colour of the printed words, respectively, as quickly and as accurately as possible. The number of correctly read words or colours out of 100 was recorded for each section, i.e. W, C and CW.

In addition, following completion on the task, the predicted CW, which is based on the individual's performance in the W and C sections, denoted as CW', was calculated using the formula indicated, (W x C) / (W + C). Inhibition ability is based on the interference score, calculated with the formula stated, CW – CW'.

Hayling sentence completion test (HSCT) (Burgess & Shallice, 1997)

Participants were required to provide either the expected word or an unrelated word to complete a high cloze sentence. The test consisted of two parts, each with a set of 15 sentences with the last word missing; for example, '*The captain wanted to stay with the sinking...*'. In Part 1, participants had to produce a word that best finished each sentence (Initiation condition), e.g. "ship". In Part 2, participants had to complete each sentence by inhibiting an impulse to give the word that best completed the sentence by instead giving an unconnected word (Inhibition condition), e.g. "colour". A prerecording of all the sentences was played to the participants and paused whilst they were being audio recorded for their verbal answers to be collected. Immediately after a participant gave a response, the next sentence was played. The overall task duration was dependent on the speed of the participant in producing a word for all the sentences but was usually between 7- and 10-min. Performance was measured by the total time taken to produce the words in both parts, and the incorrectness of the words to the sentences in part 2. Furthermore, the task generates its own derived performance score by adding the scaled score of the RTs of the two sections, and the errors produced in the incongruent section, part A scaled score + part

A scaled score + part B errors scaled score. Part B errors were scored as 'any category A (connected, related word) errors' + 'any category B (unconnected, unrelated word) errors'.

3.2.4.3 Shifting

Task switching test (Rogers & Monsell, 1995)

In this computerised task, ran in Presentation software (version 18.1.06.09.15, www.neurobs.com), participants were required to perform two test conditions, a repetition, and a shifting, where the stimulus, a '1' or '2' printed in the colours blue or yellow were presented. In the repetition condition, participants had to complete 4 blocks of 30 trials. Two separate cued blocks were performed, numerical and colour. In the cued numerical block (they performed 2 blocks of this), the participants had to response with either a '1' or '2', and in the cued colour block (they performed 2 blocks of this), with either 'blue' or 'yellow', as seen in Table 3.1, below. The QWERTY keyboard 'Z' key represented '1' and 'blue' and 'M', '2' and 'yellow'. Instructions were displayed on the screen at the start of each block until the participant started the task. The stimuli were presented on a black screen for 300ms until the participants responded or timeout after 9000ms from stimulus onset, where an error was recorded.

Table 3.1. The task switching test conditions

Stimuli / Cue	1	1	2	2
Number	1	1	2	2
Colour	Blue	Yellow	Blue	Yellow

In the task switching condition, the two repetition conditions were mixed and presented randomly within a trial. Participants were cued as to which task to perform next, e.g. number or colour. There were 30 mixed trials per block and 4 blocks of the switching task. Each stimulus was presented on a black screen for 300ms until the participants responded / timed out, otherwise an error was recorded.

The repetition and switching blocks were presented in a pseudo-randomised order in the test. The overall task duration was dependent on the response speed of the participant.

Performance was assessed by the average RTs and error rates produced during the repetition and switching conditions. The shifting cost was then determined using the formula 'shifting – repetition' for both the RT and error rate, where smaller values represent better shifting performance. The local shift (difference between shifting and non-shifting trials within a shifting block), global shift (difference between the combined shifting trials and the pure repetition trials), and mixing task cost (difference between the repetition trials within the pure repetition trials and within the combined shifting and repetition blocks) were assessed.

Trail making test (TMT) Parts A and B (Reitan, 1992)

The pen-and-paper TMT for cognitive flexibility encompassed two parts, A and B, consisting of 25 small open circles randomly distributed over a sheet of paper. In TMT part A, the circles are numbered 1–25, and the participant is asked to draw lines to connect them in ascending order as quickly as possible. In TMT part B, the circles include both numbers (1–13) and letters (A–L). The participant has to draw lines to connect the circles in ascending order as quickly as possible while alternating between the numbers and letters (i.e. 1, A, 2, B, etc). The completion time and the number of errors were recorded. Data from this task were excluded when participants made more than 2 mistakes in either part. The overall task duration was dependent on the completion times of both parts by the participant. The shifting cost was then determined using the formula 'switching (TMT part B) - repetition (TMT part A)' for the RT, where smaller values represent better shifting performance. Similarly for error rates, 2 errors were equated to an error rate of 100% in each part, hence the error rate cost was also determined.

3.2.4.4 Updating

N-Back test (Kirchner, 1958)

In this computerised spatial task, ran in Presentation software (version 18.1.06.09.15, www.neurobs.com), participants were instructed to select the position of the stimulus, a yellow circle, presented to them on a black computer screen. The task involved 4 conditions where the participant must respond with the position of the yellow circle seen at N screen to the present screen. The N positions used in this research were 0 (the present screen), 1-, 2-, and 3-back screens prior, as seen in the Figure 3.3. Participants were instructed to select

the corresponding QWERTY keyboard button they thought was the position of the circle, i.e. 'V' for the first (left-most) position, 'B' for the second, 'N' for the third and 'M' for the fourth.

Target (circle) were presented on a black computer screen for 2000ms or until the participants responded, otherwise it was recorded as an error. There were 5 blocks for each n-back condition, i.e. 20 blocks in total. One block consisted of 16 trials, so in total 320 trials (i.e. 20 x 16). Conditions were always presented in the fixed order, blocks 1-5: 0-back, blocks 6-10: 1-back, blocks 11-15: 2-back, and blocks 16-20: 3-back. Instructions were presented on the screen at the start of each block until the participant started the task. Thus, a trial took a maximum of 2750ms in the case of time-out, or shorter if responded before the time-out.

Performance was assessed by the average RTs and error rates produced during each n-back condition. Analysis was then conducted by comparing the n-back conditions among each other, e.g. 0 vs 1, 0 vs 2, 0 vs 3, 1 vs 2, etc, with the RTs and error rates.

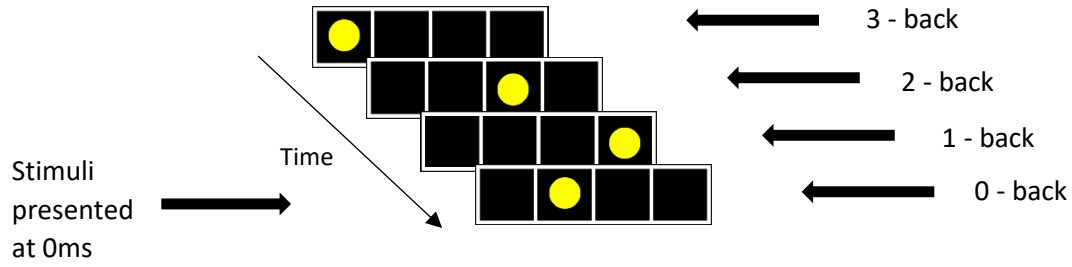


Figure 3.3. The N-Back test. In this spatial n-back test, the participant is required to indicate at what position on the screen the yellow circle appears by selecting an appropriate button on the keyboard. In the 0-back condition, the position at t = 0ms is recorded for all trials within the block. In the 1-back, the participant must respond to the circle's position on the previous screen, in the 2-back, its position two screens before, and in the 3-back, three screens prior.

Backward digit recall span (BDS) (Baddeley & Hitch, 1974)

In the pen-and-paper BDS, participants are required to recall a list of numbers in reverse order immediately following presentation from a pre-recording on a computer or laptop. The examiner paused the recording after each list to allow the participant to respond. The minimum length of the list is 2 and maximum 8, and there are two trials per length. The longest correct list of numbers the participant can recall backward once is recorded as a measure of their working memory capability. Performance assessment is determined by

scoring ‘1’ for each correctly recalled length, thus ranging 1 to 14, e.g. if all trials are performed correctly then the score would be ‘14’ for 2 trials for all 7 lengths.

3.2.5 Statistical Analysis

The data was assessed by using the Statistical Package for Social Sciences (SPSS), version 26.0.0.0 (IBM SPSS Statistics, IBM Corp, Armonk, NY). Participants were excluded from analysis on each task if they performed above or below 3 standard deviations (SDs) from the rest of the groups’ mean performance. Additionally, participants who produced an error rate of 60% or greater in either condition of the TEA test and/or 50% or greater in either task condition of the PRP tasks were removed from analysis.

Descriptive data and the study behavioural data were collected. Performance analysis in each age group was performed separately (please refer to the Supplementary chapter for more detail on the analysis of the young adults). Paired-samples t-tests, and one-way repeated measures analysis of variance (ANOVA) were used to test whether congruent and incongruent conditions differed significantly from each other.

In comparing performance between young and older adults, chi-squared, χ^2, tests were used to assess gender and handedness. For all other task measures, analysis was first conducted using multivariate analysis of variance (MANOVA) on all task conditions collectively, where the interaction value was focused on as it revealed any performance differences. Independent t-test was then conducted on individual task conditions.

The cost measures were primarily used for this cross-sectional analysis of the EF tasks as it eliminates unwanted cognitive and nonexecutive processes by analysing the difference between congruent and incongruent, or simple and complex task conditions of the same EF. Examples of such measures include the DT costs (DT minus ST condition measures), inhibition costs (incongruent minus congruent), shifting costs (shifting minus repetition condition measures) (Wylie & Allport, 2000), updating cost (3-back minus 0-back) or equivalent. Some derived test scores were also assessed where applicable. The significant effects for the tests were reported at $p < 0.05$, unless stated otherwise.

The *p*-value used in the n-back pairwise comparison analysis was Bonferroni corrected due to the numerous pairwise assessments conducted to reveal the new (corrected) alpha level

needed to be passed, i.e. 6 (number of comparisons). It was calculated using an online calculator, https://www.easycalculation.com/statistics/bonferroni-correction-calculator.php.

To determine the trajectory of cognitive decline of the four EFs, the z-scores of both groups' outcome measures were calculated and compared with the use of paired-samples and independent t-tests.

The effect size, Cohen's *d*, and partial eta squared, η_p^2, of the EF costs and/or equivalent t-tests were also collected to assess the strength of the difference between the young and older adults. Cohen's *d* was calculated with the use of an online calculator (https://www.easycalculation.com/statistics/effect-size-t-test.php), and η_p^2 calculated within SPSS. For the trajectory analysis of the z-scores, the effect size, *e*, (https://www.easycalculation.com/statistics/effect-size-t-test.php) was used. The effects were classified as small, if less than or equal to 0.2, moderate, if above 0.2 and less than or equal to 0.5, large, if above 0.5, and less than or equal to 0.8, and very large if greater than 0.8 (J. Cohen, 1988).

3.3 Results

3.3.1 Demographics and Screening data

The groups' demographic data and the descriptive summary of the results can be seen in Table 3.2.

Table 3.2. Demographic Data and results of the screening tests of the Young and Older Adult Participants

Characteristic	**Young Adults** (Mean/SD)	**Older Adults** (Mean/SD)	**Young vs Old, *p*-value**
Age (years)	21.18 (4.43)	71.56 (6.63)	< 0.001[a]
Gender (M/F)	5/23	11/14	0.038[b]
Education, years	14.46 (1.32)	14.68* (2.08)	0.425[a]
Handedness (L/R)	2/26	2/23	0.906[b]
Mini-Mental State Examination	28.46 (1.29)	28.64 (1.52)	0.651[a]

Montreal Cognitive Assessment	26.71 (2.27)	26.80 (2.00)	0.885[a]
Geriatric Anxiety Scale	19.75 (9.99)	7.12 (5.49)	< 0.001[a]
Geriatric Depression Scale	12.32 (3.40)	17.92 (1.47)	< 0.001[a]
Activities of daily living scale	6.00 (0.00)	5.80 (0.41)	0.012[a]
Instrumental activities of daily living scale	7.18 (1.28)	7.92 (0.28)	0.006[a]
Hopkins Verbal Learning Test, Part A	7.38 (1.63)	7.47 (1.62)	0.849[a]
Hopkins Verbal Learning Test, Part B	11.07 (1.18)	10.28 (1.43)	0.032[a]
Hopkins Verbal Learning Test, Discrimination index	18.45 (2.23)	17.75 (2.73)	0.306[a]
Spot-the-word test	28.96 (3.11)	28.68 (1.25)	0.671[a]

*n = 24 as one individual's educational level was unknown, [a] Independent t-test, t(51), [b] Chi-squared test $\chi^2(1)$, n=53.

The older adult group consisted of less female participants, 56%, in comparison to in the young adult group with 88%, $\chi^2(1) = 4.28$, $p = 0.038$. A comparable level of education was observed in the groups, $t(50) = -0.80$, $p = 0.425$. Similarly, there was no difference in the cognitive status between the groups, the MMSE score, $t(51) = -0.45$, $p = 0.651$, or the MoCA score, $t(51) = -0.15$, $p = 0.885$.

Differences were reported in the quality-of-life assessments, ADL and IADL. The ADL test reported the young adults were better at completing everyday self-care tasks, such as bathing, dressing, and eating, $t(51) = 2.60$, $p = 0.012$. Whereas for more complex daily tasks, including cooking, shopping, laundry, and housework, assessed with the IADL test, the older participants were better, $t(51) = -2.84$, IADL, $p = 0.006$. Nonetheless, these differences should not greatly affect the cognitive function required of them in completing this study.

In the evaluation of both groups' anxiety and depression level, the GAS and GDS were employed. The GAS (0 to 75 scale range) revealed that young adults showed significantly more anxiety than the older adults, $t(51) = 5.61$, $p < 0$ .001, however both had fairly low mean levels. The GDS (0 to 30 scale range) suggested a moderate level depression in the

older participants, $t(51) = -7.62$, $p < 0.001$. Thus, significant differences were attained for both measures between the groups. Nevertheless, no participant was reported to been clinically diagnosed (e.g. by a medical profession) with anxiety or depression. Furthermore, participants regularly complained about some of the questions asked in both assessments, as they did not apply to them, i.e. concerning children and/or spouse, as well as the limited response choice of the GDS of 'yes' and 'no', as they would have preferred more choices, such as 'sometimes'.

Verbal learning and memory were examined with the Hopkins verbal learning test. In part A, the free recall section, performance was comparable between the groups, $t(51) = -0.19$, $p = 0.849$, but not in part B, the recognition section, $p = 0.032$, [$t(51) = 2.20$]. The young participants were better at remembering the words that had been presented to them in part A. Paired-samples t-test between part A and B performance showed significance in both groups. In the young, $t(27) = -10.97$, $p < 0.001$, and in the old, $t(24) = 10.25$, $p < 0.001$. A 2 (young, old) x 2 (part A, part B) ANOVA indicated no main group effect between their performances, $F(1, 51) = 1.07$, $p = 0.306$, $\eta_p^2 = 0.02$. There was a main effect for the test part, $F(1, 51) = 218.07$, $p < 0.001$, $\eta_p^2 = 0.81$, and for the interaction, $F(1, 51) = 3.97$, $p = 0.052$, $\eta_p^2 = 0.07$, confirming a difference in the task performance between the groups.

Still, insignificant difference in their total scores of parts A and B, which represents the test discrimination index, was observed, $t(51) = 1.04$, $p = 0.306$. In sum, the groups' performed similarly in part A, i.e. in immediate recall, however the older adults did not perform as well in part B, delayed recall, as the younger group.

No difference was found in the estimated premorbid IQ assessment with the utilisation of the spot-the-word test, $t(51) = 0.43$, $p = 0.671$.

In conclusion, all scores represented normal functional ability and within normal cognition function ranges. The groups had fairly similar cognitive statuses as observed by the MMSE and MoCA scores, and education level. Likewise, performance in the spot-the-word and Hopkins verbal learning task parts were comparable. Although, there was a difference in the level of anxiety and depression, and quality of life, particularly with the young adult's lack of independence in performing everyday tasks. Nonetheless, the groups' cognitive ability was deemed equivalent and ideal for the comparison study detailed here.

3.3.2 Executive Function Abilities in Young and Older Adults, A Cross-sectional study

3.3.2.1 Dual-Tasking

The TEA telephone search subtest and PRP paradigm results can be viewed in Table 3.3 below.

Table 3.3. Dual-Tasking Results of the Young and Older Adult Participants

Task	**Young Adults**		**Older Adults**		**Young vs Old, *p*-value**
	n	Mean (SD)	n	Mean (SD)	
Test for Everyday Attention, telephone, auditory ST, count accuracy (%)	24	N/A	20	97.50 (7.69)	-
Test for Everyday Attention, telephone, auditory DT, count accuracy (%)	24	90.42 (13.34)	20	92.50 (11.18)	0.582
Test for Everyday Attention, auditory DT accuracy cost (%)	24	N/A	20	-5.00 (10.88)	-
Test for Everyday Attention, telephone count ST, code count accuracy (%)	24	N/A	20	71.43 (17.34)	-
Test for Everyday Attention, telephone count DT, code count accuracy (%)	24	79.17 (15.12)	20	75.88 (15.26)	0.479
Test for Everyday Attention, telephone count DT cost, count accuracy (%)	24	N/A	20	4.45 (20.89)	-
PRP paradigm, auditory ST RT (ms)	24	616.97 (199.59)	22	657.28 (152.67)	0.449
PRP paradigm, auditory ST error rate (%)	24	7.33 (7.91)	22	3.00 (5.94)	0.043
PRP paradigm, auditory DT (SOA 0ms) RT1 (ms)	24	1079.62 (365.27)	22	1097.13 (287.27)	0.858
PRP paradigm, auditory RT1 DT cost (SOA 0ms), RT (ms)	24	462.65 (323.27)	22	439.85 (245.96)	0.790
PRP paradigm, auditory DT (SOA	24	10.75 (9.81)	22	3.91 (6.66)	0.009

0ms) RT1 error rate (%)					
PRP paradigm, auditory DT (SOA 0ms RT2) error rate cost (%)	24	3.42 (6.92)	22	0.09 (3.53)	0.134
PRP paradigm, visual ST RT (ms)	24	503.54 (109.17)	22	553.77 (59.37)	0.062
PRP paradigm, visual ST error rate (%)	24	3.42 (4.55)	22	0.64 (1.14)	0.008
PRP paradigm, visual DT (SOA 0ms) RT2 (ms)	24	1312.99 (418.22)	22	1459.13 (311.22)	0.189
PRP paradigm, visual RT2 DT cost (SOA 0ms), RT (ms)	24	809.45 (381.28)	22	905.37 (292.60)	0.347
PRP paradigm, visual DT (SOA 0ms) RT2 error rate (%)	24	7.75 (7.13)	22	2.36 (2.36)	0.002
PRP paradigm, visual DT (SOA 0ms) RT2, error rate cost (%)	24	4.33 (5.71)	22	1.73 (2.41)	0.054
PRP paradigm, DT (SOA 0ms) RT2-RT1, RT cost (ms)	24	233.37 (134.72)	22	362.00 (113.90)	0.001
PRP paradigm, DT (SOA 0ms) RT2-RT1, error rate cost (%)	24	-0.03 (0.08)	22	-0.02 (0.06)	0.483
PRP paradigm, visual DT RT2 (SOA 1000ms) (ms)	24	743.43 (360.35)	22	726.62 (209.67)	0.849
PRP paradigm effect, SOA 0 – 1000ms, visual task, RT2 (ms)	24	569.56 (254.83)	22	732.51 (250.94)	0.034
PRP paradigm, visual DT RT2 (SOA 1000ms) rate (%)	24	9.08 (11.25)	22	1.27 (2.10)	0.003
PRP paradigm effect, SOA 0 – 1000ms, RT2 error rate (%)	24	-1.33 (9.60)	22	1.09 (2.20)	0.254
PRP ANOVA, RT2, SOA 0ms, SOA 1000ms	-	< 0.001	-	< 0.001	0.486
PRP ANOVA, RT2, error SOA 0ms, SOA 1000ms	-	0.503	-	0.030	0.001

RT - Reaction time; SOA - Stimulus Onset Asynchrony.

In the TEA telephone code search subtest, the young adult participants performed the tasks as DT only, i.e. no ST condition of the auditory and telephone code count tasks were completed, whereas the older adults completed the tasks as ST and DT.

Paired-samples t-tests between the ST and DT conditions in the auditory task was marginally significant in the older adult's performance $t(19) = 2.06$, $p = 0.054$, for accuracy (and error rate). With the telephone code search task, no significance was observed, $t(19) = 0.95$, $p = 0.352$. Therefore, the DT condition caused this group to produce more performance errors during the completion of the auditory task.

A 2x2 ANOVA for the TEA DT [group (young, older adults) x task (auditory, code count)], found no main group effect, $F(1, 42) = 0.04$, $p = 0.835$, $\eta_p^2 = 0.00$. A main effect for the TEA task, $F(1, 42) = 20.68$, $p < 0.001$, $\eta_p^2 = 0.33$ was revealed as participants performed better in the auditory task. An insignificance for interaction $F(1, 42) = 0.77$, $p = 0.386$, $\eta_p^2 = 0.02$, was observed. Thus, DT performance between the young and older group was comparable in both TEA tests.

Independent t-tests confirmed this. During the auditory task, $t(42) = -0.55$, $p = 0.582$, $d = 0.17$, and the telephone code count task, $t(42) = 0.72$, $p = 0.479$, $d = 0.22$. Interestingly, both groups performed better, i.e. with more accuracy, in the auditory task in comparison to the telephone search task. This was confirmed by a further paired-samples t-test between the two tasks accuracy during DT performance. In the young adults, $t(23) = 2.54$, $p = 0.018$, and the older adults, $t(19) = 4.05$, $p = 0.001$.

Please note, as only the older adult participants completed these two tasks as STs, the DT cost was only obtained for that population. Nevertheless, since the performance in the more difficult DT condition was comparable, thus it seems unlikely that a DT cost would have revealed an age effect.

In the PRP paradigm, two DT conditions were assessed at SOAs of 0 and 1000ms.

To test whether there were significant age effects in the RT DT between the ST and DT performance at SOA 0ms where participants had to respond to RT1 before RT2, two 2x2 ANOVA [group (young, older adults) x task (ST, DT)] were calculated separately for RT1-auditory and RT2-visual.

For the RT1 costs, no main effect for the group was observed, $F(1, 44) = 0.19$, $p = 0.662$, $\eta_p^2 = 0.00$. A main effect for the task condition was found, $F(1, 44) = 111.96$, $p < 0.001$, $\eta_p^2 = 0.72$ as DT resulted in longer RTs in both groups. There was no interaction $F(1, 44) = 0.07$, $p = 0.790$, $\eta_p^2 = 0.00$. Similarly, for RT2, no main group effect was observed, $F(1, 44) = 2.54$, $p = 0.118$, $\eta_p^2 = 0.06$, but was for the task condition, $F(1, 44) = 288.85$, $p < 0.001$, $\eta_p^2 = 0.87$ for the same reason as stated with the RT1. There was no interaction $F(1, 44) = 0.90$, $p = 0.347$, $\eta_p^2 = 0.02$.

With the RT1 mean error rate cots, a main group effect, $F(1, 44) = 6.79$, $p = 0.012$, $\eta_p^2 = 0.13$, and for the PRP task, $F(1, 44) = 6.94$, $p = 0.012$, $\eta_p^2 = 0.14$, was shown, due to the older adults producing less errors in both task conditions, as well as both groups producing more errors during the DT. However, there was no significance for interaction $F(1, 44) = 2.33$, $p = 0.134$, $\eta_p^2 = 0.05$. For the RT2, a main group effect was also shown, $F(1, 44) = 12.43$, $p = 0.001$, $\eta_p^2 = 0.22$ with the older adults performing more accurately, and main effect for the PRP task condition, $F(1, 44) = 21.28$, $p < 0.001$, $\eta_p^2 = 0.33$, as DT resulted in an increased proportion of errors. No significance for interaction $F(1, 44) = 394$, $p = 0.054$, $\eta_p^2 = 0.08$, was found. Thus, the groups performed comparably in both tasks.

Paired-sampled t-test between ST and DT in the young adults for RT1 showed significance for the RTs, $t(23) = -7.01$, $p < 0.001$, and error rates, $t(23) = -2.42$, $p = 0.024$, and for RT2, $t(23) = -10.40$, $p < 0.001$, and error rates, $t(23) = -3.72$, p = 0.001, indicating overall performance difference between the two task conditions. Whereas in the older adults, significance was revealed in the RTs for RT1, $t(21) = -8.39$, $p < 0.001$, and RT2, $t(21) = -14.51$, $p < 0.001$, and the RT2 error rates, $t(21) = -3.36$, $p = 0.003$, but not for RT1 error rates, $t(21) = -1.21$, $p = 0.241$.

Assessment between the DTs at SOA 0ms with a 2x2 ANOVA [group (young, older adults) x DT (RT1, RT2)] was conducted. For the mean RTs, no main group effect was observed, $F(1, 44) = 0.64$, $p = 0.427$, $\eta_p^2 = 0.01$ as the groups performed comparably. There was a main effect for the task condition as the participants were explicitly instructed to respond first to the RT1 before RT2, $F(1, 44) = 259.48$, $p < 0.001$, $\eta_p^2 = 0.86$. A significance for interaction $F(1, 44) = 12.11$, $p = 0.001$, $\eta_p^2 = 0.22$, was found which revealed a difference in the RT costs (RT2-RT1) between the groups. This was confirmed by an independent t-test, $t(44) = -3.48$, $p = 0.001$, $d = 1.05$, see Figure 3.4.

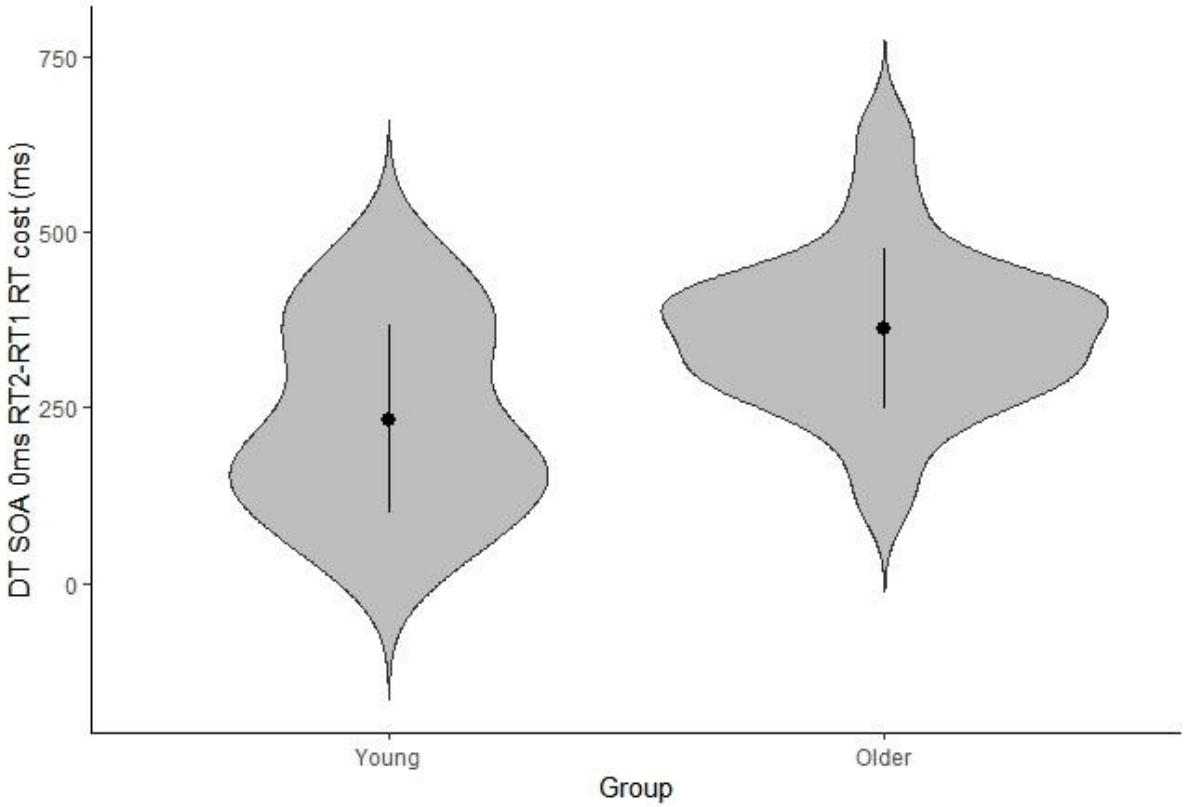


Figure 3.4. Psychological Refractory Period (PRP) Paradigm, SOA 0ms RT (RT2-RT1) cost group comparison. This figure presents the difference in RT performance between the two DTs (RT2-RT1) at SOA 0ms, between the young adults (skewness 0.28, kurtosis -1.16), and older adult groups (skewness 0.36, kurtosis 1.09). The round black circle presents the groups means and the line is ± the standard deviation. The grey kernel density plot is the data frequency, i.e. the skewness of the data, where wider areas represent a higher percentage of observations at a given value and the thinner areas, lower percentages. The tails are the ends of the data distribution.

With the error rates, a main group effect was shown, $F(1, 44) = 11.22$, $p = 0.002$, $\eta_p^2 = 0.20$, the older adults performed with better accuracy. There was also a main effect for DT, $F(1, 44) = 4.89$, $p = 0.032$, $\eta_p^2 = 0.10$, as RT2 was performed with less errors. However, no significance for interaction $F(1, 44) = 0.50$, $p = 0.483$, $\eta_p^2 = 0.01$ was observed.

The second DT ability was assessed at SOA 1000ms. Here only the visual stimuli, RT2, was considered as it is presented at 1000ms (Pashler, 1994; Schubert & Szameitat, 2003; Szameitat et al., 2011).

In comparing performance between the DTs at different SOAs, a 2x2 ANOVA [group (young, older adults) x RT2 SOA (0ms, 1000ms) was completed. For the mean RTs, there was no main group effect observed, $F(1, 44) = 0.49$, $p = 0.486$, $\eta_p^2 = 0.01$. However, there was for the SOA, $F(1, 44) = 304.07$, $p < 0.001$, $\eta_p^2 = 0.87$, as the SOA 1000ms was completed faster.

Significance for interaction, $F(1, 44) = 4.76$, $p = 0.034$, $\eta_p^2 = 0.10$ was observed which showed the PRP effect was different. Independent t-tests confirmed this difference in the RT between the groups, $t(44) = -2.18$, $p = 0.034$, $d = 0.66$, see Figure 3.5. The older adults produced a higher RT cost.

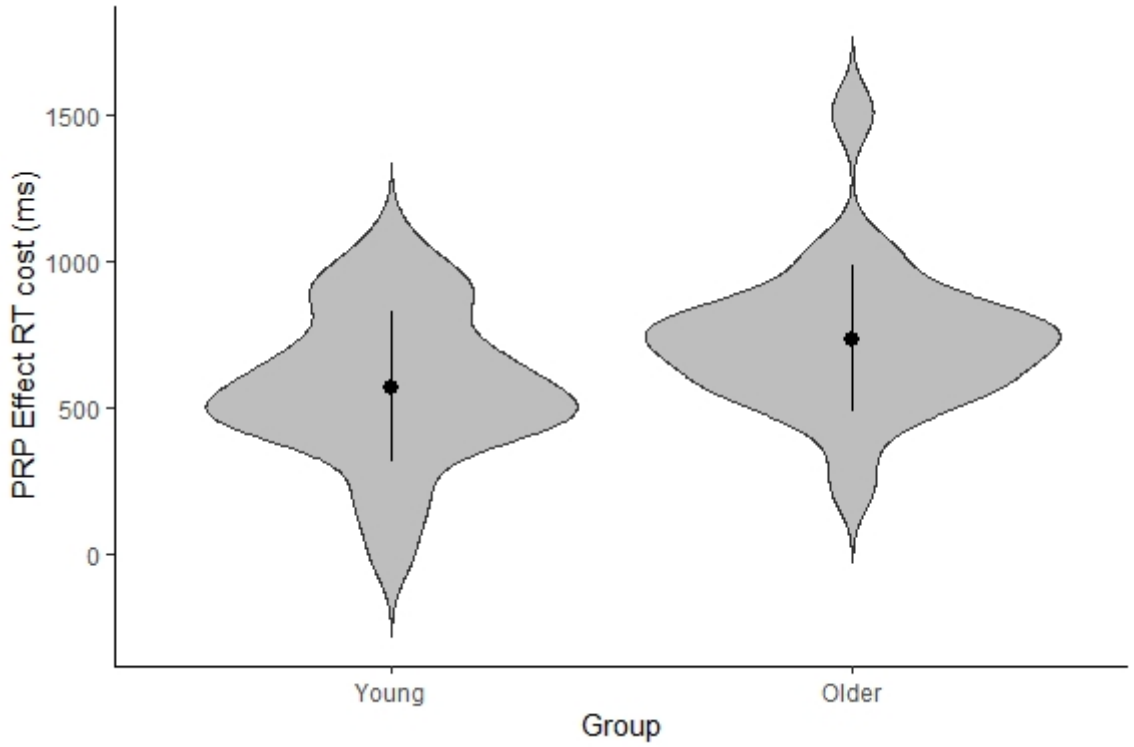


Figure 3.5. Psychological Refractory Period (PRP) Paradigm, PRP Effect RT group comparison. This figure presents the difference in RT performance between the two DTs at SOA 0ms and SOA 1000ms for RT2, between the young adults (skewness -0.15, kurtosis 0.11), and older adult groups (skewness 1.12, kurtosis 3.78).

With the error rate, no main group effect, $F(1, 44) = 0.27$, $p = 0.608$, $\eta_p^2 = 0.01$, SOA task effect, $F(1, 44) = 0.01$, $p = 0.908$, $\eta_p^2 = 0.00$, or for interaction $F(1, 44) = 1.34$, $p = 0.254$, $\eta_p^2 = 0.03$ were observed. Thus, there was a comparable error rate cost generated by the PRP effect in the groups.

To conclude, in the assessment of DT ability, an age-associated effect was observed with the PRP task in the RT DT SOA 0ms (RT2-RT1) cost, and effect RT PRP effect (RT2 SOA 0 – 1000ms) measures but not with the DT cost comparing ST and DT for RT1 or RT2. Accuracy performance was comparable between the groups for all these analyses. Similarly, no age effect was found with the accuracy performance in the TEA DT.

3.3.2.2 Inhibition

The HSCT and Stroop task results can be viewed in Table 3.4 below.

Table 3.4. Inhibition Results of the Young and Older Adult Participants

Task	**Young Adults**		**Older Adults**		**Young vs Old, *p*-value**
	n	Mean (SD)	n	Mean (SD)	
Hayling sentence completion test, Part A RT (s)	26	22.27 (8.22)	23	19.00 (3.37)	0.082
Hayling sentence completion test, Part A RT completion score	26	4.73 (1.08)	23	5.35 (0.71)	0.024
Hayling sentence completion test, Part B RT (s)	26	29.04 (18.53)	23	47.30 (21.79)	0.003
Hayling sentence completion test, Part B RT score	26	5.92 (0.84)	23	5.22 (0.90)	0.007
Hayling sentence completion test, inhibition RT cost (s)	26	6.77 (17.80)	23	28.30 (21.10)	<0.001
Hayling sentence completion test, Part C, Error score	26	6.00 (1.98)	23	5.48 (2.04)	0.369
Hayling sentence completion test, overall score	26	5.38 (1.36)	23	5.00 (1.41)	0.337
Stroop, Word (no. out of 100)	26	93.19 (10.00)	25	90.24 (13.74)	0.383
Stroop, Colour (no. out of 100)	26	71.54 (13.97)	25	65.44 (11.29)	0.093
Stroop, Colour-Word (no. out of 100)	26	47.04 (10.92)	25	32.28 (10.01)	< 0.001
Stroop, Colour-Word' (no. out of 100)	26	39.69 (5.39)	25	37.80 (5.69)	0.228
Stroop, CW-W	26	-46.15 (14.71)	25	-57.96 (11.81)	0.003
Stroop, CW-C	26	-24.50 (14.19)	25	-33.16 (9.15)	0.013
Stroop, ANOVA	-	< 0.001[a]	-	< 0.001[a]	0.003[b]
Stroop, Interference	-	6.92 (10.48)	-	-5.60 (7.71)	< 0.001

[a] - one-way repeated measures, [b] - two-way repeated measures.

Please note in addition to the outliers, one young and one older adult participant were removed from analysis due to audio recording issues. The test score for part A of the HSCT suggested both groups performed 'moderately average', while in part B the young adults were deemed 'average' indicating they performed better in this inhibition section of the test for some unknown reason. The older adults were classified as 'moderately average' in both task parts. A 2x2 ANOVA [group (young, older adults) x HSCT part (part A, part B)] was conducted. A main group effect, $F(1, 47) = 5.33$, $p = 0.025$, $\eta_p^2 = 0.10$, a main effect for the HSCT part, $F(1, 47) = 39.83$, $p < 0.001$, $\eta_p^2 = 0.46$, and for interaction $F(1, 47) = 15.01$, $p < 0.001$, $\eta_p^2 = 0.24$, were observed. The significant of the interaction shows that the costs of the two parts differed between the groups.

Independent t-test analysis between the groups in part A showed there to be no difference in their RTs, $t(47) = 1.78$, $p = 0.082$, but in part B, a substantial difference was seen with the mean RTs, $t(47) = -3.17$, $p = 0.003$. Thus, confirming the significance of the MANOVA analysis, and the better performance of the young adults.

A paired-samples t-test between the RT cost of the two parts in the young adults showed an insignificant difference in performance, $t(25) = -1.94$, $p = 0.064$, but significance in the older adults, $t(22) = -6.43$, $p < 0.001$, indicating that the older adults were affected more by the inhibition condition of the task. Thus, comparison of the RT inhibition cost between the groups was statistically significant, $t(47) = -3.88$, $p < 0.001$, $d = 1.13$, see Figure 3.6.

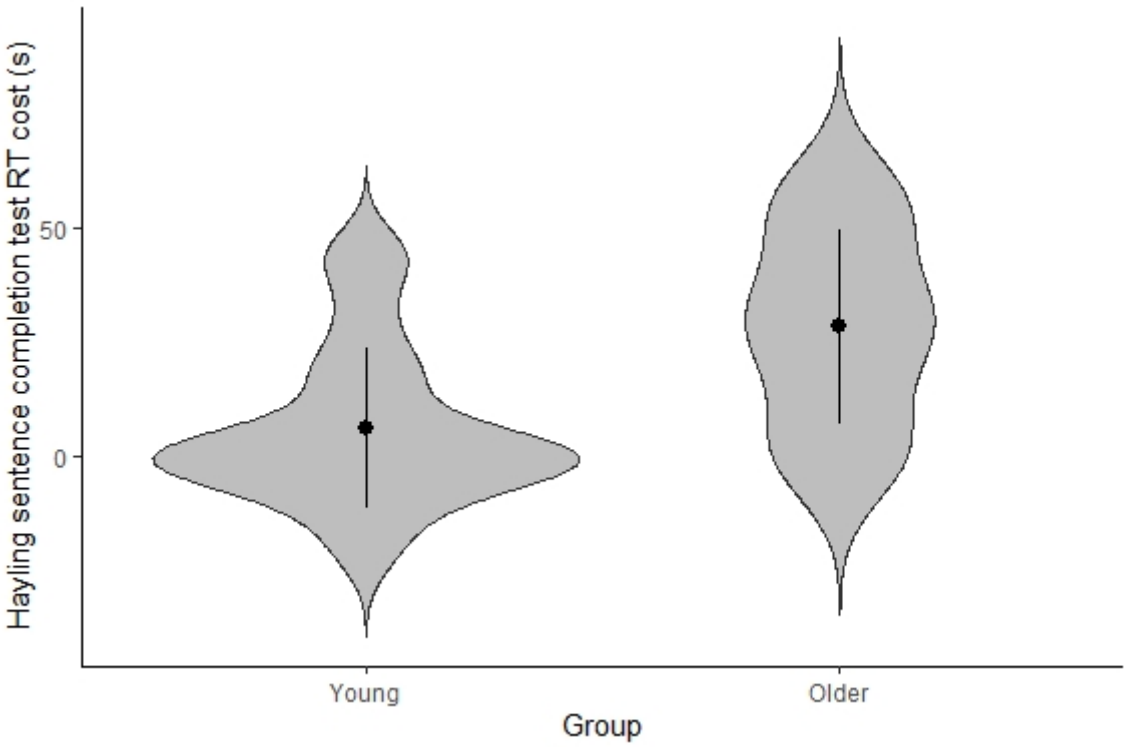


Figure 3.6. Hayling sentence completion test (HSCT) RT cost group comparison. This figure presents the RT (s) difference between non-inhibitory (part A) and the inhibition section (part B) of the test for the young adults (skewness 1.25, kurtosis 1.07), and older adult groups (skewness -0.30, kurtosis -1.22).

The error rate for part B performance in the young adult group was classified as 'moderately average', and 'average' for the older adult group. Though, an insignificant difference was observed between the groups' performance, $t(47) = 0.91$, $p = 0.369$.

Inhibitory ability was further assessed with the utilisation of the Stroop task. A one-way repeated measures ANOVA [conditions (C, W, CW)] comparing performance across the three task sections revealed significance in their performance, $F(2, 50) = 124.78$, $p < 0.001$, $\eta_p^2 = 0.83$, in the young, and $F(2, 48) = 378.55$, $p < 0.001$, $\eta_p^2 = 0.94$, in the old.

A two-way repeated measures ANOVA [group (young, older adults) x conditions (C, W, CW)], found a main group effect, $F(1, 49) = 9.74$, $p = 0.003$, $\eta_p^2 = 0.17$, as the younger group were better performers. There was a main effect for the Stroop section, $F(2, 98) = 412.56$, $p < 0.001$, $\eta_p^2 = 0.89$, which is understandable as the performance in the two repetition sections, C and W, were less demanding than the inhibition section, CW. Thus, interaction $F(2, 98) = 5.67$, $p = 0.005$, $\eta_p^2 = 0.10$, was significant confirming the performance difference between the groups.

A MANOVA comparing the inhibitory costs [group (young, older adults) x conditions (CW-C, CW-W)], showed a main group effect, $F(1, 49) = 11.53$, $p = 0.001$, $\eta_p^2 = 0.19$, and main effect for cost type, $F(1, 49) = 151.26$, $p < 0.001$, $\eta_p^2 = 0.76$. No significance for interaction was found, $F(1, 49) = 0.69$, $p = 0.409$, $\eta_p^2 = 0.01$, thus there was no difference between the groups' costs. Both groups performance better in the W section in comparison to the C.

Independent t-tests confirmed the insignificant difference, CW-C, $t(49) = 2.58$, $p < 0.013$, $d = 0.79$, and CW-W, $t(49) = 3.15$, $p < 0.003$, $d = 0.90$, as well as in the performance of the W ($p = 0.383$) and C ($p = 0.093$) sections. However, significance was revealed with performance in the CW section, $t(49) = 5.03$, $p < 0.001$. Thus, the Stroop effect was observed as expected. However, Inhibitory ability is based on the calculated interference score of the test. A positive calculated value indicates satisfactory ability in inhibiting interfering information, as seen with the young adults, whereas a negative interference value, shows worsen inhibition ability, as seen with the older adults (Scarpina & Tagini, 2017; Stroop, 1935). Accordingly, this difference was statistically significant, $t(49) = 4.84$, $p < 0.001$, $d = 1.38$, as seen in Figure 3.7. These findings indicated that while inhibition capacity was demonstrated by both groups, it had deteriorated with advance age.

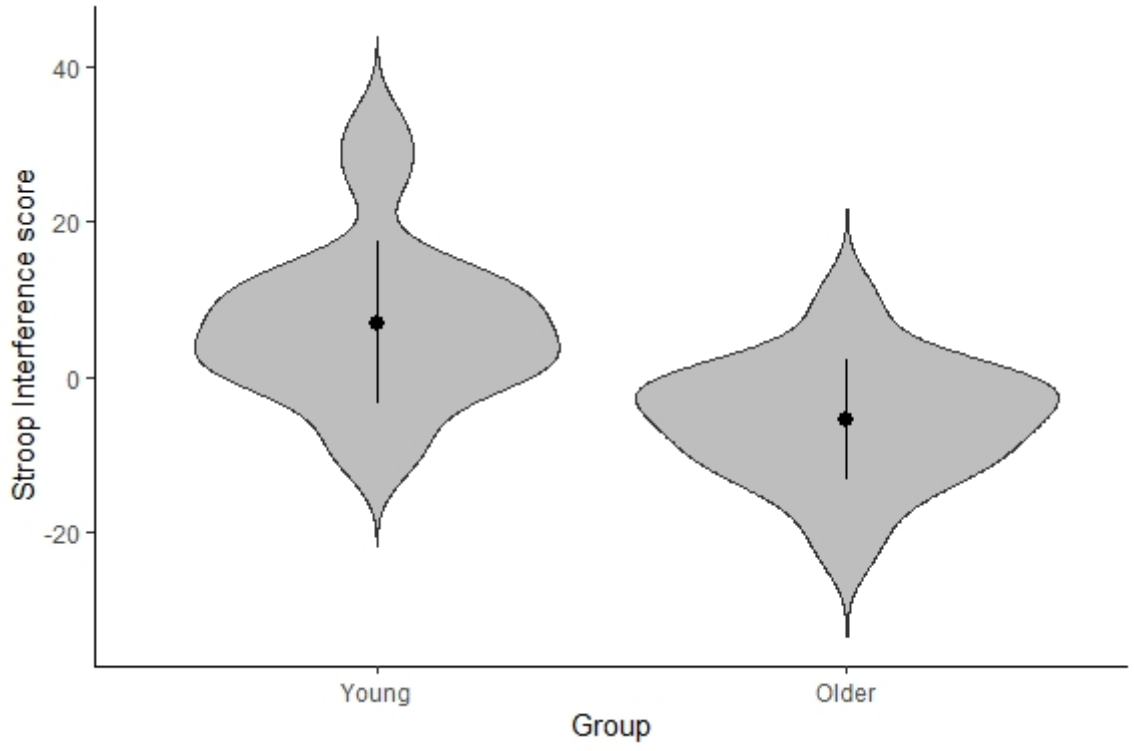


Figure 3.7. Stroop task Interference score group comparison. This figure presents the calculated inhibitory control for the Stroop task in the young adults (skewness 0.80, kurtosis 0.92), and older adult groups (skewness -0.18, kurtosis 0.34).

In sum, significant differences were observed in inhibitory abilities, i.e. the incongruent conditions of both the Stroop task and the HSCT. In the Stroop task, performance in the CW section and the derived Stroop interference score demonstrated age effects. The young adults possessed a more positive mean value, which equates to better performance. Similarly, decreased inhibition ability was observed in the older adults in the HSCT. An age effect was found in the RT cost. However, insignificant differences were shown in the errors produced in the inhibition section of task and in the overall HSCT score between the groups.

3.3.2.3 Shifting

The task switching test and TMT results can be viewed in Table 3.5 below.

Table 3.5. Shifting Results of the Young and Older Adult Participants

Task	**Young Adults**		**Older Adults**		**Young vs Old, *p*-value**
	n	Mean (SD)	n	Mean (SD)	
Task Switching, local shift - repetition RT (ms)	26	1253.00 (350.88)	23	1492.41 (370.63)	0.025
Task Switching, local shift - repetition error rate (%)	26	3.69 (4.22)	23	7.91 (10.80)	0.072
Task Switching, local shift - shifting RT (ms)	26	1328.95 (340.29)	23	1699.59 (524.40)	0.005
Task Switching, local shift - shifting error rate (%)	26	8.42 (7.72)	23	10.83 (11.59)	0.392
Task Switching, local shift - cost (RT)	26	75.96 (84.29)	23	207.18 (228.92)	0.009
Task Switching, local shift - error rate cost (%)	26	4.77 (5.92)	23	3.04 (4.44)	0.259
Task Switching, mixing task - repetition RT (ms)	26	966.32 (179.70)	21	1071.00 (133.12)	0.031
Task Switching, mixing task - repetition error rate (%)	26	2.85 (2.74)	21	1.43 (1.33)	0.035
Task Switching, mixing task - shifting RT (ms)	26	1253.00 (350.88)	21	1475.14 (336.95)	0.033

Task Switching, mixing task - shifting error rate (%)	26	3.69 (4.22)	21	6.14 (9.12)	0.229
Task Switching, mixing task - cost (RT)	26	286.67 (222.77)	21	404.14 (314.73)	0.142
Task Switching, mixing task - error rate cost (%)	26	0.88 (3.71)	21	4.81 (8.44)	0.038
Task Switching, global shift - repetition RT (ms)	27	963.08 (177.01)	21	1071.00 (133.12)	0.024
Task Switching, global shift - repetition error rate (%)	27	3.04 (2.86)	21	1.43 (1.33)	0.021
Task Switching, global shift - shifting RT (ms)	27	1312.44 (349.75)	21	1690.79 (496.87)	0.003
Task Switching, global shift - shifting error rate (%)	27	8.96 (7.94)	21	8.86 (9.97)	0.968
Task Switching, global shift - shifting cost (RT)	27	349.36 (219.29)	21	619.79 (457.52)	0.010
Task Switching, global shift - shifting error rate cost (%)	27	5.85 (5.72)	21	7.52 (9.14)	0.441
Task Switching, RT cost ANOVA	-	< 0.001	-	< 0.001	< 0.001
Task Switching, error rate ANOVA	-	< 0.001	-	< 0.001	0.001
Trail Making Test, Part A RT (s)	24	32.29 (10.80)	23	32.70 (10.34)	0.896
Trail Making Test, Part A error rate (%)	24	2.08 (10.21)	23	6.52 (17.22)	0.286
Trail Making Test, Part B RT (s)	19	64.11 (19.54)	19	57.53 (15.12)	0.253
Trail Making Test, Part B error rate (%)	19	15.79 (33.55)	19	26.32 (45.21)	0.421
Trail Making Test, RT Shifting cost (s)	19	31.00 (17.68)	19	25.89 (11.99).	0.305
Trail Making Test, global error rate shifting cost (%)	19	13.16 (36.67)	19	18.42 (47.76)	0.705

In the examination of shifting ability with the task switching task, three shifting types were assessed, local shift, mixing task, and global shift. Please note in addition to the outliers, two older adult participants were removed from analysis due to computer issues.

In comparing repetition and shifting performance amongst the shift types, paired-samples t-tests on the young adults revealed significance in all the RTs, local shift, $t(25) = -4.60$, $p < 0.001$, mixing task, $t(25) = -6.56$, $p < 0.001$, global shift, $t(26) = -8.28$, $p < 0.001$, and all but one of the error rates, the local shift, $t(25) = -4.08$, $p < 0.001$, mixing task, $t(25) = -1.19$, $p = 0.247$, and the global shift, $t(26) = -5.26$, $p < 0.001$. Whereas in the older adults, significance

was found in all the RTs, local shift, $t(22) = -4.34$, $p < 0.001$, mixing task, RT, $t(20) = -5.88$, $p < 0.001$, global shift, $t(20) = -6.21$, $p < 0.001$, and error rates, local shift, $t(22) = -3.18$, $p = 0.004$, mixing task, $t(20) = -2.56$, $p = 0.019$, global shift, $t(20) = -3.75$, $p = 0.001$.

Analysis of the local shift performance with a 2x2 ANOVA [group (young, older adults) x task switching part (repetition, shifting)] for the RTs, revealed a main group effect, $F(1, 47) = 7.42$, $p = 0.009$, $\eta_p^2 = 0.14$, a main effect for task condition, $F(1, 47) = 34.56$, $p < 0.001$, $\eta_p^2 = 0.42$, and for interaction $F(1, 47) = 7.42$, $p = 0.009$, $\eta_p^2 = 0.14$. The older adults spent longer performing the repetition and shifting conditions, and thus had higher shifting costs in comparison to the young adults. For error rate, there was no main group effect revealed, $F(1, 47) = 1.85$, $p = 0.180$, $\eta_p^2 = 0.04$ but a main effect for the task condition, $F(1, 47) = 25.80$, $p < 0.001$, $\eta_p^2 = 0.35$. No interaction, $F(1, 47) = 1.46$, $p = 0.233$, $\eta_p^2 = 0.03$ was shown, indicating both groups produced more errors by the same amount in the shifting condition.

A 2x2 ANOVA of the RT mixing task performance, showed a main group effect, $F(1, 45) = 5.70$, $p = 0.021$, $\eta_p^2 = 0.11$, and a main effect for the task condition, $F(1, 45) = 77.44$, $p < 0.001$, $\eta_p^2 = 0.63$. However, not for interaction $F(1, 45) = 2.24$, $p = 0.142$, $\eta_p^2 = 0.05$. Thus, performance between the groups was comparable. For error rate, there was no main group effect, $F(1, 45) = 0.19$, $p = 0.664$, $\eta_p^2 = 0.00$. A main effect for task condition, $F(1, 45) = 9.22$, $p = 0.004$, $\eta_p^2 = 0.17$, and for interaction $F(1, 45) = 4.46$, $p = 0.040$, $\eta_p^2 = 0.09$, were found, indicating there was a difference in the accuracy performance between the groups.

For global shift, RTs, a main group effect, $F(1, 46) = 9.78$, $p = 0.003$, $\eta_p^2 = 0.18$, a main effect for task condition, $F(1, 46) = 93.87$, $p < 0.001$, $\eta_p^2 = 0.67$, and for interaction $F(1, 46) = 7.31$, $p = 0.010$, $\eta_p^2 = 0.14$, were revealed. The older adults generated a much longer mean RT performing the shifting condition. For error rate, there was no main group effect found, $F(1, 46) = 0.31$, $p = 0.583$, $\eta_p^2 = 0.01$. However, there was a main effect for task condition, $F(1, 46) = 38.17$, $p < 0.001$, $\eta_p^2 = 0.45$ as the shifting condition was completed with less accuracy. Insignificance for interaction $F(1, 46) = 0.48$, $p = 0.490$, $\eta_p^2 = 0.01$ was seen, thus performance was comparable between the groups.

The significant interactions were further analysis with independent t-tests on the shifting costs, which confirmed substantial differences amongst the groups' performances in local shift RT cost, $t(47) = -2.73$, $p = 0.009$, $d = 0.80$, mixing task error rate cost, $t(45) = -2.13$, $p =$

0.038, *d* = 0.64, and the global shift RT cost, *t*(46) = -2.70, *p* = 0.010, *d* = 0.80. The older adults had much larger shifting costs in comparison to the young adults, see Figures 3.8, 3.9, and 3.10.

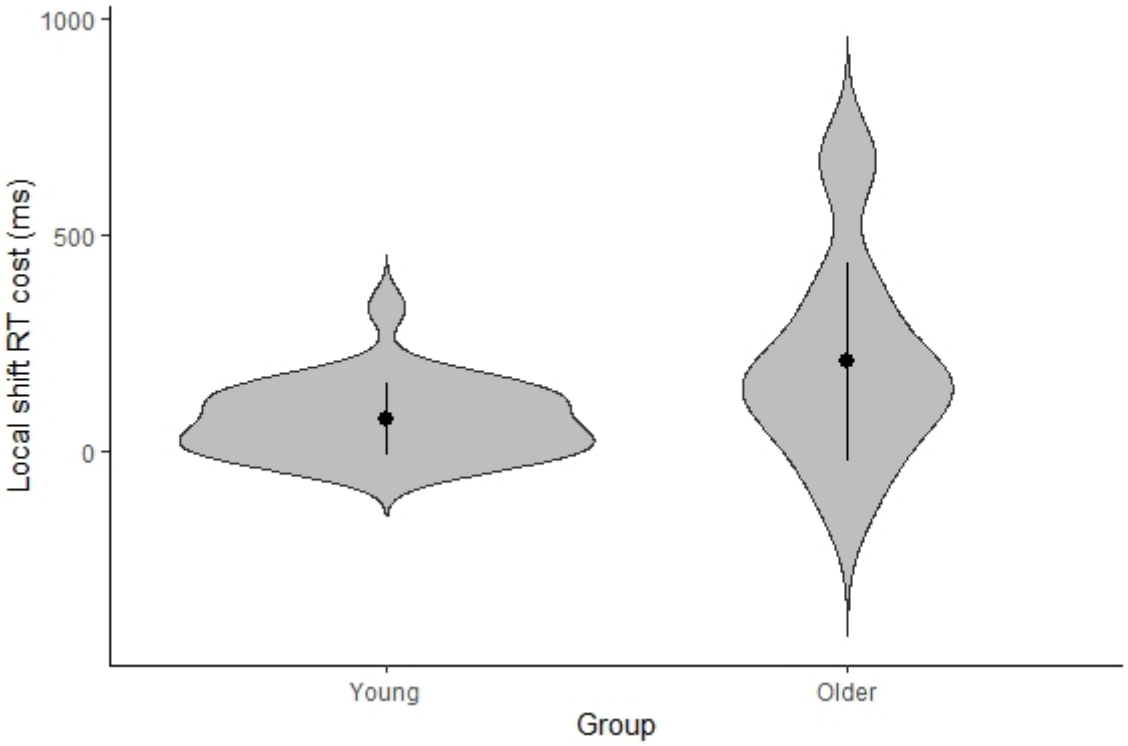


Figure 3.8. Task Switching test, local shift RT cost group comparison. This figure presents the local shift RT cost (ms) between the young adults (skewness 1.05, kurtosis 1.86), and older adult groups (skewness 0.86, kurtosis 0.39).

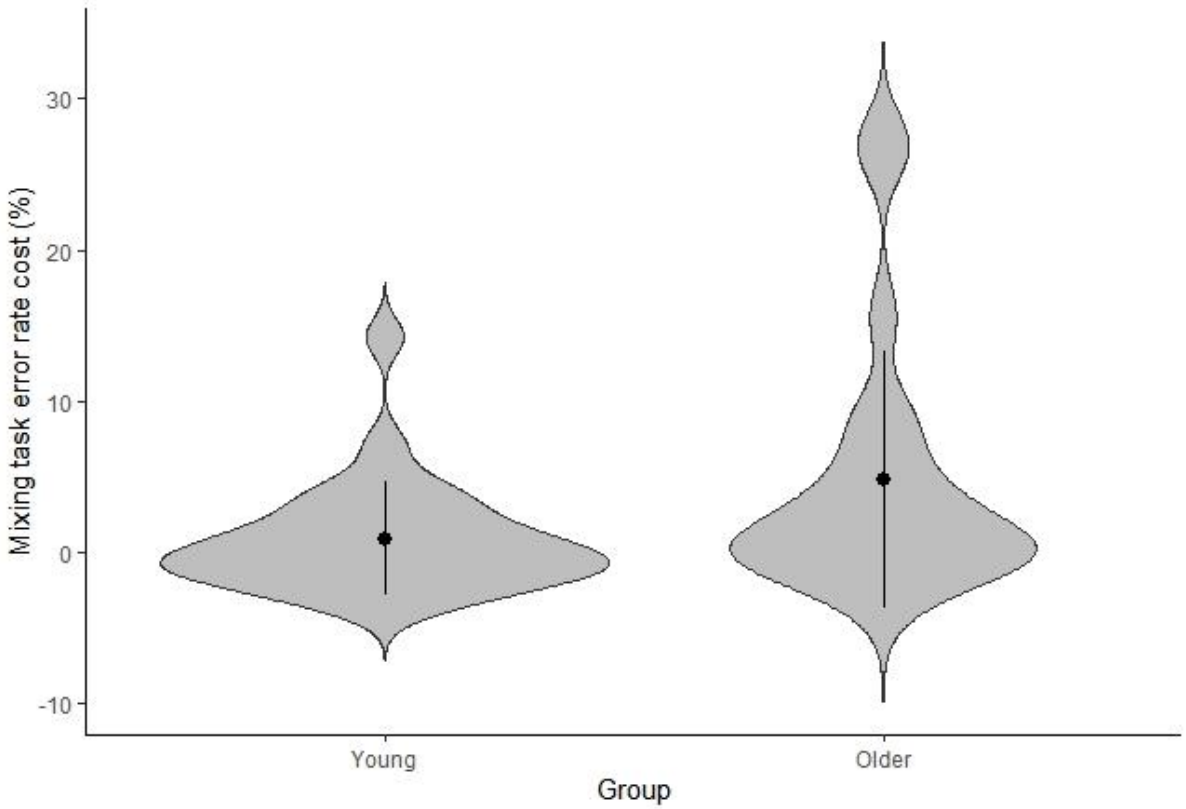


Figure 3.9. Task Switching test, mixing task error rate cost group comparison. This figure presents the mixing error rate cost (%) between the young adults (skewness 1.95, kurtosis 5.28), and older adult groups (skewness 1.87, kurtosis 2.77).

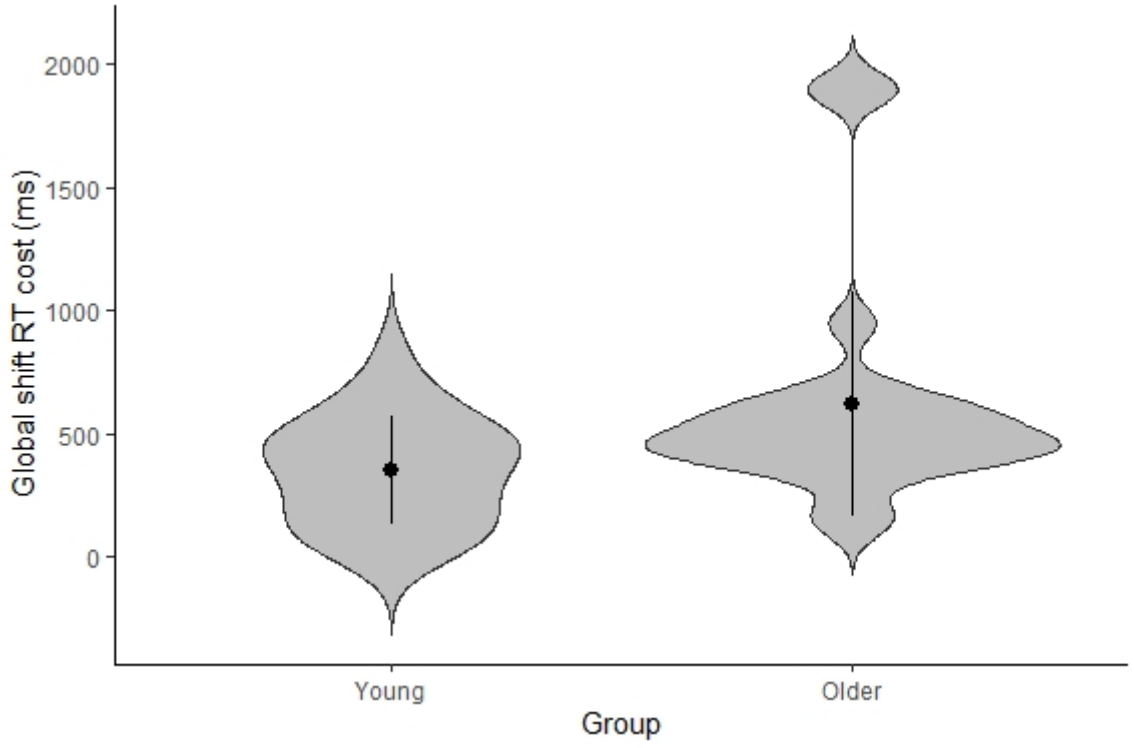


Figure 3.10. Task Switching test, global shift RT cost group comparison. This figure presents the global shift RT cost (ms) between the young adults (skewness 0.22, kurtosis -0.57), and older adult groups (skewness 2.28, kurtosis 4.94).

Both age groups' participants presented with the characteristic task-shifting costs associated with this task by producing longer RTs and more errors in the shifting task, indicating the demand on the shifting EF. The older adults were especially affected, producing higher RT costs during the local shift and global shift analyses, and a larger error rate cost during the mixing task analysis.

In the assessment of performance with the TMT, paired-samples t-tests confirmed a significant difference in the RTs between the two test parts in both age groups, $t(18) = -7.64$, $p < 0.001$ in the young adults, and $t(18) = -9.41$, $p < 0.001$ in the older adults, highlighting the demand on shifting ability generated by the task.

A 2x2 ANOVA [group (young, older adults) x TMT part (repetition, shifting)], completed on the TMT RTs found no main group effect, $F(1, 36) = 1.01$, $p = 0.321$, $\eta_p^2 = 0.01$. However, there was a main effect for the test part, $F(1, 36) = 134.75$, $p < 0.001$, $\eta_p^2 = 0.79$ due to the demand generated for shifting, but no effect for interaction $F(1, 36) = 1.09$, $p = 0.305$, $\eta_p^2 = 0.03$, was shown. Thus, there was no age effect in the overall RT test performance, which was confirmed with an independent t-test of the RT, $t(36) = 1.04$, $p = 0.305$, $d = 0.35$.

Paired-samples t-test reported insignificant differences in the analysis of the error rates produced in the two test parts in the young, $t(18) = -1.56$, $p = 0.135$ and in the older adults, $t(18) = -1.68$, $p = 0.110$.

As this test only considers the good performers of both tests, it is understandable that no differences were observed with the remaining participants, as they completed the entire test correctly.

A 2x2 ANOVA [group (young, older adults) x TMT part error rate (repetition, shifting)] showed no main group effect, $F(1, 36) = 1.29$, $p = 0.264$, $\eta_p^2 = 0.03$. A main effect for the TMT part was found, $F(1, 36) = 5.23$, $p = 0.028$, $\eta_p^2 = 0.13$ but no effect for interaction $F(1, 36) = 0.15$, $p = 0.705$, $\eta_p^2 = 0.00$. Thus, no difference in the groups' accuracy performance between the TMT parts was observed. An independent t-test of the error rate cost confirmed the groups error rates were comparable, $t(36) = -0.38$, $p = 0.705$, $d = 0.13$.

In conclusion, shifting ability was in principle maintained in both participant groups through its assessment with the task switching task and TMT. With the TMT, insignificant performance differences were observed as comparable RT and error rate shifting costs were observed. However, with the task switching paradigm, age effects in the local and global shift RT costs, and the mixing task error rate shifting cost were seen.

3.3.2.4 Updating

The BDS test and n-back task results can be viewed in Table 3.6 below.

Table 3.6. Updating Results of the Young and Older Adult Participants

Task	**Young Adults**		**Older Adults**		**Young vs Old, *p*-value**
	n	Mean (SD)	n	Mean (SD)	
Backward Digit Span Test (no. out of 14 spans)	28	7.86 (2.16)	25	7.68 (2.81)	0.797
N-back, RT ANOVA	-	0.392[a]	-	0.668[a]	< 0.001[b]
N-back, error rate ANOVA	-	< 0.001[a]	-	< 0.001[a]	< 0.001[b]
N-back, 0-, RT (ms)	26	536.86 (89.89)	24	785.18 (159.74)	< 0.001
N-back, 0-, error rate (%)	26	2.40 (2.32)	24	3.61 (3.72)	0.171
N-back, 1-, RT (ms)	26	525.91 (153.08)	24	764.81 (216.70)	< 0.001
N-back, 1-, error rate (%)	26	14.90 (8.13)	24	31.15 (22.38)	0.001
N-back, 2-, RT (ms)	26	573.06 (186.48)	24	825.30 (242.33)	< 0.001
N-back, 2-, error rate (%)	26	40.05 (18.65)	24	60.28 (20.96)	0.001
N-back, 3-, RT (ms)	26	562.74 (189.19)	24	798.87 (247.72)	< 0.001
N-back, 3-, error rate (%)	26	52.84 (14.81)	24	70.38 (14.47)	< 0.001
N-back, RT updating cost (ms)	26	25.88 (186.22)	24	6.34 (240.56)	0.751
N-back, error rate updating cost (%)	26	50.43 (14.34)	24	67.17 (14.52)	< 0.001

[a] - one-way repeated measures, [b] - two-way repeated measures.

Statistical analysis revealed no significant differences between the groups' mean BDS task performance, $t(51)= 0.26$, $p = 0.797$, $d = 0.07$. All the young and older participants were able to recall up to 4 digits backwards, see Table 3.7, which is similar to results reported by

Woods et al (2011), who observed a span of 4 to 6 in their study assessing young and middle-aged healthy adults. Only two young participants, 7%, were able to correctly recall the longest span of 8 digits, one doing so on both trials, but no member of this group scored the maximum test score of 14, i.e. correctly recall all the spans in reverse order. However, in the older group, 24%, were able to recall the maximum span of 8 digits backwards correctly. One individual was able to recall all the spans and obtained the maximum score of 14 for the test.

Table 3.7. Backward Digit Span Group Comparison Performance. The test involves the completion of seven spans (lengths 2 to 8), twice. The highest span length achieved by a participant is presented.

Span Length	**Young Adults, Highest Span Achieved** (n)	**Older Adults, Highest Span Achieved** (n)
2	0	0
3	0	0
4	6	7
5	5	8
6	12	3
7	3	1
8	2	6

In the n-back task, a one-way repeated measures ANOVA test [conditions (0-, 1-, 2-, and 3-back)] revealed an insignificant main effect between the RT n-back conditions, $F(3, 75) = 1.01$, $p = 0.392$, $\eta_p^2 = 0.04$, in the young adults, and in the older adults, $F(3, 66) = 0.52$, $p = 0.668$, $\eta_p^2 = 0.02$.

A two-way repeated measures ANOVA for the RTs [group (young, older adults) x conditions (0-, 1-, 2-, 3-back)] showed a main group effect, $F(1, 47) = 33.27$, $p < 0.001$, $\eta_p^2 = 0.41$, confirming the groups performed differently, with the older adults producing larger mean RTs. However, no main effect for n-back condition, $F(3, 141) = 1.34$, $p = 0.263$, $\eta_p^2 = 0.03$, or for interaction, $F(3, 141) = 0.07$, $p = 0.978$, $\eta_p^2 = 0.00$ was found.

For error rate, a one-way repeated measures ANOVA test [conditions (0-, 1-, 2-, and 3-back)] showed a significant main effect for both groups. In the young adults, $F(3, 75) = 140.01$, $p < 0.001$, $\eta_p^2 = 0.85$, and in the older adults, $F(3, 66) = 130.15$, $p < 0.001$, $\eta_p^2 = 0.86$. Thus, the classic effect of this task was observed, as there was an increase in errors produced with increased task difficulty.

A two-way repeated measures ANOVA [group (young, older adults) x conditions (0-, 1-, 2-, 3-back)] revealed a main group effect for error rates, $F(1, 47) = 17.33$, $p < 0.001$, $\eta_p^2 = 0.27$. As well as a main effect for n-back condition, $F(3, 141) = 268.68$, $p < 0.001$, $\eta_p^2 = 0.85$, and for the interaction, $F(3, 141) = 6.66$, $p < 0.001$, $\eta_p^2 = 0.12$. The groups performed the different n-back task conditions with different accuracy, with the older adults generating more errors throughout.

The combined performance of all the RTs, as well as the error rates for the young adults is seen in Figure 3.11, and for the older adults in Figure 3.12.

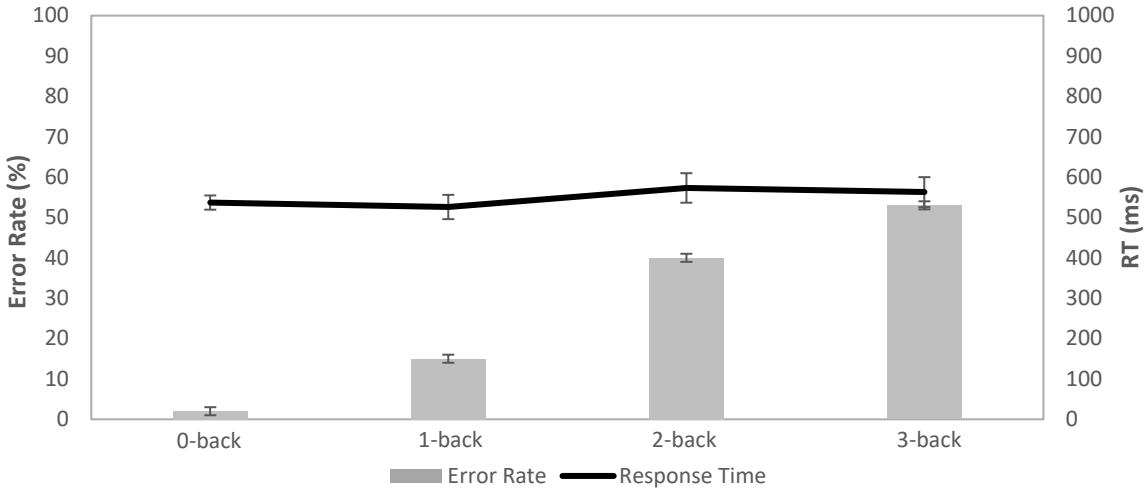


Figure 3.11. Young Adult Group N-Back task performance. This figure presents the relationship between the mean n-back RT in ms (line and right axis) and the error rates in % (bars and left axis) at 0-, 1-, 2-, and 3-back in the young adult group. Error bars denote SEM (standard error mean).

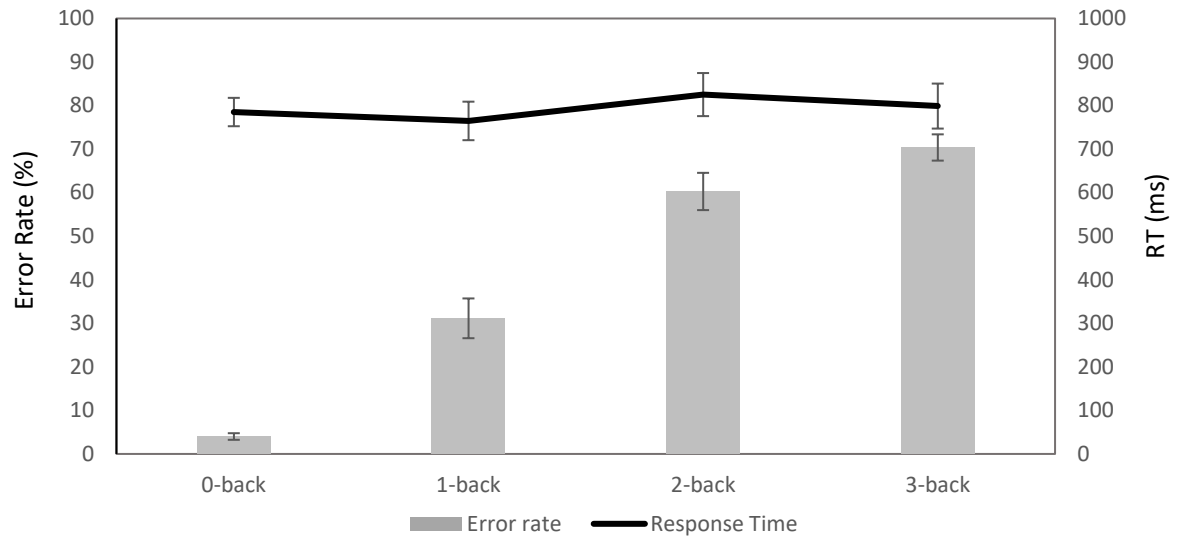


Figure 3.12. Older Adult Group N-Back performance. This figure presents the relationship between the mean n-back RT in ms (line and right axis) and the error rates in % (bars and left axis) at 0-, 1-, 2-, and 3-back in the older adult group. Error bars denote SEM.

Each n-back condition was then compared between the groups. At 0-back, significance was only found in the RTs, $t(48) = -6.84$, $p < 0.001$, but not in the error rates, $t(48) = -1.39$, $p = 0.171$, signifying that the older adults spent longer in completing the tasks but produced comparable errors with the younger adults, in the least demanding condition of the task.

Significant differences were found between the groups in the RTs and error rates during the remaining conditions, in the 1-back [RT, $t(48) = -4.53$, $p < 0.001$, error rates, $t(48) = -3.46$, $p = 0.001$], 2-back [RT $t(48) = -4.14$, $p < 0.001$, t(48) = -3.61, $p = 0.001$], and 3-back [RT $t(47) = -3.77$, $p < 0.001$, error rate $t(47) = -4.18$, $p < 0.001$] conditions. Therefore, signifying that the older adults possessed higher RTs and generated more errors during these conditions.

To further examine the groups' performances, a series of pairwise comparisons for the different conditions, i.e. 0 vs 1, 0 vs 2, 1 vs 3 etc, between the groups' RTs and error rates, was conducted. Following Bonferroni correction, all the RT comparisons were observed as being statistically insignificant, $p > 0.00851$, implying the groups had approximately the same mean RTs between all the pairwise comparisons.

However, significant differences in the error rates between all the n-back conditions in each group and between the groups demonstrated significant differences in the errors produced.

Finally, no significance in the RT updating (3-back RT minus 0-back RT) cost between the groups was found, $t(47) = 0.32$, $p = 0.751$, $d = 0.09$. Significance was observed for the mean error rate cost, $t(47) = -4.06$, $p < 0.001$, $d = 1.18$ (Figure 3.13), confirming the more errors produced by the older adults while produced spending approximately the same time completing each task condition, in comparison to the young adults.

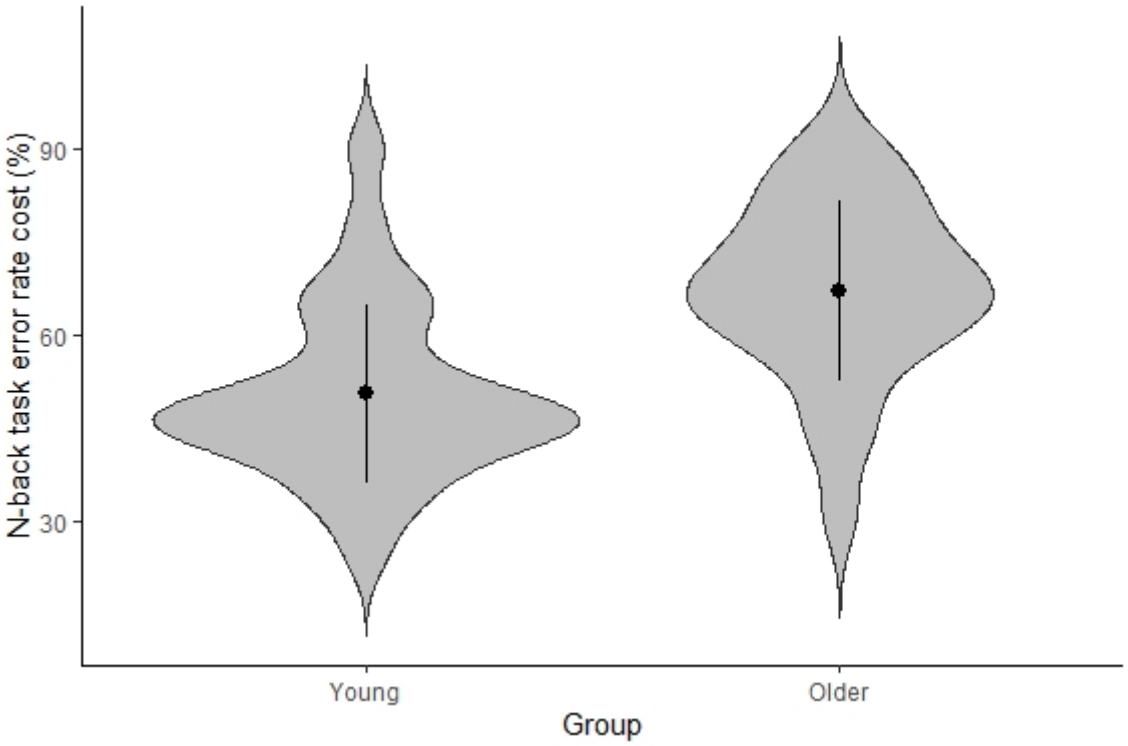


Figure 3.13. N-Back error rate costs group comparison. This figure presents the error rates (%) difference at 0-back and 3-back for the young adults (skewness 0.95, kurtosis 1.29), and older adult groups (skewness -0.57, kurtosis 0.48).

Thus, the typical effect of this task on accuracy and not RT, as shown by the individual groups' performance, as a result of the strictly timed trial procedure, was observed. Therefore, age-related performance decline was apparent in the updating error rate cost between the groups.

To summarise, updating ability was comparable in performance between the two age groups with the BDS task, where both groups obtained a mean score of 7, which equates to a span length of 5. With the n-back task however, a statistically significant difference was observed in the updating error rate costs and absolute error rates between the groups, a typical finding with this task. Age effects were also observed for all the error rate n-back pairwise comparisons, following Bonferroni correction.

3.3.3 Statistical Power of Study

The majority of the statistical powers, i.e. Cohen's *d* and the partial eta squared, η_p^2, of the many EF analyses performed were small to medium. Thus, the modest sample size in the study may have had a role in limiting the significance of some of the statistical comparisons conducted.

A power analysis using the G*power computer program (Erdfelder et al., 2009; Faul et al., 2007) was performed. It indicated that a total sample of 101 participants, 51 in each of the groups, would be required to detect medium effects (*d* = 0.50) with 80% power using the independent t-test between means with alpha at 0.05, in a one-tailed hypothesis. (A total of 128 participants, 64 per group is required in a two-tailed hypothesis.) This would apply to all the EF tasks except the Stroop and n-back tasks.

For MANOVA analysis with the Stroop and n-back tasks, power analysis indicated a total sample size of 18 participants, 9 each, for three repeated measurements, i.e. the Stroop task, and 16 participants, 8 each, for four repeated measurements, i.e. the n-back task, in a one-tailed hypothesis.

Following review of previous cognitive ageing studies that employed these tasks, the lack of statistical power observed in this study may be adequate as the employment of smaller participants than these calculated number was observed. These included the PRP task (Maquestiaux et al., 2010; Strobach et al., 2012a, 2012b), Stroop task (Albinet et al., 2012; Andrés et al., 2008; Bherer et al., 2006; Boucard et al., 2012; Damoiseaux et al., 2008; Keightley et al., 2006; Laguë-Beauvais et al., 2015; Langenecker et al., 2004; Mayas et al., 2012; Morrone et al., 2010; P. Wang et al., 2013), TMT (Damoiseaux et al., 2008; Laguë-Beauvais et al., 2015; Laguë-Beauvais, Brunet, et al., 2013; L. D. Müller et al., 2014), task switching task (Hillman et al., 2006), BDS task (Bherer et al., 2006; Chee et al., 2006; Damoiseaux et al., 2008), and the n-back tasks (Berger et al., 2017; Boucard et al., 2012; Daffner et al., 2011).

No study was found to have utilised the TEA telephone code search DT in this type of participant groups. Whereas all the studies that used the HSCT had the appropriate participant numbers (Morrone et al., 2010; Tournier et al., 2014; Z. Wang & Su, 2013).

Nevertheless, assessing more participants was not possible due to the restrictions imposed by the COVID-19 pandemic.

3.3.4 Trajectory of Decline in Executive Function Abilities

3.3.4.1 Decline in comparison to the Young Adults

In order to determine the rate of decline of EF abilities in the older adults, some measures from the tasks employed were further analysed following their normalisation, by transforming raw score values to a normalised form. This was to alleviate analytical variations of task measures as it can be challenging to compare results assessing the same construct of EF performance with different outcome metrics, e.g. RTs, error rates, completion times, and/or derived test scores (Lezak et al., 2012) to determine the amount of impairment shown for these tasks. Accordingly, the measures were transformed to comparable units and z-score transformation was the most appropriate.

This was accomplished by first normalising the young adult data by calculating the group mean and SD, then this mean was taken away from each older participant's task score and divided by the SD, i.e. [(older participant score – young adult mean)/young adult standard deviation]. Consequently, the z-scores of the older adults reflected the amount of cognitive decline (or improvement) in terms of the young groups' performance. As a consequence, the mean z-scores of the older participants will not be zero, as would be observed with the young group. The resulting older adult mean z-scores of the four pairs of EFs tasks were compared with the young adults via independent samples t-tests. (Please note the Stroop and HSCT z-scores were inverted as better performance was indicated with a higher score, whereas in the remaining assessments used, better performance was reflected by a lower score.)

In addition, the effect sizes (*e*) of the values, as proposed by Cohen (1988), were calculated (The Cohen's value, *d*, was not calculated.) The results are listed in Table 3.8.

Table 3.8. Decline in Executive Function Abilities in Older Adults in comparison to Young Adults

Task	**n**	**Older Adults z-scores**	**independent t-test *p*-value**	**Effect size, *e***
Dual-tasking				

Test for Everyday Attention, auditory dual-task, count correct - *accuracy measure*	20	-0.64	0.020	0.35
Test for Everyday Attention, telephone code dual-task, count correct - *accuracy measure*	20	-0.34	0.229	0.19
PRP, SOA 0ms auditory dual-task cost, RT1 - *time cost*	24	-0.11	0.639	0.07
PRP, SOA 0ms dual-task cost, RT1 error rate - *accuracy cost*	24	-0.36	0.067	0.27
PRP, SOA 0ms visual dual-task cost, RT2 - *time cost*	24	0.25	0.135	0.22
PRP, SOA 0ms dual-task cost, RT2 error rate - *accuracy cost*	24	-0.46	0.093	0.25
PRP Effect, SOA 0 – 1000ms, visual task**,** RT2 - *time measure*	24	0.64	0.013	0.36
PRP Effect, error rate - *accuracy measure*	24	0.25	0.370	0.14
Inhibition				
Stroop Colour-Word - *inhibition measure*	25	1.35	< 0.001	0.58
Stroop Interference - *test score*	25	1.19	< 0.001	0.57
Hayling sentence completion test, RT inhibition cost - *time cost*	23	1.21	< 0.001	0.49
Hayling sentence completion test, overall score - *test score*	23	-0.28	0.337	0.01
Shifting				
Task Switching Test, local shift RT shifting cost - *time cost*	23	1.56	0.009	0.37
Task Switching Test, local shift error rate shifting cost - *accuracy cost*	23	-0.29	0.254	0.17
Task Switching Test, mixing RT shifting cost - *time cost*	21	0.53	0.142	0.22
Task Switching Test, mixing error rate shifting cost - *accuracy cost*	21	1.04	0.042	0.30
Task Switching Test, global shift RT shifting cost - *time cost*	21	1.23	0.010	0.37
Task Switching Test, global shift error rate shifting cost - *accuracy cost*	21	0.30	0.426	0.12
Trail Making Test, RT shifting cost - *time cost*	19	-0.34	0.253	0.19
Trail Making Test, error rate shifting cost - *accuracy cost*	19	-0.29	0.305	0.17
Updating				

Backward Digit Span Test - *updating measure*	25	-0.08	0.797	0.04
N-Back, RT cost - *time cost*	23	-0.11	0.751	0.05
N-Back, error rate cost - *accuracy cost*	23	1.17	< 0.001	0.51

TEA - Test for Everyday Attention, PRP - Psychological Refractory Period paradigm.

The significant findings observed with this analysis, confirms the statistical analysis performed in section 3.3.2.

Independent t-test found a significant difference in the TEA auditory DT accuracy measures, z-score = -0.64, $p = 0.020$, $e = 0.35$, where the negative z-score reflected better performance in the older adults, i.e. higher scores in comparison to the young adults. Additionally, with the other PRP DT condition, the PRP effect, the older adults had greater decline in the time measure (PRP effect RT2), z-score = 0.64, $p = 0.013$, $e = 0.36$.

Worsened inhibition ability was apparent in the older adults, with the evaluation of the incongruent CW condition of the Stroop task, z-score = 1.35, $p < 0.001$, $e = 0.58$, and the derived Stroop interference score, z-score = 1.19, $p < 0.001$, $e = 0.57$, both with a large effect size. Also, the HSCT time cost was statistically significant, z-score = 1.21, $p < 0.001$, $e = 0.49$.

Significant decline in shifting ability with the task switching task was observed in the local shift RT shifting cost - time cost, z-score = 1.56, $p = 0.009$, $e = 0.37$, mixing error rate shifting cost - accuracy cost, z-score = 1.04, $p = 0.042$, $e = 0.30$, and global shift RT shifting cost - time cost, z-score = 1.23, $p = 0.010$, $e = 0.37$.

Lastly, significant decline in updating ability was observed with the n-back accuracy cost, z-score = 1.17, $p < 0.001$, $e = 0.51$, which presented with a moderately large effect size.

In sum, it seems the greatest decline of EF ability among the four EFs ability due to healthy ageing was in shifting ability assessed with the task switching local shift RT shifting cost, z-score = 1.56. Followed by inhibition ability measures from the two tasks, the Stroop task interference, z-score = 1.19, and the CW condition, z-score = 1.35, as well as the HSCT time cost score, z-score = 1.21. Then updating ability with the accuracy cost, z-score = 1.17 of the n-back task and last DT ability with in the RT2, PRP effect measure, z-score = 0.64.

3.3.4.2 Pairwise comparison of Decline amongst the Older Adults

In order to determine the extent of decline in EF ability in the older adults across the four EFs examined, the differences between the tasks that presented with the most deterioration in the older adults were examined in a repeated-measure design. The reason for this is that this study is interested in the individual trajectory rate of decline amongst the EFs due to cognitive ageing. Thus, the tasks that appeared to be the most sensitive to age effects were used for this analysis. Therefore, one score from each of the four EF tasks was selected based on the z-score value from the data presented in Table 3.8 for this purpose. These were for DT, the PRP effect RT2 measurement (z-score = 0.64), for inhibition, the Stroop task CW (z-score of 1.35), for shifting, the local shift RT shifting cost (z-score = 1.56), and for updating, the error rate cost of the n-back task (z-score of 1.17).

Paired-samples t-tests were employed to test pairwise comparisons between all the four EF tests, i.e. DT compared with inhibition, DT with shifting, DT with updating, and so on, with the use of these scores. The effect sizes were also calculated. The results are shown in Table 3.9 and Figure 3.14.

Table 3.9. Decline in Executive Function Abilities amongst the Older Adults

Pairwise comparison	***df***	**Paired-samples t-test p-value**	**Effect size, *e***
Dual-tasking (PRP Effect RT) vs Inhibition (Stroop CW)	21	< 0.001	0.84
Dual-tasking (PRP Effect RT) vs Shifting (Task Switching Test, local shift RT shifting cost)	19	0.231	0.27
Dual-tasking (PRP Effect RT) vs Updating (N-Back, error rate cost)	19	0.123	0.35
Inhibition (Stroop CW) vs Shifting (Task Switching Test, local shift RT shifting cost)	22	< 0.001	0.73
Inhibition (Stroop CW) vs Updating (N-Back, error rate cost)	22	< 0.001	0.13
Shifting (Task Switching Test, local shift RT shifting cost) vs Updating (N-Back, error rate cost)	22	0.532	0.86

Substantial differences were only observed between DT (PRP effect) and inhibition (Stroop CW), *p*-value of < 0.001 with a fairly large effect size of 0.84, between inhibition and shifting

(local shift RT shifting cost), *p*-value of < 0.001, large effect size of 0.73, and between inhibition and updating ability (n-back, error rate cost), *p*-value of < 0.001, small effect size of 0.13, as seen in Table 3.9 and presented in Figure 3.13. Thus, inhibition differed from the other three EFs.

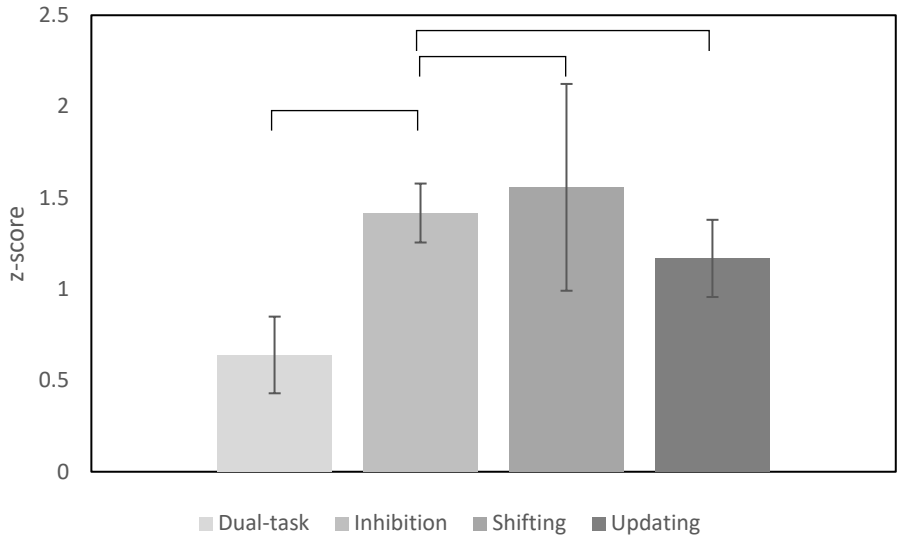


Figure 3.14. Significant differences in decline in Executive Function Abilities amongst the Older Adults. The bars represent the z-score data from the four EF tasks presented in Table 3.9. The three statistically significant paired-samples t-test analyses, p < 0.05, are shown by the black line above each EF pair. Error bars represent SEM.

Whereas the remaining analysis found no difference between the abilities, i.e. between DT and shifting, *p* = 0.231 and moderate *e* = 0.27, DT and updating *p* = 0.123 and moderate *e* = 0.35, DT and shifting ability, *p* = 0.113 with moderate *e* = 0.36, and between shifting and updating ability, *p* = 0.532, with a very large *e* of 0.86.

Of note is while the analysis between DT and inhibition, and between inhibition and shifting was significant, between DT and shifting was not. This may be due to the larger variances of DT and shifting z-scores, whereas inhibition presented with a smaller variance.

Based on these findings and Figure 3.14, shifting ability appears to have the numerically greatest decline. Although inhibition displayed significantly less decline than shifting and updating showed significantly less decline than inhibition. While DT ability demonstrated a significantly smaller decline rate from all three.

In conclusion, the results of these EF comparisons demonstrated that shifting seemed to be the most affected EF ability due to ageing, displaying the highest numerically z-score. A significant finding of the analysis conducted.

However, it is important to note that the findings observed here are based solely on the tasks and task measures used. The trajectory of decline of the four EF may differ if a different set of tasks is used.

3.4 Discussion

This cross-sectional study assessed age decline on a range of tasks assessing the EFs dual-tasking, inhibition, shifting and updating between young and older adults. The results indicated the older adults performed poorer in comparison to the young adults. In general, age-associated decline was observed, where tasks were completed slower and with less accuracy. However, this was also dependent on the task utilised and the condition of the task being examined.

A further aim of this study was to compare the trajectory of decline of these abilities in the older adult population between the four EFs. Shifting was observed to have the highest decline rate, followed by inhibition, and then updating, although collectively they all appeared to decline at a similarly high rate. Whilst DT had the smallest rate of decline, based on the calculated z-scores of the one of the tasks employed.

3.4.1 Dual-Tasking

An age effect in DT performance was observed in the RT of the PRP effect, with the PRP paradigm (Pashler, 1984; Welford, 1952). The older group produced a higher mean RT difference between performance in the SOA 0ms and 1000ms, which has similarly been reported by a number of researchers in cross-sectional studies (Allen et al., 1998; Glass et al., 2000; Hartley, 2001; Hartley et al., 1999; Hein & Schubert, 2004; Verhaeghen et al., 2003). The theory is young adults are better at bypassing the central bottleneck for the simultaneous processing of the stages required for the completion of the two tasks (Pashler, 1984, 1992, 1993, 1994; Schubert, 2008; Schubert et al., 2008). No difference was observed with the mean error rate.

Although the groups had similarly RT cost measures when comparing ST and DT (SOA 0ms) performance for the auditory and visual tasks, significance was observed when the two DT task performances were compared. This showed that the tasks were completed differently by the age groups, with the older adults generating a higher cost.

There were insignificant performance differences observed in the accuracy performance of the TEA DT task (Robertson et al., 1994), and in the RT and error rate of the DT cost of the PRP task. Researchers have reported increased variations in female performance when completing DT due to menstruation as a result of varying hormonal levels (Kaur et al., 2014; Mäntylä, 2013; Poromaa & Gingnell, 2014; Wong-Goodrich et al., 2020; Wozniak et al., 2014). Thus, as the young adult group consisted of a high proportion of female participants of menstrual age, this may account for the overall poorer performance of this group.

In conclusion, an age effect was observed with the RT of the PRP effect and during comparison of the two PRP DT costs. The older adult group performed with the same level of accuracy as the young adults in the TEA, and the DT cost measures of the PRP task (auditory and visual) were comparable, demonstrating maintained DT ability in the older adults.

3.4.2 Inhibition

Age-related decline in inhibitory control was observed in the performance of the incongruent section and interference score of the Stroop task (Golden, 1978), and in the inhibition RT cost (RT difference between incongruent and congruent section) of the HSCT (Burgess & Shallice, 1997). This is well supported by previous research (Albinet et al., 2012; Amer & Hasher, 2014; Borella et al., 2009; Boucard et al., 2012; Bruyer et al., 1995; Bugg et al., 2007; Clarys et al., 2009; Graf et al., 1995; Houx et al., 1993; Laguë-Beauvais et al., 2015; Maquestiaux et al., 2010; Mayas et al., 2012; D. P. McCabe et al., 2005; Morrone et al., 2010; Pettigrew & Martin, 2014; Uttl & Graf, 1997), and correlates with the inhibition deficit hypothesis in that older adults are less capable of suppressing or ignoring irrelevant thoughts and actions when compared to young adults (Rey-Mermet & Gade, 2018).

The age-related decline in inhibitory control found in the RT inhibition cost is in line with what has been reported with this test (Bielak et al., 2006; Borella et al., 2011; Cervera-Crespo & González-Alvarez, 2017; Tournier et al., 2014; Zimmermann et al., 2017),

particularly in the inhibitory section. Although, typically older participants are known to also produce more errors, which was not observed here, as part A errors were not collected or scored, like part B.

However, although both these tasks assess inhibitory abilities, they measure different aspects. Interference is thought to refer to the disruptiveness of the stimulus, but not the susceptibility to disruptiveness which may not require the active suppression of thought (Borella et al., 2009). This is assessed in the Stroop task. While inhibition requires the active suppression of processes to withhold irrelevant information from entering WM (Borella et al., 2009). Which is measured in the HSCT. This may be the reason why the HSCT is thought of as a more difficult task, as individuals have to consciously suppress words to sentences they are accustomed to. Nonetheless, both tasks showed age-associated decline.

Therefore, it can be concluded that inhibition is greatly affected by increasing age, as both tests observed decline.

3.4.3 Shifting

With the task switching test (Rogers & Monsell, 1995), age-related decline in shifting ability was evident with the local and global shift RT shifting costs, and the mixing task shifting error rate. This is consistent with the findings of many studies with this test (Brandt & Benedict, 2001; Hirsch et al., 2016; A. F. Kramer et al., 1999; Kray et al., 2002; Kray & Lindenberger, 2000; Moretti et al., 2018; Reimers & Maylor, 2005; Wasylyshyn et al., 2011).

The three shift types differ in cognitive processes as they represent the performance differences between three different non-shifting and shifting conditions. Resulting in different task demands, whilst maintaining and selecting between the two possible response sets (Reimers & Maylor, 2005). Thus, the RT global shift cost reflects the maintenance of multiple task configurations in WM, particularly during the pseudo-random presentation of the shifting task with two response sets in one trial block in comparison to one in each repetition trial block (Huff et al., 2015; Wasylyshyn et al., 2011). Similarly, local shift cost assesses this ability within shifting blocks, where the ability to suppress the response requirement of the prior trial to complete the current trial is in focus (Monsell, 2003). Hence, a time deficit is observed for this cognitive process or processes (including inhibition), i.e. transient cost (Monsell, 2003), leading to significant age effects. Whereas the

error rate costs, but not RT costs, found with the assessment of mixing shifting costs may reflect reduction in executive control to completing multiple task conditions (Braver et al., 2003; W. P. Chang et al., 2020).

Decline in older adults' performance is thought to be a result of general slowing attributed to decreased cognitive functioning, as higher level cognitive performance has been associated with better performance (Salthouse et al., 1998). Accordingly, the reorganisation of WM processes due to age-associated deterioration of the PFC has been indicated to be the cause of this shifting deficit. Older adults are thought to be able to recruit the cognitive processes required to complete shifting tasks, however are unable to efficiently maintain and coordinate two tasks in WM (Bopp & Verhaeghen, 2009; Gajewski, Ferdinand, et al., 2018; Kray et al., 2002; Kray & Lindenberger, 2000; Wasylyshyn et al., 2011).

Furthermore, it has been proposed that significant differences in costs are contingent on WM demands, which are reduced in the presence of task cues (Gajewski, Ferdinand, et al., 2018), as were utilised here. In line with this, it has been suggested that age-associated decline in shifting ability increases with task uncertainty, as with the removal of environmental prompts to guide behaviour in daily life (Kray et al., 2002; Moretti et al., 2018). Nonetheless, no age effects with the use of task switching paradigms have also been reported (Grange & Becker, 2019).

The absence of age effects with the utilisation of the TMT has also been reported by researchers including Ebert & Anderson (2009), Maquestiaux et al (2010) and Wecker et al (2000). Though numerous others have described age-related decline (Hamdan & Hamdan, 2009; Tom N. Tombaugh, 2004; Wecker et al., 2005; Woods et al., 2015; Zimmermann et al., 2017).

3.4.4 Updating

Lastly, an age effect in WM updating capacity was seen with the employment of the spatial n-back paradigm task (Kirchner, 1958), where a larger error rate cost was found in comparison to the younger group. Similar to shifting ability, this task is largely dependent on WM, although it is attributed to WM demand in the same task, where greater task difficulty is linked with the occurrence of an updating deficit.

Ageing is proposed to affect the recalling of immediate and delayed memory processes more than item recognition (Dennis & McCormick-Huhn, 2018). Thus, the increased demands of the task conditions with an increasing n resulted in the older adults generating more errors. Importantly, increase in n-back position over 1-back has been reported to result in increase in the demand for the storage and processing of WM (Bopp & Verhaeghen, 2018). This leads to larger performance costs in accuracy, which increases with age (Bopp & Verhaeghen, 2018; Qin & Basak, 2020; Verhaeghen & Basak, 2005), identical with the findings observed here. Moreover, it has been suggested that older adults are incapable of organising and managing new incoming information, and processing of outgoing information as fast as young individuals (Kirchner, 1958). Also, decline in attention has also been proposed to contribute to increased error rates, especially in the 2-back condition and longer spans (Kane et al., 2007; Verhaeghen & Cerella, 2002).

In sum, decline in updating ability is observed more at greater WM demands in older individuals, leading to an increased level of inaccuracies as shown with the large error cost produced with the n-back task in the older population.

3.4.5 Trajectory of EF decline

In comparing the decline of the older adults with the young adults and the trajectory of the four EFs in the older adults, shifting was showed to be the most affected by cognitive ageing. This was followed by inhibition, updating, and the most preserved ability, DT.

However, the findings suggest a comparable higher of rate of decline amongst shifting, inhibition, and updating, which is in accordance with the findings of Miyake, Friedman, et al (2000), who suggested these three EFs correlated with each other and possess a common 'unity' factor. Therefore, the decline rates may indicate decline in a common underlying factor. DT was deemed to be separate and unrelated from these three EFs, loading on its own factor, and as observed in the trajectory analysis, it showed the lowest decline rate. Thus, the analysis seems to agree with the theory of the unity and the diversity of EFs.

A criticism of the findings of Miyake, Friedman, et al (2000) was the utilisation of a specific set of DT paradigms and that their findings were task specific. It was suggested that unity of DT with the other three may have been observed with the use of other DT paradigms. However, as observed with the findings here with the use of the PRP DT paradigm, a similar

unity finding of the other three EFs was found. Thus, it seems that the findings may truly reflect the unity and diversity of these four EFs, and not be an artifact of their chosen paradigms.

To conclude, although shifting ability presented with the greatest decline rate, two different rates of age-associated cognitive decline was observed in the four EFs, one for inhibition, shifting, and updating, and another for DT. These findings may be used to monitor how these EFs decline in various clinical population, including AD and other dementias, by observing for variation from the results observed here. However, these rates of decline should be cautioned, as they might be task dependent.

3.5 Conclusion

To conclude, these findings provide evidence for age-related decline in all four of the EFs investigated, dual-tasking, inhibition, shifting, and updating, however this was largely dependent on the task used. Nevertheless, discrepancies were seen in the outcome of the pair of tasks employed. Overall, these findings indicate that older adults possess the abilities required to complete these EFs tasks, and in some instances at a level comparable with their younger counterparts.

Due to inconsistency with some of the task results for the same EF assessment, the following chapter investigates to what extent each pair of tasks correlated in their outcome, and the factor loadings of the EF between the age groups.

Lastly, the rate of decline of these EFs was also investigated. It was found based on analysis of selected measures of all the tasks used, that shifting had the greatest decline rate followed by inhibition, then updating and the least DT. Although shifting, inhibition, and updating seemed to all decline at a relatively higher rate in comparison to DT.

Chapter 4, Analysis of Executive Function Task Measures – A Correlation and Confirmatory Factor Analysis Study

4.1 Introduction

Assessing executive functions (EFs) can be problematic as there is no universal guideline nor a clear consensus amongst researchers on what tasks to utilise for a specific domain or for a certain study population. Accordingly, a variety of tasks have been employed in clinical and research settings for their assessment (Chan et al., 2008; Miyake, Emerson, et al., 2000). However, their ability to accurately predict EF deficits is not well researched. Furthermore, it is unclear whether tasks designed to assess the same EF are actually measuring the same underlying process (Salthouse, 2005), as there are no specific criteria on how such tasks are created. In addition, it is also unclear whether one EF (e.g. inhibition) is a unitary construct, or whether different types of inhibition may differ (e.g. perceptual vs motor inhibition). Therefore, since the exact nature of a task's EF processes is underspecified, i.e. the construct validities of tasks are not usually well formed, there is the issue of lack of correlation in the outcome measures or scores amongst tasks (Burgess et al., 1998, 2006; Canali et al., 2011; D. Howieson, 2019; Jansari et al., 2014; Lezak, 1982; Miyake, Emerson, et al., 2000). Furthermore, a task may not be sensitive enough in detecting executive dysfunction in a specific clinical group (Hanes et al., 1996). Thus, the validity of individual EF tasks and how well the outcome measures correlate is of interest.

4.1.1 EFs and Ageing

Of particular importance to this chapter is the process of ageing on EFs and the outcome measures of tasks used in their assessment. In children EFs are understood to be less distinct, however, in adults they are more separable but still interrelated, although the degree of separability decreases with advanced age, due to biological and pathological changes (Diamond, 2013, 2016; J. E. Fisk & Sharp, 2004; MacPherson et al., 2019; Miyake, Friedman, et al., 2000; Miyake & Friedman, 2012). One cause for this may be cognitive dedifferentiation and/or neural reorganisation (Cabeza et al., 2018; Oschwald et al., 2019), which refers to the alteration of cognitive structures due to deteriorations of neural integrity in older adults resulting in less distinction of cognitive processes (Koen & Rugg,

2019). Therefore, this would mean EFs in older populations are more similar to each other, i.e. more correlated, than in the younger generation (Glisky et al., 2020; Johnson et al., 2010; Koen & Rugg, 2019; La Fleur et al., 2018; Zanto & Gazzaley, 2019). Likewise, it would suggest that the correlations of EF abilities as assessed by EF specific tasks would differ between young and older adults.

4.1.2 Factor-analytic studies

Factor-analytic studies have further been completed to hypothesise the organisation of EFs in young and older adult populations through individual differences and comparison studies, where the resulting latent variable is used as a measure of the specific EF (Bettcher et al., 2016; Bock et al., 2019; Friedman & Miyake, 2004; Glisky et al., 2020; Hedden & Yoon, 2006; Hull et al., 2008; Miyake, Friedman, et al., 2000; Vaughan & Giovanello, 2010). In the examination of young adults only, Miyake, Friedman, et al (2000) employed confirmatory factor analysis (CFA) on task measures for dual-task (DT), inhibition, shifting, and updating. Three tasks each for inhibition (antisaccade, stop-signal, and the Stroop), shifting (plus–minus, number–letter, and local–global tasks), and updating (keep track, tone monitoring, and letter memory tasks), and one for DT (spatial scanning and word generation DT). Reporting a common underlying commonality with the EFs inhibition, shifting, and updating, however still separable and independent. It was thought that they employed common inhibitory processes leading to a degree of correlation. DT was considered to be more distinct from the other three EFs. Thus, the unity and diversity theory of EFs were suggested, in that the three EF were more similar than DT, which was more diverse from the three. Nonetheless, inconsistencies in the factor structure of these EFs have been reported across studies that examined older adults and are now discussed.

Vaughan & Giovanello (2010) was the only study found to have observed the same three-factor model in older adults as Miyake, Friedman, et al, (2000 with almost identical tasks, however, with a stronger degree of correlation. The researchers used three tasks for each EF, for inhibition (Stroop, anticue, and stop-signal), shifting (local-global, number–letter, and more–less and odd–even tasks), and updating (letter memory, n-back, and refreshing).

However, a two-factor model was commonly reported in older adults. Hedden & Yoon (2006) employed four tasks for inhibition (two prepotent response inhibition - the

antisaccade and the Stroop tasks, and two resistance to proactive interference - the excluded letter fluency 1 and 2, and the semantic fluency tasks), three tasks for assessing shifting [plus–minus, Wisconsin card sorting test (WSCT), and trail making test], updating [letter memory, backward digit span (BDS), and self-ordered pointing]. Reporting strong correlation between shifting and updating, thus a two-factor model, *inhibition and shifting/updating,* was applied. Similarly, Hull et al (2008) utilised multiple tasks to assess these three EFs, for inhibition (antisaccade, nonverbal Stroop, and verbal Stroop), three for shifting (plus-minus, nonverbal local-global, and verbal local-global), and four for updating (nonverbal keep-track, verbal keep-track, nonverbal n-back, and verbal n-back). Inhibition was removed due to weak correlations, hence a two-factor model comprising *shifting and updating* was established. Of note is that the plus-minus task measure that loaded with shifting in Miyake, Friedman, et al, (2000) with young adults, loaded with updating in this study with older adults. Whereas Bettcher et al (2016) reported a two-factor model consisting of *shifting/inhibition and updating*. They employed three inhibition tasks (antisaccade, enclosed flanker test, and the Stroop), three shifting (design fluency, number-letter, and set-shifting paradigm), and four updating tasks (BDS, dot counting, n-back, and running letter memory). Throughout these studies, inhibition and updating never strongly correlated, while shifting was either independent or associated with inhibition or updating. Hence, it may be concluded that inhibition and updating are independent from each other.

The differences in the factor structure demonstrates differences in how EF load and correlate, implicates the concept of dedifferentiation in EF processing (Koen & Rugg, 2019; Tucker-Drob, 2009). Furthermore, although these CFA studies reported similar (3-factor model), and dissimilar (2-factor model) between the age groups, none of these studies assessed and compared the factor structure between young and older adults. Two further studies were found to have completed this, Bock et al (2019) and Glisky et al (2020).

Bock et al (2019) performed exploratory factor analysis (EFA) as well as CFA on a pair of tasks on young and older adults to examine the EF structure of DT (tracking-verbal and tracking-manual tasks), inhibition (the Simon and Stroop tasks), shifting (switch-semantic and switch-spatial tasks), and updating (keep-track and n-back tasks). The EFA findings indicated some correlation (not high or low) between the four task pairs, which was higher in the older adults, suggesting an age effect. While, CFA reported no common underlying

factor between the EFs, concluding the EFs to be "*partly overlapping rather than a factorial structure*" (Bock et al., 2019, p. 1). Although the degree of loading between the age groups did differ, higher for the older adults in comparison to the younger adults.

Glisky et al (2020) examined three EFs in young, young-older, and older adults with a pair of tasks, inhibition (Simon and Stroop), shifting (global-local and number-letter), and updating (consonant updating/letter memory and keep track). As with the Miyake study, the young were found to load with three-factor model, though weakly. A different two-factor model where inhibition and updating highly correlated into one and shifting (*inhibition/updating and shifting),* was observed in the two older age groups. Which is in contrast to the previously discussed older adult CFA studies. The loading was moderately correlated in the young-older group, and strongly correlated in the older participants, indicating the increased merging of EFs with advancing age.

These findings strengthen the theory regarding the unity and diversity of EFs in that individual EFs, particularly inhibition, shifting, and updating, might possess some degree of commonality, particularly in older adults. Although the factor loading models differed, this could possibly be due to the variation in the array of tasks used by each research group as well as the age of the participants.

4.1.3 Study Aims

In the first study presented in this chapter, the data from the EF task pairs used to examine each of the four EF domains, DT, inhibition, shifting and updating, in the young and older adults presented in Chapter 3 were assessed in order to test their convergence with each other. It is hypothesised that as each pair of tasks aims to assess the same construct, a particular EF, the tasks should in theory produce the same relative level of EF performance outcome. Although it is predicted there will be an age effect resulting in increased correlation between the same EF pairs in the older adults than in the young adults.

A second aim of the research, presented in study 2, was to gain further understanding into the cognitive processes underlying the construct of the EFs to find to what extent the four EFs are similar, i.e. "unity", or separable, i.e. "diverse", i.e. their factorial structure, based on the factorial analysis study conducted by Miyake, Friedman, et al (2000). This was assessed through CFA on the four task pair measures (one for each EF) to investigate if they shared a

common EF loading factor, see the model in Figure 4.1. The correlation factor loadings between the task pairs of each EF were also explored.

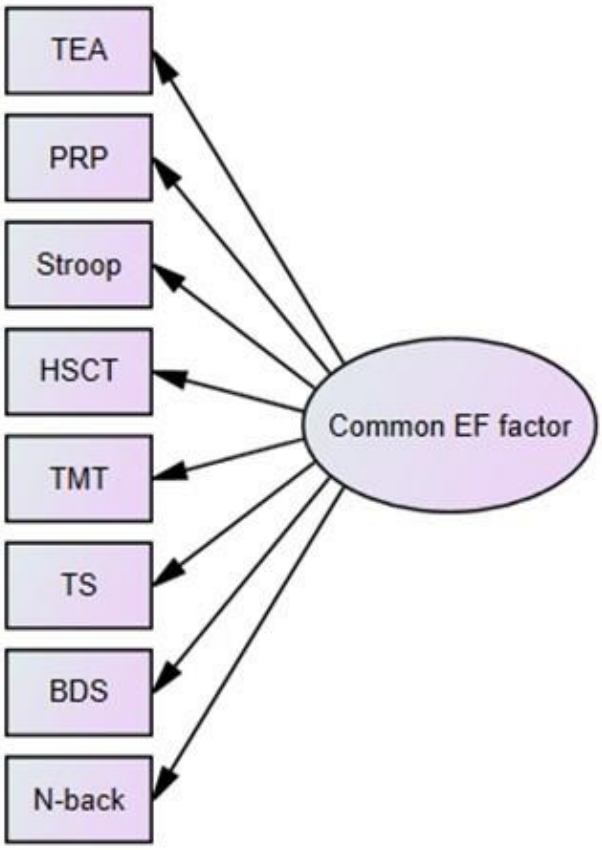


Figure 4.1. Common EF model. TEA - Test for Everyday Attention, PRP - Psychological Refractory paradigm, HSCT - Hayling sentence completion test, TMT - Trail making test, TS - task switching test, and BDS - backward digit span test.

The relations between the latent variables were assessed through the estimation of multiple correlated factors, where the level of unity and diversity is shown by the degrees of the correlations.

4.2 Methods - Study 1, Correlation Analysis

4.2.1 Participants

The young and older adult participants recruited in Chapter 3 were used for the correlation analysis, please see section 3.2.1 for more detail.

As stated in Chapter 3, participants who did not perform within 3.0 SD above or below the group mean in the individual tasks or generated an error rate of 50% or more in the PRP task, or 60% or more in the TEA task, were removed from analysis.

4.2.2 Procedure and EF Assessments

Two tasks each assessing the four EFs were utilised for both analyses, the correlation and CFA. A full description of each task can be found in section 3.2.4.

For DT ability, correlation was assessed between the computerised psychological refractory period paradigm (PRP) task, a comprehensive assessment of DT (Pashler, 1984), and a modified paper-and-pen based test for everyday attention (TEA) telephone code search subtest (Robertson et al., 1994). More specifically, the PRP DT RTs and error rate against the DT accuracy rate and error rate of the modified TEA tasks for each of the tasks, as these performances were the most similar. The DT costs could not be used as the young adults did not complete the two TEA tasks separately.

For inhibition, a paper-and-pen based Stroop task (Stroop, 1935), and a paper-and-pen based Hayling sentence completion test (HSCT) (Burgess & Shallice, 1997), were compared. In detail, the calculated Stroop interference score (calculated by using the formula CW – CW') was assessed against the HSCT score (calculated by the adding the scaled scores, derived from the task's own scales, of the individuals' RTs in part A and part B, and the errors produced in part B). These scores are designed to determine the level of inhibitory ability in an individual. As higher interference and HSCT scores indicates better inhibition ability, thus to remain consistent with the other cost measures, the scores were inverted so that a higher score signifies poorer ability. Another comparison was also conducted between the incongruent condition of the Stroop task, the colour-word (CW) section, and the RT inhibition cost, as these both assess inhibition performance.

For shifting ability, a paper-and-pen based trail making test (TMT) (Reitan, 1992) and a computerised task switching task (Rogers & Monsell, 1995) were analysed. The shifting tasks, TMT (global switch) and task switching test (mixing, local and global switch), was assessed through comparison of the RT shifting costs. Error rates were not assessed because only individuals who produced errors less than three are included in the performance

analysis of the TMT as instructed by the test. However, the shifting cost error rates of the task switching task were compared during the cross-correlation assessments.

For updating, a paper-and-pen based backward digit span test (BDS) (Baddeley & Hitch, 1974), and a computerised spatial n-back task were evaluated (P. T. Griffin & Heffernan, 1983; Jaeggi et al., 2010; Kirchner, 1958). The accuracy rate measure of the BDS was compared with the updating costs (3-back measure minus the 0-back measure) of the n-back task RT, and the error rates of both tasks was compared also. The BDS test only records the score of the correct number of span lengths the participants generate, thus these variables could only be considered. Technically, it would have been more logically to have also used the span updating cost, calculated by subtracting the score of the forward digit span test (FDS) from the BDS test score. However, the participants were not assessed with the FDS test.

4.2.3 Statistical Analysis

Correlation analyses were conducted in the Statistical Package for Social Sciences (SPSS), version 26.0.0.0 (IBM SPSS Statistics, IBM Corp, Armonk, NY) using Pearson's coefficient on the raw data of the tasks.

All analyses were conducted on the young and older adults separately.

A power analysis using the G*power computer program (Erdfelder et al., 2009; Faul et al., 2007) indicated that a total sample of 29 participants, at least 15 in each of the groups, would be required to detect medium effects (d = 0.50) with 80% power using the independent t-test between means with alpha at 0.05.

4.3 Results

4.3.1 Demographics

Please refer to section 3.3.1 for demographic detail on the young and older adult group of participants.

4.3.2 Analysis

4.3.2.1 Dual-tasking

The results of the DT correlation analysis are presented in Table 4.1. [Please note that although data from 28 (two incomplete) young adults and 25 older adults was used, SPSS only correlates between available data for each participant. For example, TEA versus PRP data from participant A. If participant B only has TEA data, it was not analysed.]

Table 4.1. Dual-task correlations

Test comparison	**Young Adults**			**Older Adults**		
	n	Pearson coefficient, *r*	*p*-value	n	Pearson coefficient, *r*	*p*-value
TEA A DT accuracy rate (%) vs PRP A DT RT (ms)	21	-0.89	0.702	19	0.03	0.903
TEA A DT error rate (%) vs PRP A DT error rate (%)		-0.02	0.918		0.31	0.201
TEA C DT accuracy rate (%) vs PRP V DT RT (ms)		-0.02	0.925		-0.27	0.269
TEA C DT error rate (%) vs PRP V DT error rate (%)		0.03	0.905		0.538	0.017

TEA – Test for Everyday Attention, PRP – Psychological Refractory Period paradigm, A - auditory task, C - telephone search code count task, DT – dual-task, RT – reaction rate, V - visual task.

Significance was only found with the older adults between the mean values of the TEA telephone search error rate and the PRP visual DT error rate, see Figure 4.2. Thus, this finding suggests this group performed similarly in their accuracy during the visual tasks of both DTs.

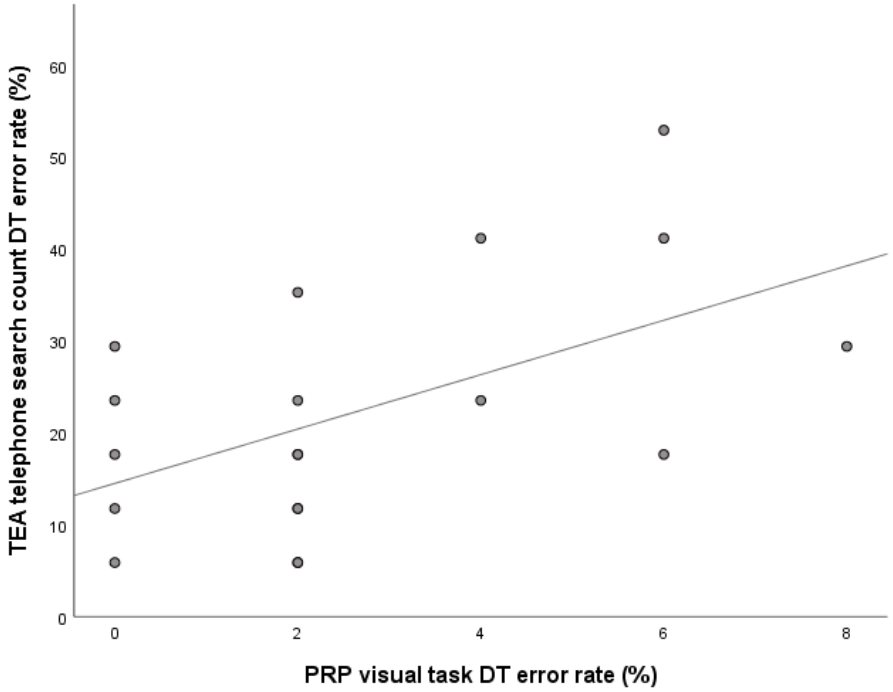


Figure 4.2. Correlation between the TEA telephone code search DT error rate (%) and the PRP visual task DT error rate (%) in the older adults.

4.3.2.2 Inhibition

The results of the inhibition correlation analysis are presented in Table 4.2.

Table 4.2. Inhibition correlations

Test comparison	**Young Adults**			**Older Adults**		
	n	Pearson coefficient, *r*	*p*-value	n	Pearson coefficient, *r*	*p*-value
Stroop interference score vs HSCT score	24	-0.30	0.156	23	-0.09	0.670
Stroop interference score vs HSCT RT cost (%)		-0.03	0.880		-0.04	0.873
Stroop CW vs HSCT RT cost (%)		0.07	0.733		-0.05	0.829

No positive correlation of the derived task scores from both the Stroop and HSCT tasks, as well as between the raw data was found. In this instance, the tasks measurements, the method of calculation of the outcome measures, and possibly their underlying cognitive process may be too dissimilar for a fair correlation to be found.

4.3.2.3 Shifting

The results of the shifting correlation analysis are presented in Table 4.3.

Table 4.3. Shifting correlations

Test comparison	Young Adults			Older Adults		
	n	Pearson coefficient, *r*	*p*-value	n	Pearson coefficient, *r*	*p*-value
TMT RT shifting cost (ms) vs TS local shift RT shifting cost (ms)	17	-0.33	0.200	18	0.01	0.980
TMT RT shifting cost (ms) vs TS mixing RT shifting cost (ms)	17	0.19	0.477	18	-0.21	0.405
TMT RT shifting cost (ms) vs TS global shift RT shifting cost (ms)	18	0.08	0.741	18	-0.14	0.578

TS - Task switching.

No significant correlations in the shifting RT costs between the TMT and all the task switching task shifting types, particularly the global shift which is considered the most comparable measure, in both the young and older adults was observed.

4.3.2.4 Updating

The results of the updating correlation analysis are presented in Table 4.4.

Table 4.4. Updating correlations

Test comparison	Young Adults			Older Adults		
	n	Pearson coefficient, *r*	*p*-value	n	Pearson coefficient, *r*	*p*-value
N-back RT cost (ms) vs BDS accuracy rate (%)	26	-0.18	0.367	23	-0.17	0.448
N-back error rate cost (%) vs BDS error rate (%)		0.06	0.768		0.13	0.561

As with inhibition and shifting, no positive correlations were seen between the BDS test and n-back task in the young and older adults.

4.3.2.5 Additional Correlation Analysis

In further assessing correlations between the EF tasks, additional cross-correlation analysis between different EFs was conducted for significant positive correlations. The results of the analysis are presented in Table 4.5.

Table 4.5. Cross EF Correlation. 208 cross correlation analysis between all the task measures used in section 4.3.2, with the inclusion of the three task switching task error rate measures, was performed in both age groups. Only the significantly positive correlations are presented in this table.

Test comparison	**Young Adults**			**Older Adults**		
	n	Pearson coefficient, *r*	*p*-value	n	Pearson coefficient, *r*	*p*-value
BDS error rate (%) vs HSCT score	26	0.40	0.044	-	-	-
TEA A DT accuracy rate (%) vs TS local shift error rate shifting cost (%)	23	0.44	0.037	-	-	-
HSCT score vs TS global shift RT shifting cost (ms)	25	0.47	0.018	-	-	-
TS mixing RT shifting cost (ms) vs TEA A DT accuracy rate (%)	23	0.44	0.037	-	-	-
TS local shift error rate cost (%) vs TS global shift error rate shifting cost (%)	26	0.77	< 0.001	-	-	-
TS local shift error rate cost (%) vs PRP A DT error rate (%)	23	0.61	0.002	-	-	-
TS local shift error rate shifting cost (%) vs PRP V DT error rate (%)	23	0.72	< 0.001	-	-	-
TS mixing RT shifting cost (ms) vs PRP A DT RT (ms)	23	0.44	0.023	-	-	-
TS mixing RT shifting cost (ms) vs PRP V DT RT (ms)	23	0.59	0.003	-	-	-
TS global shift RT shifting cost (ms) vs PRP A DT RT (ms)	23	0.51	0.014	-	-	-
TS global shift error rate shifting cost (%) vs PRP A DT error rate (%)	23	0.47	0.025	-	-	-
TS global shift RT shifting cost (ms) vs PRP V DT RT (ms)	23	0.59	0.003	-	-	-
TS global shift error rate shifting cost (%) vs PRP V DT error rate (%)	23	0.59	0.003	-	-	-

TS local shift RT shifting cost (ms) vs PRP A DT error rate (%)	23	0.61	0.002	-	-	-
TS local shift error rate shifting cost (%) vs PRP V DT error rate (%)	23	0.72	< 0.001	-	-	-
BDS error rate (%) vs TMT RT cost (%)	-	-	-	19	0.48	0.040
BDS error rate (%) vs Stroop CW	-	-	-	25	0.63	0.001
BDS error rate (%) vs Stroop interference score	-	-	-	25	0.40	0.045
TMT RT cost (%) vs Stroop CW	-	-	-	19	0.49	0.033
TEA A DT error rate (%) vs Stroop CW	-	-	-	20	0.59	0.007
TEA A DT error rate (%) vs Stroop interference score	-	-	-	20	0.46	0.041
TEA C DT error rate (%) vs TS global shift error rate shifting cost (%)	-	-	-	18	0.65	0.004
HSCT RT cost (ms) vs PRP A DT RT (ms)	-	-	-	21	0.46	0.036
HSCT RT cost (ms) vs PRP V DT RT (ms)	-	-	-	21	0.45	0.041
N-back RT cost (ms) vs TS local shift error rate shifting cost (%)	-	-	-	23	0.45	0.033
N-back error rate cost (ms) vs TS mixing RT shifting cost (ms)	-	-	-	21	0.51	0.018
N-back error rate cost (ms) vs PRP A DT RT (ms)	-	-	-	20	0.53	0.015
N-back error rate cost (ms) vs PRP V DT RT (ms)	-	-	-	20	0.49	0.029
TS mixing error rate shifting cost (%) vs PRP A DT error rate (%)	-	-	-	20	0.55	0.013
TS global shift error rate shifting cost (%) vs PRP A DT error rate (%)	-	-	-	20	0.61	0.004

Fifteen significant cross correlations were observed in both age groups but between different task pairs. These correlations may relate to the issue of task impurity, in that one or more EF process was utilised during task completion of a specific EF. Similarly, the concept of an underlying cognitive component between the EFs, such as the theory of the unity and diversity of EFs suggested by Miyake, Friedman, et al (2000), may be the cause of these large number of significant correlations.

Additionally, the differences in these cross correlations between the ages may also highlight an age effect, as reported by Glisky et al (2020). It was explained that ageing causes decreased efficiency in the processing of EFs, resulting in the reallocation of limited resources to enhance performance. As observed with the DT correlation in the older adults and not young adults, in that the EFs have changed in structure due to the ageing process, where EFs have started to merge, resulting in a difference in the correlation between tasks. However, this same pattern might also occur with the assessment of a second independent young adult sample, as these correlations might be due to random variation.

Nonetheless, as only a single correlation was observed between task measures of the same EF in the older adults, and none in the young adults, these significant cross correlations may possibly be false positives, as there is a 5% possibility of these correlations occurring. This would account for 10 of the 15 significantly positive correlations observed in both age groups.

4.4 Discussion

This first study aimed to examine if any of the four separate pairs of EF tasks correlated in their examination of their intended EF, i.e. DT, inhibition, shifting and updating. Insignificant positive correlations were observed between all the EF pairs in the young adults age groups. Whereas in the older adults, a positive significant correlation was observed between the DT error rate measures for the visual tasks, specifically the TEA telephone code search count and PRP visual task. Thus, implying that performance of this DT condition was comparable, in that the participants recruited similar cognitive processes to complete the task, i.e. differentiate between numbers in the PRP and the visual scanning for a particular symbol and number combination, as with the TEA subtest. However, as the correlation was only observed in the older group, an age effect is suggested, i.e. dedifferentiation and neural

reorganisation, as EFs become less distinct because of merging in older individuals, causing reduction of selectivity of responses, resulting in more homogenous responses (Grady, 2012). Possibly highlighting the change and reallocation of cognitive processes in older adults. Although it is unknown why this was the only association observed.

Moreover, significant positive correlations may have also been seen in the auditory condition of the DTs by comparing the cost measures as the cognitive processes utilised in the performances are similar, if not identical. However, this was not possible because the TEA tasks were not performed as STs in the young adults.

Whilst there was no sizable correlation between the tasks assessing the same EF, particularly in the young adults, it does not necessarily infer that the tasks did not efficiently assess their intended EF, as they may have been examining different aspects of the same EF. As with inhibitory control, the Stroop interference measure assesses the disruptiveness of a stimulus which is not required for the active suppression of thought (Borella et al., 2009; Diamond, 2013; Friedman & Miyake, 2004). It largely relies on the notion that reading is an automatic process and therefore participants tend to read words instead of the colour of the words during the incongruent section of the task. Whereas the HSCT entails response inhibition and cognitive inhibition for the suppression of active processes to stop or limit irrelevant information from entering WM (Borella et al., 2009; Diamond, 2013; Friedman & Miyake, 2004). Including relying on the knowledge of how sentences are formed and how to make them comprehensible, so when presented with a sentence, the missing word is familiar and automatically available in memory. Similarly, with updating, the tasks utlilised different measures in their assessment of updating. The BDS task is a WM span task that requires individuals to temporaily store previously verbally presented information and immediately recall, with the span increasing every two performances, until a span of eight digits. Measuring performance accuracy only. However, the n-back task examines speed and accuracy. Participants perform a number of trials of the same condition for a period of time before proceeding to the next n-back condition, in this case up to 3-back. Thus, although both require the temporary storage of information in WM, the BDS test is much shorter and easier to administer. Accordingly, in the performance of the BDS, participants are required to listen, pay attention, use short-term memory (STM), manuipulate the information in STM, and recall. Whereas the n-back task requires attention, visuospatial sequencing,

psychomotor speed, in addition to the use of STM, manuipulation of the information is STM, and recall.

Alternatively, perhaps only one of the tasks may have actually been assessing the EF in question, however, it is unknown which of the tasks was 'correct'. Similarly, possibly neither task may have actually examined the EF at all which would greatly impact correlation analysis studies. Thus, the assessment of more than two tasks per EF would strengthen such comparison studies (Miyake, Friedman, et al., 2000). Nevertheless, it is impossible to determine if more positive correlations may exist with larger sample sizes, and doubtful a huge effect would be observed.

Furthermore, variations in the requirement and measures of EF tasks assessing the same construct questions how these tasks and EF abilities can be likened between studies and participant groups. The stimuli used for the tasks may further impact how a task is performed by different participant groups, such as between digits and images, or auditory stimuli versus non-auditory. Thus, improved task methods or the choice of stimuli may increase positive significant correlation between tasks.

Nonetheless, further correlation analysis yielded a substantial amount of significant positive associations between the four EFs tasks assessing different EF ability, indicating that the study design was sufficiently powered. The large proportion of null-findings observed with the age groups with tasks assessing the same EF ability suggested lack of statistical power.

These significant cross correlations might be due to task impurity or the concept of a mutual underlying EF factor, 'unity' as suggested by Miyake, Friedman, et al (2000). For instance, in the young adults, significant positive correlations were found between the TEA DT auditory accuracy rate and the task switching local shift error rate shifting cost (r = 0.44), and the mixing RT shifting cost (r = 0.44), i.e. shifting. Whereas in the older adults, the TEA auditory DT error rate correlated with the Stroop CW (r = 0.59), and Stroop interference score (r = 0.46), i.e. inhibition, as well as between the TEA telephone code search error rate and the the task switching global shift error rate shifting cost (r = 0.65), i.e. shifting. The higher correlation coefficients and more correlations (3 in comparison to 2) in the older adults indicate an age effect also.

Of note is that the Stroop task measures failed to correlate with any of the other EF task measures in the young. Whereas in the older group, in addition to the TEA measures, the Stroop CW further correlated with the TMT RT cost shifting measure (r = 0.49), and BDS error rate updating measure (r = 0.63), and the Stroop interference score correlated with the BDS error rate measures (r = 0.40). Thus, the ability of inhibition may have increased involvement in older individuals as suggested by the inhibition-deficit hypothesis (Hasher & Zacks, 1988; Lustig et al., 2007). It states that impairment in inhibition is the primary source of age-associated deficits reported in the performance of numerous cognitive tasks, especially those involving WM (Campbell et al., 2020; Hasher et al., 2008). Gilsoul et al (2019) also reported inhibition partly mediated the effect of ageing in DT, shifting, and updating.

In summary, although no significant positive correlations were observed in the young adults, and only a single positive association was found in the older adults in the tasks assessing the same EF, the large proportion of cross correlations amongst both groups indicated the study had significant statistical power. The correlation in the older adults may be due to dedifferentiation and neural reorganisation as a consequence of cognitive ageing.

The reasons for the amount of cross correlations found may include, false positives, task impurity, or as discussed in Chapter 3, be attributed to the concept of unity amongst EFs, namely that inhibition, shifting, and updating, possess some common underlying factor as proposed by Miyake, Friedman, et al (2000). In addition, the inhibition specific task, Stroop measures, correlated with all the other three EF task measures in the older adults only, which is in line with the inhibition-deficit hypothesis of inhibition being the cause of age-related performance deficits.

4.5 Methods - Study 2, Confirmatory Factor Analysis (CFA)

4.5.1 Participants

For the CFA, due to the software used not allowing for missing data, only participants that completed all the task pairs successfully were analysed. Hence, the task measures of 12 young adults (3M/9F), aged 18-31 years (mean of 21.50, SD 3.90), and 15 older adults (6M/9F), aged 60-84 years (mean of 71.67, SD 6.90) were used.

As stated in Chapter 3, participants who did not perform within 3.0 SD above or below the group mean in the individual tasks or generated an error rate of 50% or more in the PRP task, or 60% or more in the TEA task, were removed from analysis.

4.5.2 Procedure and Assessments EF

See section 4.2.2.

4.5.3 Statistical Analysis

Following z-score transformation to normalise the measures, CFA was completed in SPSS AMOS, version 26 (IBM SPSS Statistics, IBM Corp, Armonk, NY).

CFA goodness-of-fit was evaluated with the chi-square (χ^2) value, Akaike's Information Criterion (AIC), and Root Mean Square Error of Approximation (RMSEA), calculated within AMOS. Insignificant χ^2 values (Byrne, 1998), low AIC values, and RMSEA values below 0.05 are considered good indicators of a good fit of the observed data to the model (Hull et al., 2008; MacCallum & Austin, 2000). χ^2 and AIC values signify the degree of difference between the observed and predicted covariance matrices.

All analyses were conducted on the young and older adults separately.

4.6 Results

4.6.1 Demographics

The groups' age difference was confirmed by an independent t-test, $t(25) = -22.42$, $p < 0.001$. There was no difference in the gender composite, $\chi^2(1) = 0.675$, $p = 0.411$ (n=27).

4.6.2 Analysis

The z-score data from 12 young adults and 15 older adults was analysed. Table 4.6 shows the descriptive statistics for the EF task measures of both groups.

Table 4.6. Descriptive statistics of CFA sample

Task	Group	Mean (SD)	Range	Skewness	Kurtosis
TEA A DT accuracy rate (%)	Young	92.50 (10.55)	70-100	-1.15	0.13

	Old	93.33 (11.75)	60-100	-1.98	3.82
TEA A DT error rate (%)	Young	7.50 (10.55)	0-30	1.15	0.13
	Old	6.67 (11.75)	0-40	1.98	3.82
TEA C DT accuracy rate (%)	Young	78.43 (16.32)	47.06-100	-0.42	-0.48
	Old	78.82 (12.14)	58.82-94.12	-0.34	-0.99
TEA C DT error rate (%)	Young	21.57 (16.32)	0-52.94	-0.42	-0.48
	Old	21.18 (12.14)	5.88-41.18	0.34	-0.99
PRP A DT RT (ms)	Young	1075.70 (476.70)	635.62-1884.32	0.87	-1.14
	Old	1141.74 (315.72)	765.66-1848.95	1.21	1.22
PRP A DT error rate (%)	Young	11.17 (11.26)	00.00-32.00	0.86	-0.78
	Old	1.33 (2.23)	00.00-8.00	2.21	5.44
PRP V DT RT (ms)	Young	1292.67 (532.42)	699.36-2119.59	0.65	-1.35
	Old	1475.05 (334.43)	1003.71-2219.00	0.86	0.90
PRP V DT error rate (%)	Young	7.33 (6.89)	2.00-20.00	0.90	-0.82
	Old	2.13 (2.33)	00.00-8.00	1.43	1.95
Stroop interference score	Young	51.50 (14.07)	23.00-68.00	-0.93	-0.31
	Old	64.87 (9.86)	44.00-88.00	0.33	2.03
Stroop CW	Young	-8.42 (14.23)	-33.00-11.00	-0.52	-0.69
	Old	4.80 (7.41)	-7.00-23.00	1.06	1.56
HSCT score	Young	4.83 (1.59)	3.00-8.00	0.82	-0.26
	Old	5.27 (1.58)	4.00-9.00	1.12	0.46
HSCT RT cost (%)	Young	12.42 (21.51)	-14.00-51.00	0.97	-0.55
	Old	33.73 (21.41)	00-61.00	-0.28	-1.34
TMT RT shifting cost (ms)	Young	33.50 (19.64)	13.00-82.00	1.50	2.45
	Old	24.60 (12.32)	7.00-50.00	0.35	-0.57
TS local shift RT shifting cost (ms)	Young	62.03 (67.98)	-27.08-166.82	0.01	-1.48
	Old	186.06 (191.14)	-86.74-662.46	1.06	1.51

TS mixing RT shifting cost (ms)	Young	290.51 (240.68)	56.38-815.49	1.19	0.73
	Old	353.48 (287.12)	46.66-1222.82	2.20	5.92
TS global shift RT shifting cost (ms)	Young	357.09 (227.00)	45.64-841.91	0.70	0.49
	Old	549.73 (388.20)	126.50-1879.46	3.17	11.53
BDS accuracy rate (%)	Young	60.71 (15.08)	35.71-85.71	0.31	-0.07
	Old	59.52 (22.70)	35.71-100	0.45	-1.25
BDS error rate (%)	Young	39.29 (15.08)	14.29-64.29	-0.31	-0.07
	Old	40.48 (22.70)	00-64.29	-0.45	-1.25
N-back RT cost (ms)	Young	14.04 (158.52)	-244.02-234.64	-0.07	-1.13
	Old	-57.03 (258.04)	-482.95-560.45	1.06	1.75
N-back error rate cost (%)	Young	43.23 (10.09)	25.00-62.50	0.03	0.29
	Old	65.00 (16.51)	32.25-91.25	-0.28	0.04

The common EF loading factor model was investigated in both age groups with the use of the error rate measures of PRP visual DT and the TEA telephone code search tasks for DT, the test scores of the Stroop task and HSCT for inhibition, the RT shifting cost measures of the TMT and the task switching task global shift for shifting, and the error rate of the BDS task and the error rate cost of the n-back task for updating.

The model proved inadequate for the young adults as the iteration limit of the analysis was reached. The loading and correlation analysis was deemed invalid, indicating no common EF factor existed with the measures for this group. The χ^2 goodness of fit test was $\chi^2(20) = 32.09$, $p = 0.042$, AIC = 64.09, and RMSEA = 0.23.

A better adequate fit was observed with the older adults with both the χ^2 and RMSEA tests showing adequacy, $\chi^2(20) = 20.71$, $p = 0.415$, and RMSEA = 0.05. (AIC = 52.71.) The standardised loadings of the EFs are presented in Table 4.7. All the loadings were statistically insignificant. The results suggest an age-associated change in the structure of the EFs may have occurred, becoming more similar. Also, the PRP DT factor loaded the

highest (> 0.7) and strongly for the common factor, while the two inhibition measures loaded the smallest.

Table 4.7. Older adults standardised common EF loading

Loading			Estimate
PRP	<---	EF	0.972
TEA	<---	EF	0.528
HSCT	<---	EF	-0.152
Stroop	<---	EF	0.081
TS	<---	EF	0.639
TMT	<---	EF	-0.020
N-back	<---	EF	0.472
BDS	<---	EF	0.190

The factor loading between the four EFs was explored. With the use of the task measures employed in the common EF factor analysis above, shifting failed to load in the young adults. In the older adults, the model reached iteration limit, so was not considered. However, following replacement of the task switching task global shift RT cost with the local shift RT cost, four-factor models were observed.

The model proved adequate for the young adults with the χ^2 goodness of fit test, $\chi^2(14) = 19.65$, $p = 0.142$. (AIC = 63.65, and RMSEA = 0.19.) A better fit was observed with the older adults with both the χ^2 and RMSEA tests showing adequacy, $\chi^2(14) = 11.26$, $p = 0.666$, and RMSEA = 0.00. (AIC = 55.26.)

The standardised loadings of the EFs for each group are presented in Table 4.8. The data shows the PRP factor loaded strongly with the young adults, whereas the TEA and task switching task factors loaded strongly in the older adults. Nevertheless, all the loadings were insignificant.

Table 4.8. Standardised EF loadings

EF Loading			Estimate
Young adults			
PRP	<---	DT	1.159
TEA	<---	DT	0.432
HSCT	<---	Inhibition	0.394
Stroop	<---	Inhibition	-0.877

EF Loading			Estimate
TS	<---	Shifting	0.348
TMT	<---	Shifting	-1.194
N-back	<---	Updating	0.562
BDS	<---	Updating	-0.413
Older adults			
PRP	<---	DT	0.540
TEA	<---	DT	0.959
HSCT	<---	Inhibition	0.434
Stroop	<---	Inhibition	-0.396
TS	<---	Shifting	0.685
TMT	<---	Shifting	-0.308
N-back	<---	Updating	0.241
BDS	<---	Updating	0.276

The remaining EFs loaded either low, i.e. weakly, or negatively.

The loadings of cross-correlation between the EFs were further assessed, see Table 4.9.

Table 4.9. Cross-correlations loading of the EFs

Loading correlations			Estimate
Young adults			
DT	<-->	Inhibition	0.220
Inhibition	<-->	Shifting	0.486
Shifting	<-->	Updating	0.455
DT	<-->	Shifting	-0.421
Inhibition	<-->	Updating	-0.597
DT	<-->	Updating	-1.034
Older adults			
DT	<-->	Inhibition	-0.264
Inhibition	<-->	Shifting	0.117
Shifting	<-->	Updating	-0.844
DT	<-->	Shifting	0.738
Inhibition	<-->	Updating	-3.064
DT	<-->	Updating	1.241

No substantial correlation was found with the young adults. To determine if DT loaded independently from inhibition, shifting, and updating as reported by Miyake, Friedman, et al (2000), a three-factor model CFA was conducted. This model was considered adequate following review of the χ^2 and RMSEA values, see Table 4.10. However, no significant strong

standardised EF loadings were observed. The highest estimate was seen with the HSCT measure for inhibition, 0.425. Similarly, there was no significant correlations between the three EFs: between inhibition and shifting the estimate was 0.262, inhibition and updating was -0.898, and shifting and updating was 0.044.

Thus, as there were no significant correlations in either the three- or four-factor models, either model may be considered.

In the older adults, strong but insignificant associations were observed between DT and shifting (0.738), and between DT and updating (1.241).

A three-factor model was assessed without DT as with the young, and without inhibition based on the strong correlation loadings between DT, shifting, and updating, Table 4.10 for their model adequacy.

Table 4.10. Additional goodness of fit models

Model	Group	*df*	χ^2	*p*	AIC	RMSEA
Three-factor *Inhibition- Shifting-Updating*	Young	6	3.95	0.684	33.95	0.00
Three-factor *Inhibition- Shifting-Updating*	Older	6	0.85	0.991	30.85	0.00
Three-model *DT- Shifting-Updating*	Older	6	8.57	0.199	38.57	0.18

With the *inhibition-shifting-updating* model, there were no strong standardised loadings, although the strongest loading was observed this time with the BDS measure for updating 0.421. While the HSCT measure for updating loaded second strongly, 0.393. No significant correlations were found between the EFs, between inhibition and shifting the loading was 0.623, inhibition and updating was -2.605, and shifting and updating was -1.001.

With the *DT-shifting-updating* model, stronger but insignificant standardised loadings were observed, particularly for DT with the TEA measure, 1.153, and shifting with the task switching task local shift measure, 0.926. A strong insignificant correlation loading was observed between DT and updating, 1.133. Thus, a two-factor model may be considered with the older adults, *DT/updating-shifting*.

However, it is clear from the goodness of fit analysis, that the *inhibition-shifting-updating* model is a more acceptable model.

4.7 Discussion

CFA was conducted to examine to what extent the four EFs were separable or utilised the same underlying construct by employing a common EF model to explore how similar the task measures loaded. A four-factor model containing the four task pair factors proposed by Miyake, Friedman, et al (2000) was also employed to investigate the correlation loadings between the separate EFs in both age groups.

The lack of commonality in the loadings of the measures during the common EF factor analysis in the young adults but not in the older adults may support the theory of the structural change and merging of EFs as a consequence of ageing. Furthermore, and surprisingly, the inhibition measures loaded the smallest (one low and one negatively). This is in contradiction to the inhibition-deficit hypothesis (Hasher & Zacks, 1988; Lustig et al., 2007), which considers inhibition the main source of age-associated deficits observed during the performance of numerous cognitive tasks, particularly those involving WM (Campbell et al., 2020; Hasher et al., 2008; Koch et al., 2010; Persad et al., 2002).

Similarly, the weak four-factor model observed with the young adults when the four EFs task pair measures were analysed may further confirm EFs are more independent in younger individuals. There was relatively low and insignificant loading of the task measures to their specific EFs, except for the PRP measure for DT, and during correlation analysis. Whereas in the older adults, strong insignificant EF loadings were observed with the TEA measure for DT, and between DT and shifting, and DT and updating. Following three-factor model analysis, a two-factor model was proposed *DT/updating-shifting,* as there was an insignificant strong association with DT and updating. Inhibition did not load strongly with the other three EF measures so was removed. This is similar to finding reported by Hull et al, (2008). However, as the sample used in the CFA consisted of only the participants that successfully performed all the task pairs correctly, inhibition may not have been affected by age as with the other sample used in the correlation analysis. Still, the goodness of fit

analysis of the *inhibition-shifting-updating* model, makes it a more appropriate model for the older adults.

The findings of the young adults is in agreement with the findings reported by Bock et al, (2019), with mostly weak loadings for the task measures and correlations. In the older adults, though insignificant in this analysis, a two-factor model has also been more frequently reported (Bettcher et al., 2016; Hedden & Yoon, 2006; Hull et al., 2008) in comparison to three-factor and the less studied four-factor models. This difference suggests an age effect which may be attributed to age-related neural reorganisation and dedifferentiation (Koen & Rugg, 2019). Resulting in larger brain areas being employed in older adults to accomplish a given task, leading to increased overlap of regions and/or different brain areas being activated (Cabeza et al., 2018; Grady, 2012) (this is elaborated upon in the next chapter). An age effect was similarly reported by Glisky et al (2020) who found a three-factor model in the young, but a two-factor model of increasing strength from young-old to older adults. The diversity of the EFs became more unified with advanced age.

A novel finding of this CFA was the EF correlations in the older adults. No other study has reported a two-factor model consisting of DT. Thus, the diversity of these findings may be due to the use of different EF tasks as all tasks use combinations of different executive processes during performance. Resulting in the identification of shared processes less probable, affecting the strength of the correlations between factors. Nevertheless, the *inhibition-shifting-updating* model as reported by Miyake, Friedman, et al, (2000) was found to be more applicable.

Still, all the findings observed in the study were insignificant, which could be due to the small number of participants in each group <20 in comparison to other factor studies with much larger groups, Ns > 40 (Bettcher et al., 2016; Bock et al., 2019; Hedden & Yoon, 2006; Hull et al., 2008; Miyake, Friedman, et al., 2000; Vaughan & Giovanello, 2010). Also, this study only compared two task measures for each factor, it may have been beneficial to have employed an additional task for each EF.

In summary, the results of the factor analysis are promising, and the loadings observed, particularly in the two-factor model in the older adult group, may become significant with a

substantial number of participants. Most importantly, the loadings between the EFs seem to be more diverse in the young adults, loading weakly or not at all, whilst in the older adults, there were stronger associations observed.

4.8 Conclusion

To conclude, the findings presented in this chapter show there to be a correlation issue of EF tasks alleging to be measuring the same construct. The absence of significant correlations in all four EF pair tasks in the young adults demonstrates the inconsistency of these tasks. Although the single significant positive correlation observed in the older adults between the DT error rate measures of the visual tasks provides possible evidence for the effect of dedifferentiation and reorganisation. Supplementary research is thus needed to fully understand precisely what such tasks are assessing, and the necessity for researchers to be mindful in their selection of EF tasks. Researchers should not take it for granted that all tests which claim to assess a certain EF may be used interchangeably.

The CFA further showed mostly lack of loading of the EF variables between and across the EFs in the young adults. An age-associated effect was shown in the older adults, larger loadings were found in comparison to young adults, specifically in the correlation loadings between DT and shifting, and DT and updating, although all were insignificant. It indicates that the diversity of EFs decreases with age.

Therefore, it is important to perform such correlation and factorial-analytic research on various age groups, as performed here, and with larger sample sizes, as cognitive ageing, (and possibly clinical conditions) may account for lack of significant correlations between tasks and the loading of shared and diverse executive processes. The inclusion of additional tasks in both analyses may add value to the observed findings also.

Chapter 5, Neuroanatomy and Neural Networks of Executive Function Abilities and Cognitive Decline, A Literature Review

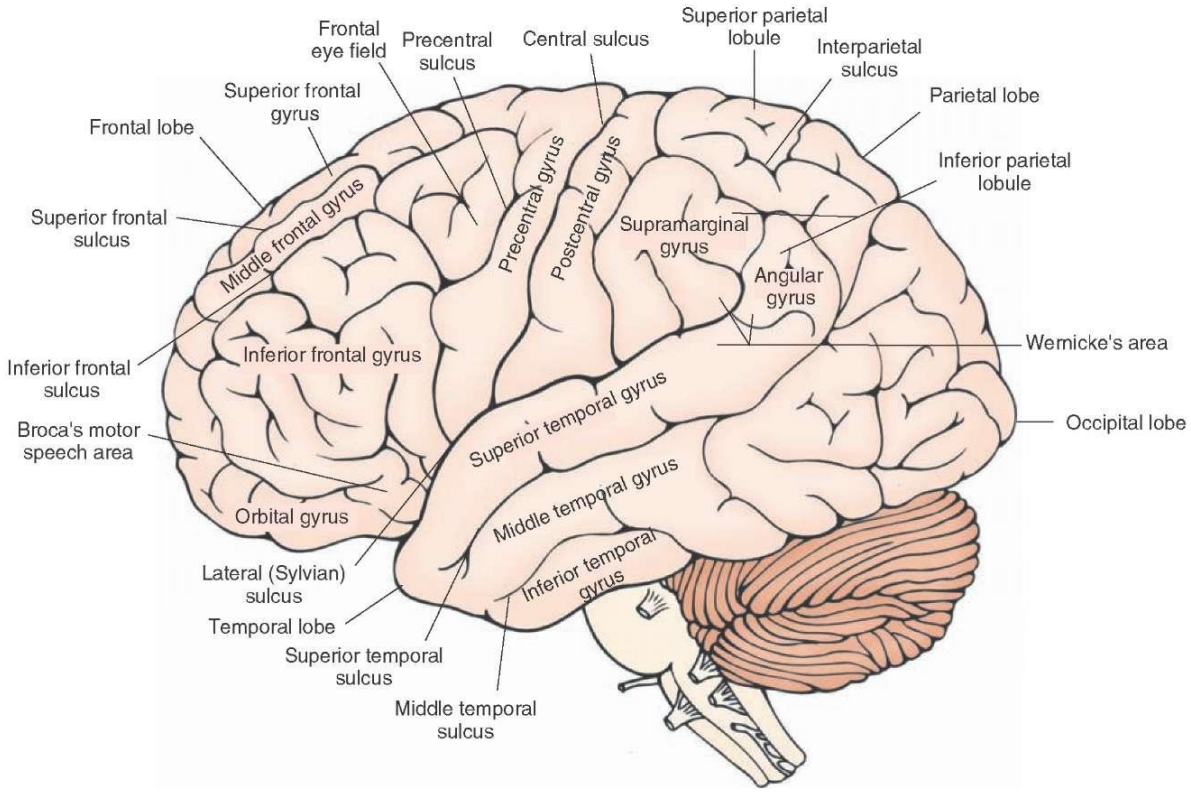
5.1. Introduction

As a consequence of ageing and neuropathological conditions, the brain typically undergoes numerous anatomical changes resulting in reduced gray matter (GM) and/or white matter (WHM) integrity, causing dysfunction of neural activity. However, the region(s) of the brain affected, and the degree of change(s) differs between individuals and by condition (Maillet & Rajah, 2013; Raz et al., 1998). The prefrontal cortex (PFC), the region associated with executive functions (EFs), is known to be heavily affected (Zanto & Gazzaley, 2019). Anatomical changes of the PFC may result in alterations in behaviour and decline in cognitive ability and performance of everyday tasks, displayed through cognitive assessment with tests like the mini-mental state examination (MMSE) (Folstein et al., 1975), and with the completion of EF tasks, as described in Chapter 3 of this thesis (Kirova et al., 2015; Mokhber et al., 2019). Furthermore, due to the structural changes of the brain, activity of the neural networks to and from the PFC is compromised, resulting in either their over- or underactivity, or in the enlistment of new networks to compensate for the structural changes and/or death of brain tissue (Abdulrahman et al., 2017; Cabeza et al., 2002).

Thus, in this chapter, the function of the PFC and its neural networks is first described before a detailed review regarding how cognitive ageing and neurodegenerative conditions impact these networks. This is followed by a review of magnetic resonance Imaging (MRI) literature of EFs, with emphasis on the cognitive abilities dual-tasking, inhibition, shifting, and updating, and how neuroanatomical deterioration as a consequence of ageing, mild cognitive impairment (MCI) and Alzheimer's disease (AD) affects these processes. The behavioural studies presented in Chapter 3 were originally planned to also include MCI and AD participants, however due to the COVID-19 pandemic this could not be accomplished. Similarly, a neuroimaging study testing all the above-named participant groups was also planned, hence, some secondary neuroimaging data, provided by the OASIS-3 study (LaMontagne et al., 2019) of these groups are analysed in the following chapter.

5.2. The Prefrontal Cortex and its Neural Networks

The PFC is thought of as the central site of our cognitive ability, connecting with networks spanning the remaining brain. It is composed laterally of the orbitofrontal gyrus (OFG), inferior frontal gyrus (IFG), middle frontal gyrus (MFG), superior frontal gyrus (SFG), and precentral gyrus (PCG) separated by the inferior frontal sulcus (IFS), superior frontal sulcus (SFS), and precentral sulcus (PCS). Medially, it contains the cingulate gyrus (CG) and the cingulate sulcus (CS) (Ulmer et al., 2015). Please see Figure 5.1 for a representation of these regions and the rest of the brain structural regions. These structures are further divided into the subregions referred to as the orbitofrontal PFC (OFC), dorsolateral PFC (DLPFC), dorsomedial PFC (DMPFC), ventrolateral PFC (VLPFC), ventromedial PFC (VMPFC), and the cingulate cortex. Please refer to Chapter 1, Figure 1.3 for a visual representation and detailed discussion in section 1.3.2. In sum, these regions are involved in the processing of several EF functions, working independently or with one or more brain regions to accomplish a task, through neural networks.



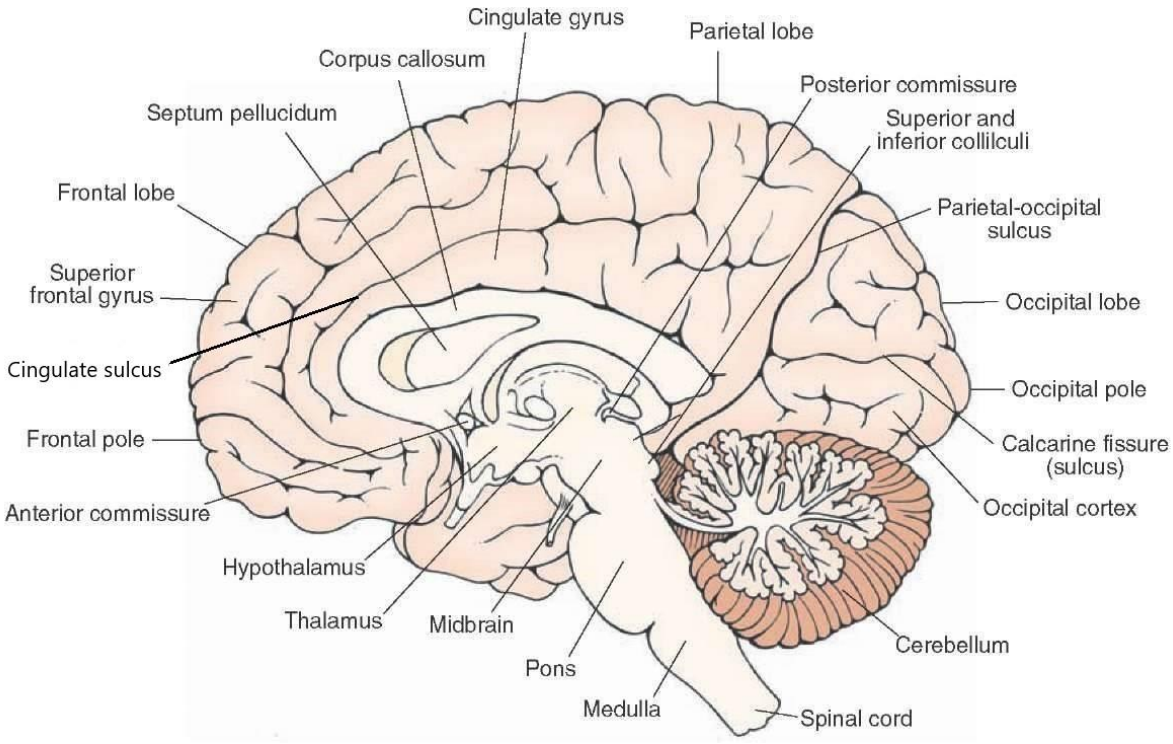


Figure 5.1. The Gyri and Sulci of the left hemisphere of human brain. The first figure represents the lateral view of the brain, and the second, the medial view (*Operative Neurosurgery*, 2019).

The PFC itself is responsible for the controlling and monitoring of many of the neural networks in other cortical and subcortical regions. First by receiving neural signals via input projections referred to as 'bottom-up' signals via afferent networks located within brain regions including the parietal and temporal lobes. In particular, the cingulate cortex, hippocampus, substantia nigra, thalamus, and medial dorsal nuclei (Collette et al., 2006). These networks relay information from low-level cognitive sensory processes, i.e. auditory input from language and/or sounds, and visual input from letters, words, digits, sentences, faces and/or scenes, to the PFC (D'Esposito & Postle, 2015). Thus, the PFC relies on environmental stimuli to influence thought and decision-making. An example of this is the limbic network (Mezzacappa, 2011), which will be discussed in the next section.

Secondly, the PFC sends command signals, output projections known as 'top-down' signals via efferent networks (Funahashi & Andreau, 2013; Sarter et al., 2001). These networks work on the basis of prior knowledge and thought to influence how an individual perceives and understands the environment. These efferent pathways originate from the PFC and connect with cortical and subcortical structures including the amygdala, basal ganglia, hypothalamus, septal nuclei, and the medial dorsal nuclei within the thalamus, amongst

others, as seen in Figure 5.2. A large part of these neural networks connecting the parietal cortex has been suggested to be associated with EFs. This is known as the fronto-parietal network (Mezzacappa, 2011; Wallis et al., 2015), and will be discussed in a later section.

Thus, the PFC is regarded as the 'central hub' of the brain, receiving all forms of information, such as sensory, internal, and environmental in an abstract form necessary for the execution of action and behaviour, specifically for the completion of EFs. These include decision-making, management of attention, and the control of emotional state.

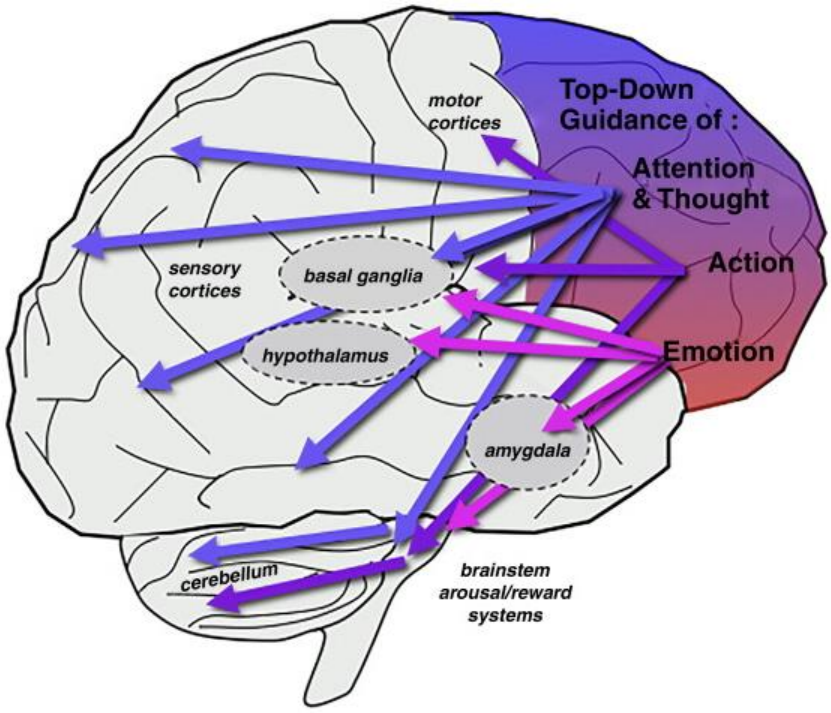


Figure 5.2. A Simplified Representation of the Prefrontal Cortex Top-Down Pathways. These are primarily conscious and intentional mental cognitive processes initiated at the level of the cerebral cortex (Berridge & Arnsten, 2015).

5.2.1 The Fronto-Parietal Network

A prominent top-down network primarily implicated in the executive control of an array of EF processes is the fronto-parietal network (Dixon et al., 2018; Marek & Dosenbach, 2018; Mezzacappa, 2011). Frontally, the DLPFC is the central region, involved in the monitoring and manipulation of cognitive processes, goal-directed behaviour, and adaptive decision-making, through inhibitory control and resistance to interference. This occurs through connections with the parietal cortex, especially the inferior parietal lobe, interior parietal

lobule, interparietal sulcus, and superior parietal lobule, as well as the medial cingulate cortex, striatum (basal ganglia) and thalamus (Barbey et al., 2013; Curtis & D'Esposito, 2003; Harding et al., 2015; Mezzacappa, 2011; Postle, 2017; Rebecca, 2003; Suchy, 2009; Wallis et al., 2015). Through the DLPFC connection with the superior parietal cortex, it is associated with saccades and spatial attention, mental rotation, and working memory (WM) (Ptak et al., 2017).

5.2.2 The Limbic Network

The PFC connections with non-frontal cortical areas such as the hippocampus and amygdala in the limbic region of the medial temporal lobe (MTL) are essential for the active organisation of memory content, emotional response regulation, mnemonic interactions, and goal salience. In addition, the nucleus accumbens and the ventral tegmental area are vital for incorporating cortical and limbic processes into goal-oriented behaviour (Cristofori et al., 2019; Mezzacappa, 2011; Rabinovici et al., 2015).

5.2.3 Other PFC Associated Networks

The cingulo-opercular network is located between the fronto-parietal network and the limbic network and functions by providing bidirectional communication between these networks. Accordingly, structurally, the anterior cingulate gyrus (ACG), and the operculum (the area along the lateral sulcus that contains sections of the inferior frontal, orbitofrontal, inferior parietal, and superior temporal lobes) are implicated. Thus, it is thought to play a critical role in cognitive control and decision-making by accounting for limbic network traits, i.e. emotion, memory of cognitive processes (Coste & Kleinschmidt, 2016; Mezzacappa, 2011; Wallis et al., 2015).

The default mode network is implicated in self-generated thought and social cognition, more precisely the ability to engage in social interaction and thought due to external and internal sources of social information. The DMPFC, VMPFC, IFG, hippocampus, inferior parietal lobe, lateral temporal cortex, and posterior cingulate cortex (PCC) are all involved in its function (Mezzacappa, 2011; Spreng & Andrews-Hanna, 2015).

5.3. Age-Associated Neuroanatomical Changes and Cognitive Decline

Ageing (as well as neurodegenerative conditions) causes the brain to undergo structural changes. Evidence from imaging studies has indicated that the frontal cortex, primarily the PFC, is more vulnerable to age-associated structural changes than posterior and subcortical brain regions (Raz et al., 1997, 2005; Raz & Rodrigue, 2006; Salat et al., 1999, 2004; Tisserand & Jolles, 2003a, 2003b). Also, the DLPFC, particularly important in the fronto-parietal network, has been observed to be one of the earliest regions to begin deteriorating (Barbey et al., 2013; Funahashi & Andreau, 2013; MacPherson et al., 2002; Mezzacappa, 2011; Nissim et al., 2017; Raz et al., 1998; Wallis et al., 2015; West, 1996). However, the midbrain structures, the thalamus, caudate nucleus, and putamen of striatum, and the temporal and parietal cortices have also been shown to be susceptible to age-associated structural changes (Greenwood, 2000; Milham et al., 2002; Raz, 2000). These changes result in the decline of an individuals' cognitive ability, especially those occurring in the PFC, and affect the neural networks associated with EFs. This process has been described in the Frontal Lobe hypothesis of Neurocognitive Ageing (Dempster & Vegas, 1992; West, 1996), and the Scaffolding Theory of Ageing and Cognition (STAC) (Park & Reuter-Lorenz, 2009; Reuter-Lorenz & Park, 2014). Although, it has been suggested that a network-based theory of cognitive ageing, examining age-associated effects on the neural networks across the brain, should be considered as an alternative (Braver et al., 2001; Greenwood, 2000). Still, structural changes are observed, which appear to cause less lateralised neural activation brain patterns in older individuals in comparison to their younger counterparts during the completion of a range of tasks (Cabeza et al., 2002). The causes of which will now be discussed.

Neuroanatomical changes and the consequential changes in neural activity are thought to be a result of a combination of factors. Structurally, these include the development of neurofibrillary tangles (NFT), the accumulation of beta-amyloid proteins in cells leading to their dysfunction, and the degradation of GM leading to brain atrophy. As well as increased occurrence of WHM lesions resulting in the disruption of WHM integrity and reduced WHM volume (Bäckman et al., 2006; Farokhian et al., 2017; Garnier-Crussard et al., 2020; Giorgio et al., 2010; Gunning-Dixon et al., 2009; Gunning-Dixon & Raz, 2000; Liu et al., 2017; Raz, 2004; Salat et al., 1999). On the neural level these include reduction in the insulating myelin

sheets of neurons, reduced neural specificity and synaptic loss, decreased levels of dendrites, reduced metabolic activity, reduced neuronal size, and decreased responsiveness of neurotransmitters. Plus neuronal death leading to diminished neural signals and reduced intra- and inter- communication (Salehi & Swaab, 1999). So, it can be seen that advanced age results in the deterioration of brain tissue and the subsequent neural networks it contains.

In more detail, reduction of GM volume [the region of the central nervous system consisting of cell bodies, dendrites, and axon terminals (Liu et al., 2017)], is believed to begin during the twenties, continuing on a linear trajectory until our fifties before leveling off in later life (Ge et al., 2002). GM regions are heavily interconnected with other brain regions, so volume deficits lead to impairment in the transmission of information via WHM tracts, as these regions are the information processing sites of the brain. GM loss has been reported to occur predominantly in the PFC and regions heavily connected with it such as the striatum and thalamus (Crivello et al., 2014; Farokhian et al., 2017; Giorgio et al., 2010; Ramanoël et al., 2018; Tisserand et al., 2004; Tisserand & Jolles, 2003a, 2003b). Accordingly, age-associated cognitive decline, particularly in attentional processes via the fronto-parietal network has been reported (Koini et al., 2018; Ramanoël et al., 2018; Tisserand et al., 2004). Similarly, decline in semantic memory, although relatively small, has been associated with decreased GM integrity (Koini et al., 2018; Ramanoël et al., 2018; Tisserand & Jolles, 2003a, 2003b).

Decline in WHM volume (the structures containing myelinated axons required for effective transmission between cortical and subcortical areas, i.e. GM regions) occurs at a different rate to GM (Liu et al., 2017; Xie et al., 2016). It increases during adulthood until the mid-forties before deterioration commences at a significantly greater rate than seen with GM (Cabeza et al., 2009; Ge et al., 2002; Miller & Corsellis, 1977; Salat et al., 1999; Salthouse, 2011a). Therefore, WHM is understood to be more susceptible to ageing. Reduced integrity of the WHM tracts and an increased proportion of microlesions in the frontal cortex and the corpus callosum results in increased disconnect in neural transmission with other cortical and subcortical regions (d'Arbeloff et al., 2019; Gunning-Dixon et al., 2009; Harada et al., 2013; Raz et al., 1998; Raz & Rodrigue, 2006). Such disconnect results in reduced processing speed of information (Birdsill et al., 2014; Bolandzadeh et al., 2012; Gunning-Dixon et al.,

2009; Gunning-Dixon & Raz, 2000; Madden et al., 2010; Raz, 2000; Raz et al., 1998; Salami et al., 2012; Turken et al., 2008) which is largely observed as increase in response times (RTs) of older adults whilst completing tasks in comparison to younger adults. As witnessed in the behavioural study described in Chapter 3. Additionally, due to reduced WHM volume in the hippocampus-fornix, decline in episodic memory has also been reported (Fletcher et al., 2013; Gunning-Dixon & Raz, 2000; Persson et al., 2006).

Regarding changes in neural networks, of importance is the reduced distribution of dopaminergic signaling in the PFC, and the depletion of dopamine receptors, especially in the caudate and putamen of the dorsal striatum. Collectively it has been implicated in the slowing of motor functions and decline in cognitive processes including EFs, particularly in learnt reward behaviour (Bäckman et al., 2006; Band et al., 2002; Cabeza et al., 2009; Deary et al., 2009; Grady, 2012; Head et al., 2008; Nyberg et al., 2012; Raz & Rodrigue, 2006; Zanto & Gazzaley, 2019). Moreover, reduced dopamine distribution and its signaling in the hippocampus has been linked to decline in episodic memory (Abdulrahman et al., 2017).

5.3.1 Consequences of Neuroanatomical Deterioration

Owing to the changes described in the last section, studies (Abdulrahman et al., 2017; Cabeza et al., 2002; Grady, 2012; Grady et al., 2006; Grady & Craik, 2000; Koen & Rugg, 2019; Park et al., 2001; Park & Reuter-Lorenz, 2009; Reuter-Lorenz & Park, 2014; Rypma et al., 2001; Rypma & D'Esposito, 2000) have indicated there to be a degree of loss of brain function due to disruption to neural networks between brain regions in older adults, especially those involving the PFC. It is assumed older individuals would have difficulty performing tasks requiring the affected cognitive processes, particularly of high complexity, in comparison to younger individuals, as decreased brain activity is associated with poorer performance. However, this is not always the case. There is the concept of compensation, where older individuals have been observed to have increased brain activity and/or greater functional connectivity[1] in the same brain region or in a different region entirely, in comparison to younger individuals. Three types have been theorised, compensation by upregulation, by selection, and by reorganisation (Cabeza et al., 2018; Grady et al., 2016;

[1] the connectivity between brain regions that share functional properties.

Phillips & Andrés, 2010). However, it is unknown under which circumstances which of these processes is active.

Upregulation refers to the enhancement of the same neural processes in older adults utilised by younger individuals when performing the same task(s). However, in younger individuals it is only thought to occur when there is an increase in task complexity and/or demand. Resulting in increased neural activity, predominantly in the frontal regions, until a particular threshold at which point activation asymptotes and eventually declines. This asymptote point is thought to represent the limit of available neural resources, thus eventual decline in neural activity represents the end in cognitive performance following the end of available resources. Older adults are reported to possess a lower asymptote of available resources than their younger counterparts (Cabeza et al., 2018).

The next type, selection, is based on delocalisation (Bishop et al., 2010) in that older adults are able to recruit secondary neural networks for cognitive processes that are also available but not utilised by young adults to complete the same task. The premise is that young adults use more efficient and demanding cognitive processes to complete tasks whereas older adults may use less efficient and demanding ones. Though, it is not known precisely which regions these may be or under what condition(s) this transpires (Cabeza et al., 2018).

The last theory, reorganisation, is based on plasticity, in that due to neural loss, older adults utilise neural mechanisms not accessible in younger brains through the creation and/or replacement of neural resources. This may possibly explain the bilateral brain activity patterns regularly observed in older brains during task performance as compared to the unilateral activation typically observed in young adults (Cabeza et al., 2018).

Thus, although age-associated neuroanatomical and neural network changes take place in older adults, performance of cognitive tasks may not be affected or be affected less than would be expected by the 'amount' of neural damage, due to neural compensatory processes. In the behavioural study presented in Chapter 3, the older adults performed comparably with the young adults in some of the tasks. Based on these theories it is hard to speculate the compensatory strategy. Nevertheless, upregulation may possibly have been used during dual-task (DT) and updating performances as age effects were observed in the more difficulty/complex tasks.

In the performance of the easier DT, during the simultaneous presentations of two tasks, the older adults performed comparable with their young counterparts in the psychological refractory period (PRP) paradigm (Pashler, 1984; Telford, 1931; Welford, 1952) and test for everyday attention (TEA) telephone code search DT (Robertson et al., 1994). However, during the PRP stimulus onset asynchrony (SOA) of 1000ms (the PRP effect: difference between the SOA0ms and 1000ms performance), where a delay between presentations was incorporated, an age-associated effect was observed. Similarly, updating ability was not shown to have an age effect with the easier backwards digit span (BDS) task (Baddeley & Hitch, 1974) but did with the harder n-back task (Jaeggi et al., 2010; Kirchner, 1958). Thus, it suggests the older adults had a lower asymptote point which was reached during performance of the more demanding tasks, while using the upregulation process.

Performance in the trail making test (TMT) (Reitan, 1992) was also comparable after elimination of the low-performing participants from both age groups. The remaining older adults may have compensated by using the reorganisation of neural pathways to successfully complete that task, whereas the brains of the bad performers had not effectively accomplished this.

The older adults' performance in the remaining tasks, the Stroop (Golden, 1978), Hayling sentence completion task (HSCT) (Burgess & Shallice, 1997), and task switching task (Rogers & Monsell, 1995) showed an age effect with longer RTs and/or error rates. Thus, they were able to complete the tasks by utilising a compensatory mechanism, although it is hard to speculate which of the three processes was employed.

Studies examining the differences in the neuroanatomical activity between young and older adults during performance of these tasks and the remaining EF tasks completed in Chapter 3 are discussed in sections 5.4.1 to 5.4.4.

In summary, older adults are thought to employ a compensatory process such as upregulation, selection, or reorganisation, when performance of the same task as young adults is comparable. Such performance was observed in the older adults of the behavioural study presented in Chapter 3 however, it is difficult to speculate which process was used by these participants, as it may be individually driven, or task driven.

5.3.2 MCI, AD, and the Neural Networks

MCI, and specifically AD affects neural networks differently than what is observed with ageing as a result of more advance neuroanatomical changes. One of the regions especially affected in these conditions is the limbic network. This is a non-unitary memory processing system where the PFC is understood to be the controlling centre for episodic memory processing through connections with the MTL, thalamus, retrosplenial cortex, and the PCC, to form the memory neural network (Bubb et al., 2017; Rugg et al., 2002; Rugg & Vilberg, 2013; B. Yuan et al., 2016). Changes to it are relatively mild in cognitively healthy older adults, however in MCI and AD deficits are more pronounced and of a greater extent as severity of AD increases.

Accumulation of NFTs over what is seen in healthy older individuals in limbic structures within the MTL has been observed in both conditions (Braak & Braak, 1991). In MCI, structural changes include decrease in WHM integrity in the MTL, the splenium of the corpus callosum and fornix (Zhuang et al., 2010), GM atrophy in the hippocampus, and hypometabolism in the inferior parietal lobules (Schroeter et al., 2009). Thus, increased neural activity in the posterior region of the MTL and fusiform have been observed as compensatory mechanisms to offset the atrophy in the anterior MTL (Han et al., 2009). Additional hypometabolism in the PCC and the precuneus are observed in both MCI and AD (Bailly et al., 2015). In AD, further changes outside of this network are observed including hypometabolism in the frontal cortex, amygdala, temporoparietal cortices (Nestor et al., 2003), and the frontomedian-thalamic network (Schroeter et al., 2009). These are areas concerned with the processing, controlling and performance of EF tasks. Hence, deterioration in these regions would affect EF ability.

The main difference between the conditions is that individuals living with MCI are usually able to perform EF tasks to relatively the same degree as healthy older adults but have an above average level of episodic memory impairment. However, these individuals may be able to compensate for such memory deficits through one of the processes described in the last section. This is not the case in AD individuals due to a greater amount of neural damage in the PFC and MTL, there is reduced opportunity for compensation. So as AD progresses effectivity in EF performance declines (Prvulovic et al., 2005). The following section will

discuss how the EF abilities DT, inhibition, shifting, and updating are affected by cognitive ageing, MCI, and AD.

In sum, this section covered how brain changes and decline in the limbic network leads to episodic memory problems in individuals living with MCI and AD. The following will describe how such changes affect the neural networks in relation to EFs.

5.4. The Neuroanatomy and Neural Networks of Executive Function Abilities

EFs enable the completion of an assortment of complex cognitive behaviours through the recruitment of other brain regions. In this section, the brain regions identified by neuroimaging to be primarily associated with the performance of DT, inhibition, shifting, and updating are examined. This will include how deterioration of these regions due to healthy ageing and the conditions MCI and AD affects the performance of these cognitive abilities.

5.4.1 Dual-tasking

The brain regions and thus neural networks believed to be involved in the process of dual-task (DT), performance, have been understood to be dependent on the tasks employed (Szameitat et al., 2011). Typically DT performances are believed to utilise the same cerebral regions activated during the performance of the same two tasks separately, however, it has been observed that there are additional newly activated regions (D'Esposito et al., 1995; Klingberg, 1998; Szameitat et al., 2002).

Nevertheless, irrespective of the task paradigm employed, several neuroimaging studies have consistently shown neural activation in the same regions (Chmielewski et al., 2014; Collette & Linden, 2002; D'Esposito et al., 1995; Dux et al., 2006; Hartley et al., 2011; Herath et al., 2001; Hesselmann et al., 2011; Jiang & Kanwisher, 2003; Klingberg, 1998; Schubert & Szameitat, 2003a; Sigman & Dehaene, 2008; Stelzel et al., 2008; Szameitat et al., 2002, 2006, 2016; Worringer et al., 2019; Yildiz & Beste, 2015). These include the right, left, or bilateral hemisphere of the lateral PFC (lPFC) (Broadmann Areas - BAs 9, 10, 44, 45, and 46), specifically the DLPFC (BAs 9 and 46), the parietal areas (BAs 7, 40), and supplementary motor areas (SMA - BAs 6, 8) (Collette, Olivier, et al., 2005; D'Esposito et al., 2000; D'Esposito & Postle, 2015; Hartley et al., 2011; Shi et al., 2014; Stelzel et al., 2008, 2009;

Szameitat et al., 2002), see Figure 5.3. These regions form part of the fronto-parietal network (Mezzacappa, 2011; Ptak et al., 2017).

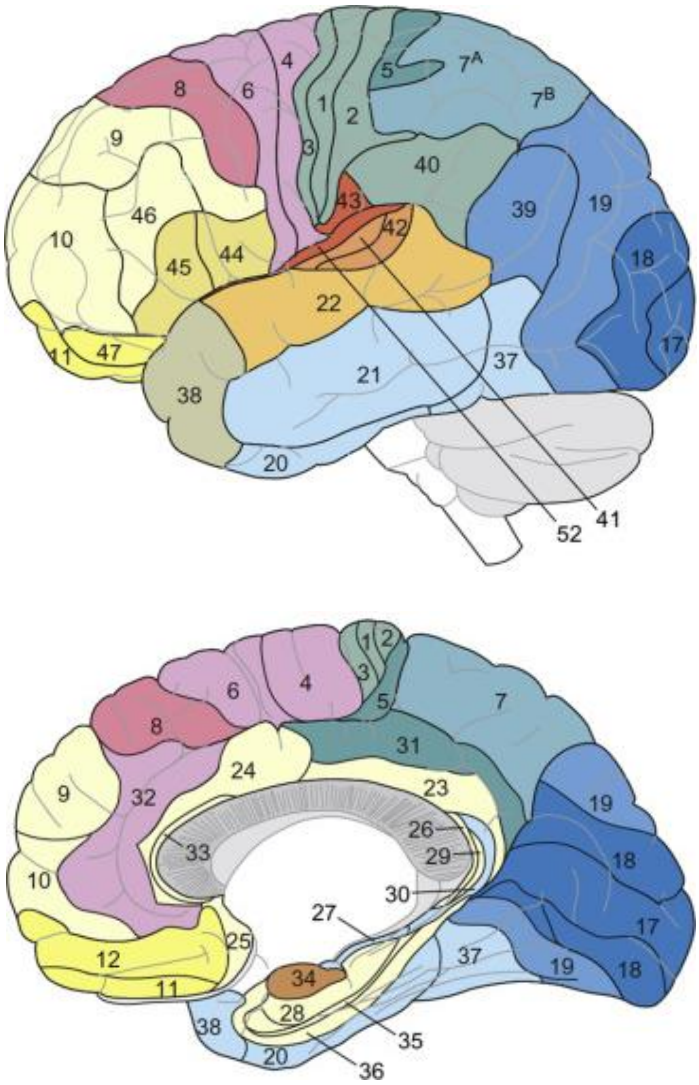


Figure 5.3. Brodmann Areas of the left hemisphere of the Human Brain. A Brodmann area is a region of the cerebral cortex characterised by its cytoarchitecture, i.e. its histological structure and cell organisation. The first figure represents the lateral view of the areas, and the second, the medial view of the areas (Gage & Baars, 2019).

Accordingly, substantial bilateral increase in activity in the DLPFC and the ACC during DT as compared to single-task (ST) performance has been attributed to the process of allocating and coordinating attentional resources and response selection, respectively (D'Esposito et al., 1995; Kondo, Osaka, et al., 2004). However, the cognitive subtraction method was employed in such analysis of neural activity which has been criticized for assuming that the processing engaged in ST was unaffected by the addition of a new task. Accordingly, Szameitat et al (2002) used this and the parametric manipulation to assess DT with the PRP

paradigm (Pashler, 1984; Telford, 1931; Welford, 1952). Neural activity in the lPFC along the IFS and in the MFG, and parietal cortices including the intraparietal sulcus were associated with DT performance. This has also been reported by numerous other researchers (Dux et al., 2006; Herath et al., 2001; Hesselmann et al., 2011; Jiang & Kanwisher, 2003; Schubert & Szameitat, 2003b; Stelzel et al., 2006, 2008; Szameitat et al., 2006, 2016; Yildiz & Beste, 2015).

DT coordination has also been proposed to require the interactions of numerous specific information-processing networks (Adcock et al., 2000). Such regions and therefore networks, include the temporal areas (BA 37), anterior insula (BA 47), ACC (BAs 24/32), posterior areas such as the cuneus (BAs 18 and 19), basal ganglia, thalamus, premotor cortex, anterior insula, and the cerebellum (Chmielewski et al., 2014; Collette & Linden, 2002; Hartley et al., 2011; Hesselmann et al., 2011; Klingberg, 1998; Schubert & Szameitat, 2003a; Sigman & Dehaene, 2008; Szameitat et al., 2002, 2016; Worringer et al., 2019; Wu et al., 2013).

Neuroimaging studies involving participants with frontal lesions have further highlighted the association of brain regions and DT performance with the use of different DTs, particularly the frontal lobes (Della Sala, 1997; McDowell et al., 1997). Richer et al (1998) reported unilateral frontal and temporal regions as areas of interest. Whilst, Andrés & Van Der Linden (2002), Casini & Ivry (1999), and Vilkki et al (1996) associated DT performance with the DLPFC and medial regions, and Roca et al (2011) identified BA 10 as a specific region for multitasking performance.

As a result of ageing, differences in performance and neural activity are anticipated in older individuals as postulated by the frontal ageing hypothesis (Geerligs et al., 2014; Raz et al., 2005; West, 1996; P. Yuan & Raz, 2014). The PFC, striatium (basal ganglia), and its connections, i.e. the fronto-striatal network, undergo changes during the ageing process, which is implicated in the dopaminergic system. Changes to it have been found to contribute to DT deficits due to the depletion of dopaminergic receptors in the frontal cortex (Goh & Park, 2009).

In examining how ageing affects performance with the use of the PRP paradigm as described in Chapter 3 of this thesis, Hartley et al (2011) reported similar neural activity

between young and older participants. Such activation related to neural activity in the medial prefrontal network and lateral frontal–parietal network. Although the older adults presented with increased activity in the aPFC and occipital regions. Using the same paradigm, Chmielewski et al (2014) reported alterations in the networks involving the MFG, SFG and the anterior insula with increased task complexity, i.e. decreased SOA, during performance of their older adults. Thus, both studies indicate compensatory neural activity is involved in DT ability in older individuals with performance in the PRP task.

With the TEA telephone code search task DT, no study was found to have examined the neuroanatomical correlates of performance in either young or older adults. However, it possesses similar task conditions, i.e. auditory and visual, as the PRP. Hence, it is conceivable that the same brain regions involved in these processes might be similarly activated in both age groups. Although as the overall requirements of both DTs are quite different, the specific brain regions activated during the TEA DT is unknown.

Similarly, there was no study found to have determined how neural activity is affected by cognitive DT ability in MCI individuals. However, it is known that severely impaired individuals including AD sufferers are mostly incapable of performing these tasks, probably due to the advanced atrophy observed in the brain (Baddeley et al., 1991; Lonie et al., 2009).

To conclude, through neuroimaging studies the fronto-parietal network which contains the DLPFC, SMA and ACC, with projections to other cortical and subcortical structures, has been shown to be the associated with DT processing. Nevertheless, as a result of structural changes, such as GM atrophy in these regions, the performance of cognitively healthy older adults and individuals living with MCI may be affected. No study was found to have evaluated the neural activity of DT in AD participants, however.

5.4.2 Inhibition

In response inhibition, i.e. the suppression of dominant or prepotent processes (Miyake, Friedman, et al., 2000), neural activity is largely considered to be associated with the right hemisphere of the brain, particularly the right VLPFC, i.e. right inferior frontal cortex and right IFG (BAs 44 and 45) (Aron, 2007; Aron et al., 2014; Aron, Robbins, et al., 2004; Bender

et al., 2016; Blasi et al., 2006; Chikazoe, 2010; Derrfuss et al., 2004; Fisk & Sharp, 2004; Garavan et al., 1999; Hazeltine et al., 2003, 2000; Hughes et al., 2013; Konishi et al., 1999; Konishi, Nakajima, Uchida, Sekihara, et al., 1998; Lemire-Rodger et al., 2019; Rubia et al., 2003; Stuss & Alexander, 2000). Increased activity of the IFG was commonly identified in several studies with healthy participants during the incongruent condition of a number of inhibition tasks. These include the utilisation of the go/no-go task (Newman & Kosson, 1986), irrespective of the handedness of the individual as the researchers considered it may be a factor (Konishi et al., 1999; Konishi, Nakajima, Uchida, Sekihara, et al., 1998), the flanker task (Eriksen & Eriken, 1974; Hazeltine et al., 2000, 2003), and the stop-signal task (M. E. Hughes et al., 2013; Logan et al., 2014). While Derrfuss et al (2004) reported the inferior frontal junction (IFJ) area, the posterior frontolateral region around the junction of the IFS and the inferior PCS were important for cognitive control. However, Hampshire et al (2010) with the use of the stop-signal task, found that this region performed a more generalised role in executive functioning and not just during inhibition.

Additional significant regions of activation have been reported. These include other frontal areas, the right MFG (BAs 9 and 46) within the DLPFC, and the ACC, as well as bilaterally in the anterior insula, presupplementary motor area (pre-SMA), the frontal limbic and inferior parietal regions, the left area of the temporal lobes, and an area within right occipital lobe (Ball et al., 2011; Banich et al., 2000; Baumeister et al., 2014; Blasi et al., 2006; Chambers et al., 2009; Durston et al., 2002; Garavan et al., 1999; Gruber et al., 2002; Kolodny et al., 2017; Konishi, Nakajima, Uchida, Sekihara, et al., 1998; Konishi et al., 1999; Mostofsky & Simmonds, 2008; Rubia et al., 2003; Steele et al., 2013; Swick et al., 2011). These regions were also identified by Wager et al (2005) with the go/no-go, flanker, and stimulus–response compatibility[3] (Wager et al., 2005) tasks. Common activated regions such as the anterior insula and aPFC bilaterally, the right DLPFC, left caudate, posterior intraparietal sulcus, right anterior intraparietal sulcus, and ACC were reported.

Although, Banich et al (2000) had previously reported activation differences with the use of two versions of the Stroop task the traditional colour-word (Stroop, 1935), and a spatial-word task (Banich et al., 2000). With the traditional task, substantial activity was observed in

[3] Task involves the presentation of an arrow stimulus in the centre of the screen. In the compatible block, participants must respond in the direction of the arrow, and in incompatible block, in the opposite direction.

the ACC bilaterally, in the inferior and middle frontal cortices, and the left precuneus of the parietal lobe, thus employing the classic fronto-parietal network. Whereas the spatial-word task caused significant activity in the medial frontal, left middle frontal, part of the parietal cortex bilaterally, and the left regions of the superior temporal and middle temporal regions. Therefore, it is important to take into account the task used when examining neural activity. Nevertheless, it can be observed that the fronto-parietal network is heavily used during inhibition. Further, dopamine is thought to play a significant role, and reported to be released during task performance (Albrecht et al., 2014; Badgaiyan & Wack, 2011; Hershey et al., 2004; Logue & Gould, 2014).

Frontal lobe lesion studies have also indicated that the frontal regions mentioned above may be important in the processing of inhibitory control (Dimitrov et al., 2003; McDowell et al., 1997; Rieger et al., 2003), especially the left medial frontal lobes (McDonald et al., 2005). However, as discussed above, the areas differed with various inhibition tasks and were not limited to the frontal cortex, as the basal ganglia have been indicated to be involved (Andrés & Van Der Linden, 2002; Rieger et al., 2003). Nonetheless, the DLPFC, particularly the left side has been implicated in its performance (Andrés & Van Der Linden, 2002; Stuss et al., 2001). Other regions observed to be important include the medial orbitofrontal cortex (gyrus rectus) (Szatkowska et al., 2007), right anterior cingulate (BAs 24 and 32) (Di Pellegrino et al., 2007; Picton et al., 2007), left BA 6, and the right BAs 9 and 32 (Dimitrov et al., 2003; R. E. Roberts & Husain, 2015). Though activity in the right VLPFC (BAs 44, 45 and 47) (Godbout et al., 2005; Picton et al., 2007) has also been associated.

A variety of studies has shown that ageing affects the functional neuroanatomical correlates of inhibition (Bloemendaal et al., 2016; Coxon et al., 2012, 2016; Elderkin-Thompson et al., 2008; Kleerekooper et al., 2016; Langenecker et al., 2004; C. Li et al., 2009; Milham et al., 2002; Nielson et al., 2002; A. Sebastian et al., 2013).

In comparing young with older adults' performance with the traditional Stroop task as employed in the behavioural study in Chapter 3, age-associated decrease in neural activity in the fronto-parietal network regions, i.e. DLPFC and parietal lobes were reported. This suggested decreased attentional control. Whereas increased activation of the anterior inferior prefrontal cortices including the IFG and MFG, pre-SMA, and the precuneus and

ventral visual processing regions within the temporal cortex were observed (Langenecker et al., 2004; Milham et al., 2002). These findings suggest compensatory mechanisms were occurring in the older individuals to complete inhibition. Additionally, superior performance was associated with greater recruitment of the ACC in older participants (Elderkin-Thompson et al., 2008).

Similar age-associated effects were reported by Nielson et al (2002) with the use of the go/no-go task. Greater activity was mainly observed in the PFC, right MFG, and in numerous left frontal regions. These left frontal regions not commonly mentioned in studies with healthy young individuals may indicate either a selection or reorganisation compensatory mechanism occurring. Comparable activation was observed in other regions, such as the right MFG, left middle and inferior gyri, left putamen, bilateral caudate, thalamus and pre-SMA, although enhanced neural activity was seen in the older adults.

Likewise, Sebastian et al (2013), found with the go/no-go, Simon (Simon, 1969), and stop-signal tasks, that increased age correlated with enhanced activation in left prefrontal regions including the IFG and MFG, and parietal regions. However, decreased activity was observed with the most challenging stop-signal task indicating that a threshold for compensatory involvement may have been encountered. Nonetheless, Kleerekooper et al (2016) reported hyperactivation of the right IFG, and Bloemendaal et al (2016) included the DMPFC, i.e. pre-SMA, and basal ganglia (striatum, subthalamic nucleus) regions with performance in this task in older participants. Such enhanced neural activity has been attributed to reduced WHM integrity of subthalamic nucleus (STN) projections, important in dopaminergic neurotransmission (Bloemendaal et al., 2016; Coxon et al., 2012, 2016). Decrease in GM in the frontal cortex is also associated with decline in inhibitory ability (Adollfsdottir et al., 2014).

No study was found to have assessed the neuroanatomical correlates of the second task used in the behavioural study, the HSCT (Burgess & Shallice, 1997) in older adults. However, in young adults, the left IFG (BAs 45/47) was reported to be activated during performance in part A. Whereas in part B, increased activity in the left prefrontal regions, such as the middle (BAs 9 and 46) as well as in the IFG (BA 45) frontal areas, and bilaterally in the IFG (BA 47) (Collette et al., 2001) was reported. Thus, it may be speculated that bilateral activity of the

left activated regions and increased activity of the bilaterally activated regions may take place in older adults.

Decline in inhibition ability in individuals living with MCI is well documented (Ahn et al., 2011; Apostolova et al., 2012; Bélanger et al., 2010; Bélanger & Belleville, 2009; Borella et al., 2017; Borsa et al., 2018; N.-C. Chen et al., 2013; Garcia-Alvarez et al., 2019; Grönholm-Nyman et al., 2010; Johns et al., 2012; C. Li et al., 2009; Mudar et al., 2016; Pa et al., 2010; Peltsch et al., 2014; Puente et al., 2014; Stricker et al., 2013; Sung et al., 2012; B. Yuan et al., 2016; Zheng et al., 2012, 2014; Zhou & Jia, 2009), although there are not many neuroimaging studies. In a study by Alichniewicz et al (2013) between amnestic MCI (aMCI) participants and healthy older individuals, decreased neural activity was observed in the frontal eye fields in aMCI participants with the employment of the antisaccade task. It was therefore concluded to indicate reduced frontal lobe activity. Between the healthy young and older adults decreased activation was only observed in the parietal lobe. However, Fernandez-Ruiz et al (2018) with the same task, observed increased activity in the DLPFC and in the frontal pole in their healthy older adults which was correlated with better inhibitory control and faster RTs, respectively.

With the Stroop task, Kaufmann et al (2008) reported heighten activity in the caudate and cerebellum during interference processing in MCI participants. Whereas Puente et al (2014) witnessed hyperactivity in the DLPFC, OFC, and PCC during task performance, within the fronto-parietal network. The activity in the OFC and PPC correlated with increased RTs between the congruent and incongruent task conditions. The differences in the studies may indicate a difference in the severity of cognitive impairment in these participants, or merely a difference in the task demand and processing in the MCI brain.

Also, Li et al (2009) reported significantly heightened activity in the basal ganglia, dorsal ACC (dACC), and fronto-parietal regions, bilaterally in the middle and IFG, inferior parietal lobule and insula in their MCI participants with the Stroop task. However, decreased activity in these same regions in AD participants indicated the compensatory mechanism available to MCI individuals through the availability of more healthy brain regions. Thus, this did not occur in the AD brain due to increased neuroanatomical damage, such as advanced GM atrophy, and reduced WHM integrity.

In summary, the neuroanatomical processing of inhibition has reported to be heavily linked to the right VLPFC, particularly the right IFG, with projections to other regions including the right MFG and ACC. Due to ageing, reduction in WHM integrity and the efficiency of the dopaminergic system, decline in inhibition activity is observed. Thus, higher activity as compared to young has been reported to take place in the left hemisphere of the PFC as a compensatory process to counteract the reduced efficacy of the right hemisphere. Similar effects occur in MCI individuals but seem to be based on the severity of the condition, although hyperactivity has also been described to compensate impaired functional activity. However, no such mechanism is observed in AD participants, as the structural changes, comprising GM atrophy, are more pronounced. Although these individuals are still able to perform the tasks of this ability to some degree.

5.4.3 Shifting

The functional neuroanatomical correlates of shifting ability, the process of alternating between tasks or mental sets (Miyake, Emerson, et al., 2000) in healthy young individuals is reported to depend largely, as with DT and inhibition, on fronto-parietal structures. Primarily the left IFJ, DLPFC, posterior intraparietal sulcus, areas associated with the VLPFC, precuneus, the dACC, parietal lobe and the occipital lobe, are more consistently considered to be activated during shifting conditions (Brass et al., 2005; Brass & Cramon, 2002, 2004; Braver et al., 2003; Collette & Linden, 2002; Dove et al., 2000; Fellows & Farah, 2003; Carl Kim et al., 2017; Chobok Kim et al., 2011; Chobok Kim, Johnson, et al., 2012; Kimberg et al., 2000; Konishi, Nakajima, Uchida, Kameyama, et al., 1998; Lemire-Rodger et al., 2019; Ruge et al., 2013; Sohn et al., 2000; Von der Gablentz et al., 2015; Worringer et al., 2019).

In a study by Konishi et al (1998), shifting activity was localised in the IFS bilaterally, with the application of the Wisconsin Card Sorting Test (WCST) (Berg, 1948; Nelson, 1976), but Kimberg et al (2000) with a task switching paradigm (Kray & Lindenberger, 2000), reported several activated regions. These included the right hemisphere regions, postcentral gyrus (BA 3), inferior parietal lobule, and thalamus, and left regions, the PCG, medial frontal (BA 6), precuneus (BA 7), anterior insula, and medial occipital gyrus. So, the type of shifting task may influence the regions of precise activation during the task shifting condition (Chobok Kim, Cilles, et al., 2012). Although, Muhle-Karbe et al (2014) reported that only the ACC

seems to be associated with the use of different tasks, implying its involvement in preparatory adjustments for particular task demands.

Moreover, with the task switching task, Sohn et al (2000) identified the right lPFC (BAs 45 and 46) and superior PFC (BA 8), the superior and inferior posterior parietal cortex areas, right temporal area (BA 22), PCC (BA 31), and right occipital cortex (BA 19). More explicitly, Dove et al (2000) further reported the SMA, pre-SMA, cuneus/precuneus, and thalamus as regions activated during the task switching condition, in addition to the left intraparietal sulcus, and bilaterally in the lateral prefrontal, premotor cortex bilaterally, and anterior insula. Braver et al (2003), reported neural activity correlated with the left DLPFC, left VLPFC, left superior parietal cortex and left SMA during shifting trials, in comparison to the right medial aPFC, right lateral aPFC, and ventral ACC during repeat trials. This has also been reported in other studies (Lemire-Rodger et al., 2019; Wager et al., 2004; Worringer et al., 2019). Thus, the lPFC and parietal regions play fundamental roles in the process of shifting as well as numerous cognitive processes. Brass & Cramon (2002 and 2004) and Brass et al (2005) further reported that the left IFJ, right IFG and the right IPS are involved in task preparation and is the same for repetition and shift trials in paradigms with a high percentage of shifting trials. Also, a positive correlation in GM-WHM contrast in the left VLPFC, bilateral MFG in the DLPFC, and SFG, are considered to be indicative of good structural integrity of these regions, and thus performance (Carl Kim et al., 2017).

In addition, Von der Gablentz et al (2015) reported an interesting finding after observing activity at the locus coeruleus, an area near the brainstem. It was found to be the main source of noradrenaline, a neurotransmitter used as a circulatory hormone and a chemical neurotransmitter (Baars & Gage, 2010). Noradrenaline, as well as dopamine, can modulate action, reward, learning, memory, and vigilance processes, and so are thought to contribute to the regulation of cognitive flexibility (Baars & Gage, 2010; Ranjbar-Slamloo & Fazlali, 2020; Ruge et al., 2013). Thus, the activity was indicated to be involved in focusing attention and disconnecting from a behavioural irrelevant task, and task optimisation.

Frontal lesion studies have further correlated these brain regions with shifting performance (McDowell et al., 1997). Though some identify right and left frontal processes (Baldo et al., 2001) others suggest only involvement of the left frontal lobe (Kumada & Humphreys, 2006). More specifically, the lPFC, left inferior posterior PFC, right IFG/pars opercularis, left

MFG, and medial orbitofrontlal cortex have also been associated (Aron, Monsell, .et al., 2004; Gehring & Knight, 2002; Szatkowska et al., 2007; Yochim et al., 2007). As well as the basal ganglia (Mukhopadhyay, Pritha, Aparna Dutt et al., 2007; Yehene et al., 2008).

Age-related performance decline and its associated activation differences have been described in shifting ability (DiGirolamo et al., 2001; Gazes et al., 2012; Gold et al., 2010; Hakun et al., 2015; Jimura & Braver, 2010; Jolly et al., 2017; M. E. Perry et al., 2009; Smith et al., 2001; Z. Zhu et al., 2014). However, the neural mechanism for this decline is uncertain. Larger areas of activation in the PFC have been reported during task shifting performance in older adults (DiGirolamo et al., 2001; Hakun et al., 2015; Smith et al., 2001), particularly in the DLPFC (BA 46) and MFC (BAs 6, 24 and 32), where increased connectivity between the left DLPFC, ventral visual cortex, and temporal lobes has been correlated with better task performance in older individuals. In comparison, young adults are seen to have less widespread connectivity. Thus, this activity is thought to be compensatory, as the recruitment of areas within the left hemisphere of the PFC has also been reported in poor performing young adult participants (Smith et al., 2001).

However, decreased activity in the PFC and the PCG, but increase in the posterior brain regions, such as the occipital lobe and the cerebellar areas linked with visual and motor processes, respectively, have similarly been seen (Gazes et al., 2012; Jimura & Braver, 2010). This alternative finding is believed to indicate age-associated disruption of PFC aided processes and the utilisation of new strategies during task performance (Gazes et al., 2012; Jimura & Braver, 2010).

Gold et al (2010) described increased task completion times with their older adult group whilst performing a letter-number task. This was associated with decrease in activity in regions activated in younger individuals in predominantly left fronto-parietal regions, the DLPFC (BA 46), left anterior and posterior inferior prefrontal cortex (BAs 44, 45 and 46), ACC (BAs 24/32), inferior parietal cortex (BAs 7/40), and the caudate and putamen. This was attributed to reduced WHM integrity. Additional recruitment of regions not observed in the younger adult group was reported in the left middle temporal cortex (~BA 22) and right aPFC (~BA 45).

In contrast, findings from Zhu et al (2014) reported increased activity in all four lobes, but especially in the fronto-parietal regions, the right DLPFC and right insula in older adults, which was linked to a reduction in WHM microstructure and increased RTs, respectively with performance in the task switching paradigm (Rogers & Monsell, 1995). This directly relates to the significant increase in local and global shift RT cost of the older participants in Chapter 3. Although increased activation of these regions correlated with slower shifting performance in both older and young adults. Therefore, it has been suggested that age-associate decline in task shifting performance may be caused by a combination of structural changes to global and tract-specific, specifically fronto-parietal, cerebral WHM leading to reduced WHM integrity. Which Gold et al (2010) reported to contribute to increased RT costs in older adults. This has been linked to changes in the cardiovascular system in older individuals (Jolly et al., 2017; M. E. Perry et al., 2009). Further, Jimura & Braver (2010) found that while younger adults displayed a cue-related response while completing task-switch trials in lPFC and PPC, the older adults only had activity in the PPC. Also, during shift blocks, the older adults displayed decreased activity in the aPFC and temporary increased activity during shift trials. Hence, Hakun et al (2015) reported compensatory increased activity between the left DLPFC region and ventral visual cortex. Accuracy performance has been suggested to be localised to the bilateral precuneus, right MFG, and left lateral occipital cortex in young adults but in older adults to the left MFG, left frontal pole, left IFG, and middle and right cerebellum regions (Basak et al., 2018).

With the second task used in the behavioural study, the TMT, bilateral activity in the VLPFC and DLPFC, and engagement of the medial temporal lobe has been observed (L. D. Müller et al., 2014; Oosterman et al., 2010) has been observed. Increased RT in older adults of performance in part B has been associated with deterioration of white matter microstructure of the left anterior thalamic radiation, and the right uncinate fasciculus. As well as cortical thinning in the frontal, temporal, and inferior parietal regions, and the Sylvian fissure/insula (MacPherson et al., 2017). Reduced bilateral activity in the occipital, temporal, and parietal lobes was reported by Talwar et al (2020). L. D. Müller et al, (2014) reported additional activity in the left medial and lateral PFC.

Reduced GM in the frontal, temporal and inferior parietal regions, including the Sylvian fissure/insula have further been linked to decrease in mental processing speed (Adollfsdottir

et al., 2014; MacPherson et al., 2017). Additionally, accumulation of beta-amyloid deposits in the right PFC may contribute to decline in shifting control (Oh et al., 2016).

Performance deficits in individuals with cognitive pathological impairment have similarly been reported (Pa et al., 2010; Tsutsumimoto et al., 2015) where deterioration in GM is associated with poorer performance. In a study by Pa et al (2010), reduced GM volume of the PFC and posterior parietal cortices was observed to correlate with decline in shifting performance, i.e. greater completion time, in the D-KEFS Design Fluency (Delis et al., 2001), TMT (Reitan, 1992), and D-KEFS Colour-Word Interference task (Delis et al., 2001).

In sum, shifting ability in healthy individuals has been reported to be associated with increased activity in the VLPFC, DLPFC, though, the precise location seems to be dependent on the task utilised to assess shifting ability (Muhle-Karbe et al., 2014). As a consequence of healthy ageing, decline in WHM integrity is witness in these regions, and so increased activity is frequently observed at these same regions to compensate for structural impairment. Likewise, GM atrophy in the parietal, temporal and occipital lobes are also associated with shifting decline. These structural changes are further seen in MCI and AD participants, where it is linked to poorer task performance especially in more advance AD.

5.4.4 Updating

WM updating is primarily associated with the DLPFC (Barbey et al., 2013; D'Esposito, 2007; D'Esposito et al., 2000; D'Esposito, Ballard, et al., 1998; Wager & Smith, 2003), specifically the right DLPFC (Collette & Linden, 2002; D'Ardenne et al., 2012). Other regions implicated in its processing include the medial prefrontal cortex (mPC), particularly the DMPLC, VMPLC, dACC, and non-PFC regions, the basal ganglia, thalamus, and PPC (Nir-Cohen et al., 2019), regions involved in the fronto-parietal network (J. D. Cohen et al., 1997; Collette & Linden, 2002; D'Ardenne et al., 2012; D'Esposito, 2007; D'Esposito et al., 1999, 2000; D'Esposito, Ballard, et al., 1998; D'Esposito & Postle, 2015; Kondo, Morishita, et al., 2004; Lemire-Rodger et al., 2019; Murty et al., 2011; Nir-Cohen et al., 2019; Roth & Courtney, 2007; Salmon et al., 1996; Wager & Smith, 2003).

More precisely, load (task demand) is thought to be associated with activity in the DLPFC, task difficulty with the ACC, and non-updating demand activity and WM maintenance with

the parietal lobe (Barch et al., 1997; J. D. Cohen et al., 1997). Additionally, as previously reported with the other EFs, the dopaminergic system influences updating. Its signaling has been hypothesised to regulate the encoding of WM and thus updating, in the DLPFC (D'Ardenne et al., 2012).

Ball et al (2011) with the employment of the n-back, go/no-go, and Tower of London[4] (Shallice, 1982) tasks reported correlation in brain activity between all three tasks during the 2-back condition of the n-back task, bilaterally in the MFG. Thus, this area seems to be associated with updating.

Performance in the n-back and Tower of London tasks was also found to be sensitive to dopamine levels. Thus, it is important to be aware of the type of task utilised when examining neuroanatomical correlates of updating.

Numerous researchers have also utilised the n-back task (Jaeggi et al., 2010; Kirchner, 1958) to assess this EF (Derrfuss et al., 2004; Jansma et al., 2000; Nir-Cohen et al., 2019; Owen et al., 2005; Postle et al., 2000), in various forms, i.e. spatial, digit, verbal. The brain activity is related to its performance is understood to be independent of modality. In the meta-analysis by Owen et al (2005), six cortical regions were observed to be consistently activated with any type of n-back task. These included the DLPFC, mid-VLPFC, medial PPC, and inferior parietal lobules. These regions were similarly reported by Jansma et al (2000), with a spatial n-back task, and Postle et al (2000) were unable to report a difference in the frontal cortical activity associated with spatial and nonspatial WM, with the n-back task.

However, D'Esposito, Aguirre, et al (1998) reported activity of the left MFG (BA 46) with a nonspatial n-back task, and right MFG (BA 46) with a spatial n-back task, indicated the n-back activations are modality dependent. Similarly, with a different updating task, a so-called spatial (location) WM task, activity was correlated with higher activity in the right MFG (BA 46), whereas nonspatial WM was linked with bilateral activity in the MFG and left IFG (McCarthy et al., 1994, 1996). Also, Jansma et al, (2000) reported better performance with the spatial n-back was associated with a large area of load-sensitive activity in anterior

[4] Task requires participants to re-arrange three coloured balls from a start position to a target position, with the minimum number of moves.

cingulate, while a small area of load-insensitive activity was linked to the right parietal cortex.

Furthermore, Leung et al (2007) indicated that the process of updating and maintenance of spatial information may be similarly processed and the rostrodorsal premotor cortex and anterior IFG may play a significant role in the successful tracking of spatial information in WM.

In the assessment of verbal WM updating (task involving participants listening and then verbally recalling items, e.g. consonants) significant increases in cerebral blood flow were observed in the same common regions identified to be involved in non-verbal updating, such as the DLPFC [right MFG (BA 9) and MFG (BA 46)], the right frontopolar cortex (BA 10), right inferior parietal and angular gyri (BAs 40/39), and left supramarginal gyrus (BA 40) (Salmon et al., 1996). This included newly seen activity in the left MFG (BA 10), right thalamus, cuneus/precuneus, cerebellum and in the superior occipital gyri (BAs 18/19), bilaterally, which seem specific for this type of updating task. Similarly, Van der Linden et al (1999), in the assessment of verbal WM, identified the DLPFC (BAs 9 and 46). Whilst, Derrfuss et al (2004) with the use of a verbal n-back task reported the involvement of the IFJ. Furthermore, Ravizza et al (2004) indicated that the ventral aspect of the inferior parietal cortex was involved in the shot-term storage buffers for verbal WM tasks. However, Ivanova et al (2018) reported in their study with two verbal tasks, a verbal n-back task and a complex span, that the temporal regions was more likely the site involved.

Moreover, R. Zhu et al (2020) found that when comparing performance of a visual and auditory letter 3-back task, the left PPC was associated with the visual task only. Therefore, the type of task stimuli should also be considered in evaluation of neural activity.

Additionally, Roth & Courtney (2007) identified similarities between updating visual sensory stimuli and of updating long-term memory (LTM) finding correlation in activation in regions including the left IFJ and left MFG of the frontal lobes, intraparietal sulcus, precuneus, and SMA/pre-SMA. Concluding a single fronto-parietal network for updating. The only difference observed was in the bilateral activation of the cuneus which was attributed to LTM recall (Murty et al., 2011). Thus, it can be concluded that updating relies on a combination of

frontal and non-frontal networks, which may also overlap with other memory processing networks, including LTM.

Through lesion studies, there seems to be involvement of the ventral and dorsal parts of lPFC (N. G. Müller et al., 2002), such as the left lPFC, medial prefrontal cortex, dorsal ACC and adjacent dorsal fronto-medial cortex (Tsuchida & Fellows, 2009), and lateral and posterior portion of the left SFG (Boisgueheneuc et al., 2006). However, the right frontal lobe may also be associated (Borgo et al., 2003), as well as the thalamus (Kubat-Silman et al., 2002).

Age-related decline in updating performance is thought to be a consequence of reduced network integrity and neuroanatomical changes in the brain that lead to a compensatory mechanism (Cabeza et al., 2018; Di et al., 2014; Rypma et al., 2001; Rypma & D'Esposito, 2000; Suzuki et al., 2018). Yaple et al (2019) completed a meta-analysis of studies comparing young, middle-aged, and older adult participants performance with the n-back task, one of the updating tasks utilised in the Chapter 3. Involvement of the WM regions, the parietal and cingulate cortices, were observed in all three groups, as well as in the non-WM regions, the claustrum, insula, and cerebellum. However, the activity within the DLPFC (e.g. BAs 9 and 10) was highest in the young participants, decreased in middle-aged adults, and absent in older adults, indicating a gradual decline in PFC engagement and WM activity with advancing age.

Qin & Basak (2020) also examined age-related differences with the use of an updating task that consisted of comparing a non-updating trial (current digit presented is the same as previous one) with an updating trial (current digit presented is different from the previous one). It was reported that young adult participants presented with significantly greater activity in the left PCG and the right cerebellum during performance in the updating trials. Decreased neural activity was observed in these regions in the young-old participants but was absent in the old-old participants. Furthermore, increased activity in the right PCG (a region linked with task sensitivity in young adults) and in some default mode network regions was seen in the old-old participants. It was concluded the overactivation in these regions was compensatory for the decrease in hemispheric specificity during updating trials. Thus, both these studies show how ageing causes a reduction in the efficiency of updating processes in the PFC.

With performance in the BDS task used in the behavioural study, in comparing bran activity between young and older adults, it has been reported that young adults exhibit greater activity in the left PFC (BA 9), and left occipital visual cortex, as well as activity in the right IFG. Whereas the older adults showed greater activity in most brain regions, the frontal, parietal, occipital, and temporal cortices, particularly in the right IFG (BAs 44/45) (Sun et al., 2005).

Decline in updating ability as a result of a neurodegenerative condition has also been reported. In examining the brain activity of the default mode network with the n-back task where decreased neural activity correlated with task performance, Rombouts et al (2005) observed activity differences in healthy old, MCI and AD participants. The healthy old participants showed decreased activity in the anterior frontal lobe, precuneus, and PCC, while the MCI showed decreased activity in these same regions but a lesser extent the healthy old and more than the AD participants. Activity in the anterior frontal lobe was greatly affected in the AD brain. The gradual decrease in activity of the default mode network from healthy to MCI to AD signifies the deterioration of the brain in these neurodegenerative conditions.

Migo et al (2015) assessed healthy and aMCI participants with the n-back task. Results for the healthy group were consistent with the studies already described for this group, for example, increased activity in the DLPFC, inferior parietal lobule, and lateral premotor cortex. However, the aMCI participants had fewer dispersed clusters and less significant activation, as well as reduced activity in the CC, IFG, MFG, and SFG. Increased activity in the right insula and lingual gyri was concluded to be a compensatory system. Nevertheless, Döhnel et al (2008) only reported significant increased activity in the right precuneus in their study on the updating of emotional WM in aMCI participants, which was attributed as a compensatory mechanism.

To summarise, updating ability has been reported to correlate with neural activity in the DLPFC, particularly the MFG, mid-brain structure such as the basal ganglia, thalamus and cuneus/precuneus, as well as parietal regions, collectively part of the fronto-parietal network. Other regions seem dependent on the type of WM task employed in updating assessment, i.e. nonverbal or verbal, thus temporal regions have been indicated to be involved in the processing of verbal WM tasks. Ageing resulted in compensatory activity in

the brain of older adults to offset decreased integrity of the networks usually involved in updating in younger individuals. Further deterioration and compensatory mechanisms were observed in MCI participants. AD participants seemed to produce less activity in response to updating task performance, demonstrating the reduced availability of healthy brain structures and networks to process such tasks.

5.5. Conclusion

In conclusion, this review demonstrated the importance of the PFC and its neural networks, specifically the fronto-parietal network and its vital role in the co-ordination of EFs. As a consequence of cognitive ageing and pathological impairment, neuroanatomical changes and hence disruption to the connections between the various cerebral regions associated with these changes are seen. Thus, the compensatory processes to counteract these changes were described and included a discussion on which of the processes may have been used by the older adults presented in Chapter 3 was speculated.

Most important to the research presented in this thesis, was the neuroanatomical correlates of performance in the EFs DT, inhibition, shifting, and updating, in healthy young and older adults with the task pairs employed in the behavioural studies presented in Chapter 3. Thus, based on this review, it is hypothesised that as a consequence of cognitive ageing, neural activity associated with DT performance with the PRP task would be observed in the medial prefrontal network and lateral frontal–parietal network. With compensatory increased activity in the aPFC and occipital regions in older adults including, alterations in the networks involving the MFG, SFG and the anterior insula with increased task complexity in these older individuals. As no neuroanatomical study with the TEA telephone code search DT was found, its neuroanatomical correlate is unknown. Although it can be speculated that the DLPFC is involved.

During inhibition performance with the traditional Stroop task, activity has been shown to correlate with activity in the right VLPFC, particularly the right inferior frontal cortex and right IFG. In older adults, compensatory activity has been associated with increased activation of the anterior inferior prefrontal cortices, particularly, the IFG, MFG, pre-SMA, and precuneus, as well as the ventral visual processing regions within the temporal cortex but decrease activity in the DLPFC and parietal lobes. Superior performance in this age

group was associated with greater recruitment of the ACC with the right VLPFC. No study was found to have assessed the neuroanatomical correlates of the second task used in the behavioural study, the HSCT.

Shifting performance with the task switching task has been correlated with activity in the DLPFC, VLPFC, and PPC. Age-associated decline in performance has been associated with increased activity in the right and left DLPFC, right insula and ventral visual cortex in older adults. With the TMT, bilateral activity in the VLPFC and DLPFC has been reported. Compensatory performance was linked with reduced activity bilaterally in the occipital, temporal, and parietal lobes, and additional activity in the left medial and lateral PFC of older adults.

Lastly, updating performance with the BDS task has been found to show increased activity in the left PFC and left occipital visual cortex in young adults but greater activity particularly in the right IFG, with the older adults. With the n-back task, increased activity within the PFC regions BAs 9 and 10 (DLPFC), mid-VLPFC, medial PPC, and inferior parietal lobules has been observed, in the young adults. With activity decreasing with advance age, and absent in older adults. Involvement of the parietal and cingulate cortices, as well as the claustrum, insula, and cerebellum have also been implicated.

Additional connections with other cortical and subcortical regions were observed in order for the efficient processing of these cognitive abilities. However, as reported in some studies, neural activity was observed to also be dependent on the stimulus or task employed.

Review of the neuroanatomical correlates of performance of these four EFs in participants living with the conditions MCI and AD was also conducted but not relevant to the overall research presented as these individuals were not assessed in the behavioural studies.

Instead, the following chapter used neuroanatomical and neuropsychological performance data from the OASIS-3 database (LaMontagne et al., 2019) to examine the neuroanatomical changes in older adults ranging from a diagnosis of cognitively healthy to advanced AD, in a voxel-based morphometry (VBM) study.

Chapter 6, VBM Study: Neuroanatomical changes with increasing Cognitive Decline

6.1. Introduction

Cognitive decline is deemed to be the result of neuroanatomical changes in the brain, particularly in the prefrontal cortex (PFC) (Christoff & Gabrieli, 2000; Funahashi & Andreau, 2013; Postle, 2017; Salat et al., 1999, 2004; Tisserand & Jolles, 2003a; P. Yuan & Raz, 2014; Zanto & Gazzaley, 2019). Such changes, including atrophy of cerebral gray matter (GM) and white matter (WHM) tracts, occur as part of healthy ageing, becoming progressively worse in pathological conditions such as mild cognitive impairment (MCI) and Alzheimer's disease (AD) (Cabeza et al., 2009; Gauthier et al., 2006; Petersen et al., 1997). Hence, the rate of atrophy in the brain has been considered a promising biomarker for tracking disease progression in ante-mortem individuals. Accordingly, neuroimaging techniques which have the capacity to detect such structural deviations, like magnetic resonance imaging (MRI), have become an important tool in the diagnosis of Alzheimer's disease (AD) (Frisoni et al., 2010; Furukawa et al., 2016; B. C. P. Lee et al., 2003).

Structural changes in the PFC are believed to correlate with decreased executive function (EF) ability and cognitive decline, as this region is predominantly involved in their processing (Jack et al., 2009; Spulber et al., 2010). Consequently, the frontal lobe hypothesis of neurocognitive ageing (Dempster & Vegas, 1992; West, 1996) associates cognitive function deficits in cognitively healthy (CH) older adults to changes in the PFC. Whilst the Scaffolding Theory of Ageing and Cognition (STAC) (Park & Reuter-Lorenz, 2009; Reuter-Lorenz & Park, 2014) describes how older brains compensate for this change. For example, by recruiting additional neural systems, as seen with the bilateral activation of frontal regions of the brain during task performance, as compared to only the left or right frontal region in younger individuals (Grady et al., 2006).

Such cognitive shortfalls result in increased performance impairments in everyday tasks, particularly in EF tasks (Mortamais et al., 2017) in CH older adults in comparison to younger adults (McAlister & Schmitter-Edgecombe, 2016; Wecker et al., 2000), as shown with the findings from Chapter 3 of this thesis. However, some researchers have found no

association between neuroanatomical changes and performance (Alvarez & Emory, 2006; Salthouse, 2011a; Van Petten, 2004), while others have even found a negative correlation (Salat et al., 2002), where a larger PFC volume was linked to reduced working memory (WM) performance.

Individuals living with MCI are usually considered to perform as well as the CH in everyday living but not in cognitive/clinical testing, although this may depend on the severity of the condition. However, tasks requiring episodic memory are usually negatively affected, especially in individuals living with amnestic MCI (aMCI). The hippocampal structures within the medial temporal lobes (MTLs), important in visual memory, auditory language and speech comprehension systems, and the processing of emotion (Brownsett & Wise, 2010; Lynch et al., 1977; Wagner et al., 2005) are typically more affected by atrophy (Tromp et al., 2015; Martial Van der Linden et al., 2000). The atrophy becomes extremely pronounced in sufferers that transition to AD (Jack et al., 2005; Kaye et al., 1997; Mufson et al., 2012), before spreading to other brain regions and increasing in severity as AD progresses (Frings et al., 2014; Gili et al., 2011; Maillet & Rajah, 2013; Pini et al., 2016; Toepper, 2017). Hence, individuals living with AD have been found to have difficulty completing all tasks successfully (Risacher et al., 2017; Schmid et al., 2013). Cognition assessments such as the clinical dementia rating (CDR) scale (C. P. Hughes et al., 1982) and the mini-mental state examination (MMSE) (Folstein et al., 1975) have been used to monitor cognitive decline.

In the present study, the progression of GM and WHM atrophy in the brains of CH older adults, MCI, and various severities of AD was examined in relation to the CDR scale score in six areas of cognition used regularly in life. The hypothesis is that increased cognitive decline (as assessed by the scale) is associated with increased global atrophy (especially in the PFC and temporal lobes).

Originally, MRI studies with the use of some of the EF tasks mentioned in the behavioural studies (Chapter 3) were planned as part of this PhD project with CH, MCI, and early-stage AD participants. However, due to the COVID-19 pandemic this was not possible. Hence, the analyses performed in this chapter were based on secondary data derived from the Open Access Series of Imaging Studies-3 (OASIS-3) database (for details, see the Methods section).

6.2. Methods

6.2.1 Participants

Structural MRI T1-weighted data was obtained from a sample of 16 CH (CDR score 0, mean age of 73.23 years, SD of 8.99), 12 MCI (CDR score 0.5, mean age of 73.22 years, SD of 6.16), 16 mild AD (CDR score 0.5, mean age of 76.09 years, SD of 6.03), 16 mild-moderate AD (CDR score 1, mean age of 76.44 years, SD of 7.79), 16 moderate AD (CDR score 2, mean age of 75.45 years, SD of 8.98), and 10 severe AD participants (CDR score 3, mean age of 75.16 years, SD of 6.76), selected from the OASIS-3 open-source dataset, https://www.oasis-brains.org (LaMontagne et al., 2019). The dataset comprises a total of 1098 participant data collected from several ongoing studies at the Washington University Knight Alzheimer Disease Research Centre over a period of 15 years. Thus, this study was based on secondary data analysis.

6.2.2 Screening Assessments

The participants of the OASIS3-3 study were screened for their cognitive status with the CDR scale described below, and the MMSE (Folstein et al., 1975) to assess cognitive status. For a full description of the MMSE, please refer to section 3.2.2.

Clinical Dementia Rating (CDR) scale (C. P. Hughes et al., 1982)

This assessment is used to measure global function in dementia and MCI sufferers. It is based on a semi-structured interview, where a named relative or next of kin is interviewed to complete the first section of the test and the participant is interviewed to complete the second section. It comprises six different functional domains: memory, orientation, judgment, community, hobbies, and personal care, where each domain is rated either, 0 = no impairment, 0.5 = questionable impairment, 1 = mild impairment, 2 = moderate impairment, or 3 = severe impairment, except for personal care which does not use the questionable impairment option. The test score is the sum of all the individual ratings of the six domains. Total scores range from 0 for no impairment to 18 for maximum impairment in all the domains. The score of each domain and the collective total test score may be used as outcome measures. It takes approximately 20 minutes to administer.

In addition, the participants were further screened for depression, and their functional and dementia health status with following tests.

Geriatric Depression Scale (GDS) (Yesavage et al., 1983)
Please see section 3.2.3. for a full description.

Functional Activities Questionnaire (FAQ) (Pfeffer et al., 1982)
This test assesses the performance of older adults in activities of daily living based on 10 questions covering areas including the preparation of balanced meals and managing personal finances. Each question is scored on a scale ranging from 0 to 3. Answers "normal" and "never did (activity) but can now" - 0, "never did and would have difficulty now" and "has difficulty but does by self" - 1, "requires assistance" - 2, and "dependent" - 3.

Total score ranges from 0 to 30. A cutoff point of 9, i.e. dependent in three activities indicates function and probable cognitive impairment.

Neuropsychiatric Inventory Questionnaire (NPI-Q) (Kaufer et al., 2000)
This briefer version of the standard NPI in questionnaire form. It is an informant-based assessment of neuropsychiatric symptoms and associated caregiver distress of 12 domains: delusions, hallucinations, agitation/aggression, dysphoria/depression, anxiety, euphoria/elation, apathy/indifference, disinhibition, irritability/lability, aberrant motor behaviors, nighttime behavioral disturbances, and appetite/eating disturbances.

Each question is answered "yes" or "no". If yes, the severity of the symptom of the participant is rated using a three-point scale, 1 - mild, 2 - moderate, and 3 - severe. The total severity score is the sum of individual symptom scores, ranging from 0 to 36.

The caregiver's distress associated with the symptom is rated on a scale scoring from 0 (not distressing at all) to 5 (extremely distressing). The total NPI-Q distress score is the sum of individual symptom scores, ranging from 0 to 60.

The NPI-Q takes approximately 5 minutes to complete.

6.2.3 Neuropsychological Assessments

As part of the neuroimaging study, the participants completed a series of neuropsychological assessments.

Boston Naming Test (BNT) (Goodglass et al., 1983)

Participants are required to name drawings of common objects. The test assesses language retrieval from semantic memory.

Category Fluency test (Binetti et al., 1995)

Participants are required to name as many words as they can that belong to a specific category, i.e. animal and vegetable, in 60 seconds. The test assesses semantic memory and language.

Digit Span (Elwood, 1991)

Participants are required to immediately recall a series of digits presented forward (FDS) and backwards (BDS) in order to assess attention and WM. (The BDS is described in section 3.2.4.4.) Scores are based on the number of trials repeated correctly forwards and backwards, as well as the longest length the participant is able to repeat back.

Logical Memory - Story A (Elwood, 1991)

Participants are required to immediately recall as many details as possible from a short story containing 25 items of information after it is read aloud by the examiner and again following a 30-minute delay. This subtest of the Wechsler Memory Scale-Revised assesses episodic memory. Scores range from 0 (no recall) to 25 (complete recall).

Trail Making Test (TMT) Parts A and B (Reitan, 1992)

A full description of this shifting assessment test can be viewed in section 3.2.4.3. It is scored by the completion time in seconds where a max of 150s for Trails A and 300s for Trails B is required. Also, the number of commission errors and number of correct lines is recorded.

WAIS-R Digit Symbol test (Wechsler & De Lemos, 1981)

Participants are assessed by the total number of digit symbol pairs completed in 90 seconds. This test assesses psychomotor speed.

6.2.4 Magnetic Resonance Imaging (MRI)

6.2.4.1 Image acquisition

All the neuroimaging scans were conducted by the Knight Alzheimer Research Imaging Program at Washington University in St. Louis. The MRI scans were collected on two different Siemens scanner models (Siemens Medical Solutions USA, Inc), the Vision 1.5T and the TIM Trio 3T (2 different scanners of this model). The images underwent cortical reconstruction and volumetric segmentation of T1-weighted images with the use of the FreeSurfer image analysis suite (http://surfer.nmr.mgh.harvard.edu/). The images from the 1.5T scanners were processed with FreeSurfer v5.0 or v5.1, and those from the 3T scanners with the FreeSurfer 5.3 (freesurfer.net) (LaMontagne et al., 2019).

6.2.4.2 Voxel-based morphometry (VBM)

Using the cortical-reconstructed and volumetric-segmented T1-weighted images provided by OASIS-3 the following voxel-based morphometry (VBM) analysis was conducted. Structural data was processed for VBM analysis (Ashburner & Friston, 2000). Pre-processing and analysis were performed using the Computational Anatomy Toolbox - CAT12 toolbox (http://www.neuro.uni-jena.de/cat/) within the Statistical Parametric Mapping (Friston et al., 1995) implemented in SPM12 (The FIL Methods Group, Wellcome Trust Centre for Neuroimaging, Institute of Neurology, UCL, London, England) running under MATLAB R2020b (MathWorks, Natick, MA, USA).

Default settings in CAT12 and SPM12 were used. Spatial normalisation to the Montreal Neurological Institute (MNI) template using the Diffeomorphic Anatomic Registration Through Exponentiated Lie algebra (DARTEL) algorithm and segmentation of the images into GM, WHM, and cerebrospinal fluid (CSF) was performed in CAT12, while images were smoothed with an 8 mm full width half maximum Gaussian kernel in SPM12. Total intracranial volume (TIV) was calculated automatically for each participant by summing global tissue volume (i.e. GM, WHM, and CSF) within CAT12. To minimise any possible edge

effects between the three regions, the absolute threshold for masking was adjusted to 0.1. The voxel-level uncorrected *p*-value was set as 0.001.

6.2.4.3 Statistical analysis

Statistical analysis was performed on the demographic, clinical characteristics, screening, and neuropsychological assessment results of the six groups using univariate, non-parametric and repeated measures analysis of variance (ANOVA), chi-square (χ^2), Mann-Whitney *U*, and independent t-tests in the statistical program SPSS for Windows version 26 (IBM SPSS Statistics, IBM Corp, Armonk, NY).

T-tests were further performed in CAT12 to compare GM and WHM differences between the healthy controls, MCI, and the AD groups. TIV was included as a covariate. The outputs were visualised using the xjView toolbox, version 9.7 (https://www.alivelearn.net/xjview). The uncorrected *p*-value was set as 0.001.

6.3. Results

6.3.1 Demographics

Demographic and clinical characteristics of the participants are presented in Table 6.1.

Data from the OASIS-3 dataset was selected based on their diagnosis, i.e. CH, uncertain dementia or 0.5 memory only CDR score, and AD dementia. The groups were matched for age and gender, where possible. Univariate ANOVA confirmed an insignificant difference, $F(5, 80) = 0.49$, $p = 0.783$, $\eta_p^2 = 0.03$, for the groups' ages. Chi-square testing reported significance for gender in the CDR score of 3 group only, $\chi^2(5) = 1.52$ (n = 86), $p = 0.911$.

Table 6.1. OASIS-3 Demographic Data

	Cognitively Healthy (n = 16)	**Mild Cognitive Impairment** (n = 12)	**Alzheimer's Disease**				***p* - value**
			AD0.5 (n = 16)	**AD1** (n = 16)	**AD2** (n = 16)	**AD3** (n = 10)	
Age	73.23 (8.99)	73.22 (6.16)	76.09 (6.03)	76.44 (7.79)	75.45 (8.98)	75.16 (6.76)	0.783
Gender (M/F)	8/8	5/7	8/8	8/8	8/8	3/7*	0.911[a]

MMSE score	28.84 (0.80)	28.08 (1.74)	25.50 (3.03)	21.42 (3.67)	15.00 (4.49)	5.25[#] (5.31)	<0.001
CDR score	0	0.5	0.5	1	2	3	<0.001[b]

CDR – Clinical Dementia Rating scale, MMSE – Mini-Mental State Examination. The p-value column displays the univariate ANOVA tests across the 6 groups, unless otherwise stated. [*]$p < 0.05$, [#]n = 8 as two participant scores are unknown, [a] Chi-square test, [b]Kruskai-Wallis test.

Univariate ANOVA reported a significant difference in the MMSE scores between the groups, $F(5,78) = 78.13$, $p = <0.001$, $\eta_p^2 = 0.83$, which is consistent with the decline in cognitive status being examined with increasing CDR score. Independent t-tests between all the neighbouring participant groups, with the exception of the comparison between the CH and MCI, $t(26) = -1.55$, $p = 0.134$, were observed to be significantly different in scores. Between MCI and AD0.5, $t(26) = 2.64$, $p = 0.014$, AD0.5 and AD1, $t(30) = 3.43$, $p = 0.002$, AD1 and AD2, $t(30) = 4.43$, $p < 0.001$, and AD2 and AD3, $t(22) = 4.73$, $p < 0.001$.

A non-parametric ANOVA (Kruskai-Wallis test) between the five CDR scores also showed significance, $\chi^2(4) = 69.00$, $p <0.001$. (CDR score of 0.5 was used for two groups, MCI, and AD0.5.) Mann-Whitney *U* tests between all the neighbouring participant groups, except between MCI and AD0.5, $U = 96$, $p = 1.000$, indicated significance. Between CH and MCI, $U = 192$, $p < 0.001$, AD0.5 and AD1, $U = 256$, $p < 0.001$, AD1 and AD2, $U = 256$, $p < 0.001$, and AD2 and AD3, $U = 160$, $p < 0.001$.

A breakdown of how the participants performed in the six different cognitive domains of the CDR scale was assessed, see Table 6.2 and Figure 6.1. As the participant's cognitive status progressed to advanced AD, decline in multiple cognitive domains increased. The least affected domain was shown to be personal care, while memory was affected at the highest rate.

Table 6.2. CDR Sub-score Group Comparisons. The first number is the CDR score, and in brackets is the number of participants.

CDR / Group	Community	Hobbies	Judgment	Memory	Orientation	Personal care
CH (n = 16)	0 (16)	0 (16)	0 (16)	0 (16)	0 (16)	0 (16)
MCI (n = 12)	0 (6) 0.5 (6)	0 (9) 0.5 (3)	0 (5) 0.5 (7)	0.5 (12)	0 (10) 0.5 (2)	0 (12)
AD0.5 (n = 16)	0 (7) 0.5 (9)	0 (4) 0.5 (9)	0 (2) 0.5 (9)	0.5 (11) 1 (5)	0 (5) 0.5 (7)	0 (16)

		1 (3)	1 (5)		1 (4)	
AD1 (n = 16)	0.5 (4) 1 (12)	0.5 (1) 1 (12) 2 (3)	0.5 (1) 1 (13) 2 (2)	1 (16)	0.5 (3) 1 (11) 2 (2)	0 (9) 1 (6) 2 (1)
AD2 (n = 16)	1 (3) 2 (13)	1 (2) 2 (12) 3 (2)	1 (4) 2 (12)	1 (1) 2 (15)	1 (4) 2 (11) 3 (1)	0 (2) 1 (11) 2 (2) 3 (1)
AD3 (n = 10)	2 (4) 3 (6)	2 (1) 3 (9)	2 (1) 3 (9)	2 (2) 3 (8)	2 (1) 3 (9)	2 (1) 3 (9)

It can be seen that in the CH older adult group, cognition was maintained in all the six domains examined, community, hobbies, judgment, memory, orientation, and personal care. The memory domain was initially the most affected in all the participants with MCI, followed by judgment, and acts relating to community. The memory domain continued to be extensively affected through the transition to AD and its progression.

Additional non-parametric ANOVA analysis between the groups' performance in these CDR subparts (community, hobbies, judgment, memory, orientation, and personal care) confirmed significance, all yielded $U = 85$, $p < 0.001$ ($df = 5$).

Pairwise analysis also revealed significance following Bonferroni correction between the groups except amongst the following.

Community, between CH and MCI, $p > 0.999$, CH and AD0.5, $p > 0.999$, MCI and AD0.5, $p > 1.000$, MCI and AD1, $p = 0.154$, AD0.5 and AD1, $p = 0.136$, AD1 and AD2, $p = 0.869$, AD1 and AD3, $p = 0.102$, and AD2 and AD3, $p > 0.999$.

Hobbies, between CH and MCI, $p > 0.999$, CH and AD0.5, $p = 0.731$, MCI and AD0.5, $p > 0.999$, AD0.5 and AD1, $p = 0.455$, AD1 and AD2, $p > 0.999$, AD1 and AD3, $p = 0.129$, and AD2 and AD3, $p > 0.999$.

Judgment, between CH and MCI, $p > 0.999$, CH and AD0.5, $p = 0.156$, MCI and AD0.5, $p > 0.999$, AD0.5 and AD1, $p = 0.977$, AD1 and AD2, $p > 0.999$, AD1 and AD3, $p = 0.077$, and AD2 and AD3, $p > 0.999$.

Memory, between CH and MCI, $p = 0.867$, CH and AD0.5, $p = 0.054$, MCI and AD0.5, $p > 0.999$, MCI and AD1, $p = 0.299$, AD0.5 and AD1, $p > 0.999$, AD1 and AD2, $p = 0.661$, and AD2

and AD3, $p > 0.999$. The comparison between AD1 and AD3 was just at significance, $p = 0.049$.

Orientation, between CH and MCI, $p > 0.999$, CH and AD0.5, $p = 0.690$, MCI and AD0.5, $p > 0.999$, AD0.5 and AD1, $p = 0.839$, AD1 and AD2, $p > 0.999$, AD1 and AD3, $p = 0.073$, and AD2 and AD3, $p > 0.999$.

Personal care, between CH and MCI, $p > 0.999$, CH and AD0.5, $p > 0.999$, CH and AD1, $p = 0.696$, MCI and AD0.5, $p > 0.001$, MCI and AD1, $p = 0.945$, AD0.5 and AD1, $p = 0.638$, AD1 and AD2, $p = 0.437$, AD2 and AD3, $p = 0.570$.

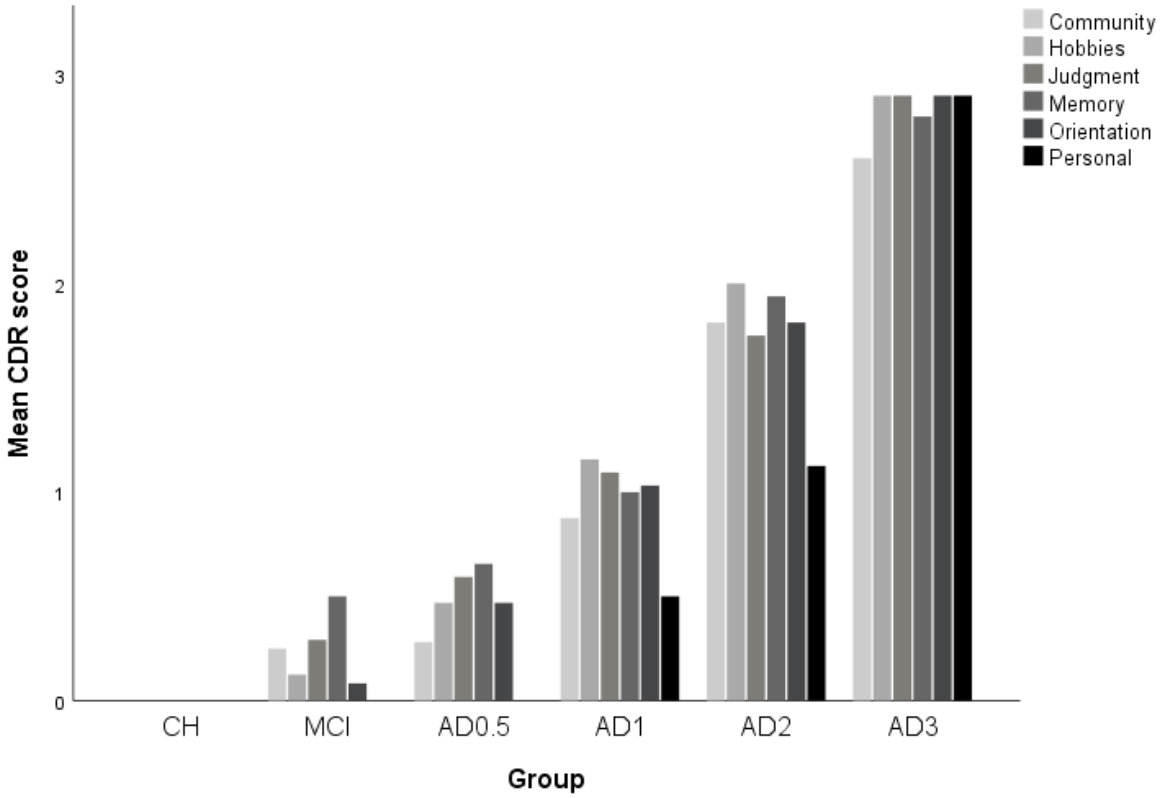


Figure 6.1. CDR Sub-score Group Data. The graph represents the data presented in Table 6.2.

Performance in the GDS, FAQ and NPI-Q is presented in Table 6.3.

Table 6.3. OASIS-3 Screening Assessment Results

	CH (n = 15)	**MCI** (n = 8)	**Alzheimer's Disease**				***p* - value**
			AD0.5 (n = 13)	**AD1** (n = 15)	**AD2** (n = 15)	**AD3** (n = 10)	

GDS	0.80 (0.86)	2.38 (1.92)	1.69 (1.55)	2.20 (2.88)	1.80 (1.21)	3.20 (2.44)	0.072
FAQ	0.07 (0.26)	2.75 (2.82)	4.00 (2.86)	14.60 (4.19)	21.07 (6.35)	23.80 (9.85)	<0.001
NPI-Q	1.73 (1.53)	5.38 (5.93)	7.92 (3.88)	12.07 (9.48)	12.27 (8.20)	12.40 (7.47)	<0.001

GDS – Geriatric Depression Scale, FAQ Functional Activities Questionnaire, NPI-Q Neuropsychiatric Inventory Questionnaire. The p-value column displays the univariate ANOVA tests across the 6 groups.

Univariate ANOVA between the GDS means indicated no differences amongst the groups, $F(5,70) = 2.13$, $p = 0.072$, $\eta_p^2 = 0.13$. Although t-tests between the neighbouring groups found a significant difference between the CH and MCI groups, CH and MCI, $t(21) = -2.74$, $p = 0.012$. The remaining comparisons yielded insignificant differences, MCI and AD0.5, $t(19) = 0.90$, $p = 0.382$, AD0.5 and AD1, $t(26) = -0.57$, $p = 0.576$, AD1 and AD2, $t(28) = 0.50$, $p = 0.624$, and AD2 and AD3, $t(23) = -1.91$, $p = 0.068$.

A significant difference between the groups' FAQ mean scores showed significance, $F(5,70) = 48.17$, $p < 0.001$, $\eta_p^2 = 0.78$. This is evident by the gradual increase in mean score from CH to AD3. However, between the neighbouring groups, significance was found between CH and MCI, $t(21) = -3.74$, $p = 0.001$, AD0.5 and AD1, $t(26) = -7.70$, $p < 0.001$, and AD1 and AD2, $t(28) = -3.29$, $p = 0.003$. An insignificant difference was shown from the comparisons between MCI and AD0.5, $t(19) = -0.98$, $p = 0.340$, and AD2 and AD3, $t(23) = -0.85$, $p = 0.406$.

Significance was further found between the NPI-Q mean scores between the groups, $F(5,70) = 5.85$, $p < 0.001$, $\eta_p^2 = 0.30$, though following t-test, significance was only shown between CH and MCI, $t(21) = -2.28$, $p = 0.033$. No substantial difference was found amongst the remaining group comparisons, MCI and AD0.5, $t(19) = -1.20$, $p = 0.246$, AD0.5 and AD1, $t(26) = -1.47$, $p = 0.154$, AD1 and AD2, $t(28) = -0.06$, $p = 0.951$, and AD2 and AD3, $t(23) = -0.04$, $p = 0.967$.

6.3.2 Neuropsychology assessments

The results of the neuropsychological assessments can be viewed in Table 6.4.

Table 6.4. Neuropsychological Results

Group / Task	CH (n=9)	MCI (n=8)	AD0.5 (n=13)	AD1 (n=15)	AD2 (n=11)	AD3 (n=9)	p-value
Logical Memory	13.78 (2.99)	7.00[a] (5.77)	6.62 (4.25)	3.60 (3.81)	1.55 (1.63)	4.50[f] (2.33)	<0.001
Digit Span F	8.56 (2.35)	7.14[a] (2.54)	6.92 (2.72)	6.87 (1.88)	7.36 (2.84)	6.11 (2.76)	0.454
Digit Span B	6.89 (2.42)	5.57[a] (1.51)	5.00 (2.68)	3.93 (2.46)	3.50[c] (2.59)	4.00[f] (1.77)	0.028
Category Fluency test A	19.89 (6.64)	16.38 (6.09)	13.08 (4.65)	8.53 (5.15)	7.64 (5.41)	9.50[f] (3.25)	<0.001
Category Fluency test V	13.89 (5.30)	9.43[a] (4.47)	9.54 (3.10)	5.60 (3.56)	4.60[c] (2.59)	6.88[f] (3.91)	<0.001
Boston Naming Test	27.78 (0.83)	23.14[a] (6.04)	21.69 (6.09)	17.00 (8.20)	14.45 (4.91)	18.50[f] (6.82)	<0.001
WAIS-R Digit Symbol test	46.00 (10.44)	40.57[a] (24.62)	37.33[b] (16.25)	29.00[b] (15.54)	23.22[d] (13.60)	20.88[f] (17.21)	0.012
TMT Part A (secs)	40.22 (12.90)	44.88 (25.59)	47.08 (18.65)	62.73 (36.59)	80.00[c] (58.38)	115.13[f] (45.53)	<0.001
TMT Part B (secs)	96.56 (25.45)	157.63 (110.29)	190.40[c] (116.01)	244.78[d] (90.36)	231.67[e] (79.15)	263.80[g] (80.95)	0.007

The p-value column displays the univariate ANOVA tests across the 6 groups. [a] n=7, [b] n=12, [c] n=10, [d] n=9, [e] n=6, [f] n=8, [g] n=5.

Comparison between the neighbouring groups, found significance between the CH and MCI groups during performance in logical memory, $t(14) = 3.05$, $p = 0.009$, and the Boston naming tests, $t(14) = 2.30$, $p = 0.038$. Significance between the AD0.5 and AD1 groups was seen in the category fluency tests, animals, $t(26) = 2.44$, $p = 0.022$, and vegetable, $t(26) = 3.10$, $p = 0.005$. [Logical memory just failed to reach significance, $t(26) = 1.98$, $p = 0.059$.] Between the AD2 and AD3, a significant difference was only shown in logical memory performance, $t(17) = -3.26$, $p = 0.005$. Comparable performances were observed between the MCI and AD0.5 groups, and between the AD1 and AD2 groups, $p > 0.05$, in all these tests.

Analysis of performance in the different parts of the same test found no main group effect between the groups following a six-way repeated measures ANOVA [group (CH, MCI, AD0.5, AD1, AD2, AD3) x digit span (forward, backward)] was found, $F(5, 56) = 1.81$, $p < 0.001$, $\eta_p^2 = 0.14$. Although a main effect for span condition, $F(1, 56) = 59.46$, $p < 0.001$, $\eta_p^2 = 0.52$ was

observed but not for interaction, $F(5, 56) = 1.35$, $p = 0.256$, $\eta_p^2 = 0.11$. This suggest the groups performed similarly but there was a difference in performance between the span conditions.

A main group effect between the groups following a six-way repeated measures ANOVA [group (CH, MCI, AD0.5, AD1, AD2, AD3) x category fluency (animal, vegetable)] was found, $F(5, 56) = 10.31$, $p < 0.001$, $\eta_p^2 = 0.48$. As well as a main effect for category fluency, $F(1, 56) = 46.09$, $p < 0.001$, $\eta_p^2 = 0.45$. However, no interaction effect, $F(5, 56) = 1.11$, $p = 0.365$, $\eta_p^2 = 0.09$ was observed. These results indicate no performance difference between the groups, only between the test categories.

A main group effect between the groups following a six-way repeated measures ANOVA [group (CH, MCI, AD0.5, AD1, AD2, AD3) x TMT (part A, part B)] was found, $F(5, 41) = 3.82$, $p = 0.006$, $\eta_p^2 = 0.32$, for TMT part, $F(1, 41) = 142.75$, $p < 0.001$, $\eta_p^2 = 0.78$, and interaction, $F(5, 41) = 3.56$, $p = 0.009$, $\eta_p^2 = 0.30$. Performance amongst the groups between the TMT parts and the groups was substantially different.

6.3.3 Neuroimaging results

Group pairwise comparisons were performed between all the groups presented in Table 6.1, e.g., CH compared with MCI participants, MCI compared with AD participants with a CDR score of 0.5, etc, for their GM and WHM structural differences. Only significant findings with an uncorrected cluster-level *p*-value of 0.001 were recorded. The results are presented in Table 6.5 below. Please note, the *p*-value was not adjusted based on the fifteen comparisons conducted, (e.g. using Bonferroni correction), given the low statistical power as the number of participants in each group was relatively small, between 10 and 16.

Table 6.5. Voxel-based morphometry results for all pairwise group comparisons

Brain Region	**Side (R/L)**	**GM/ WHM**	**BA**	**MNI coordinates x, y, z**	**T-value**	**Voxels number (K_E)**
CH v MCI						
n. s.						
CH v AD0.5						
Hippocampus	R	WHM	-	33, -7.5, -15	4.48	2213

Parahippocampal gyrus		GM	28	23, 8, -26	4.43	
Sub-lobar extra-nuclear		WHM	-	17, -8, -11	4.28	
CH v AD1						
Hippocampus	L	GM		-27, -33, -6	8.53	16484
Inferior temporal lobe		WHM	-	-38, -27, -23	7.31	
Hippocampus		WHM	-	-26, -12, -12	6.93	
Hippocampus	R	WHM	-	24, -12, -10.5	6.39	13431
Sub-lobar extra-nuclear		WHM	-	18, -5, -14	6.37	
Hippocampus		GM		23, -6, -21	5.66	
CH v AD2						
Inferior temporal lobe	L	WHM	-	-39, -27, -18	7.88	17959
Hippocampus		WHM	-	-27, -14, -14	7.83	
Hippocampus		GM		-27, -29, -11	7.39	
Sub-lobar extra-nuclear	R	WHM	-	15, -7.5, -13.5	7.52	11023
Fusiform gyrus		WHM	-	42, -35, -15	6.62	
Hippocampus		WHM	-	26, -14, -11	6.32	
CH v AD3						
Parahippocampal gyrus	R	WHM	-	25.5, -9, -27	6.72	5648
Hippocampus		GM		15, -5, -15	5.73	
Sub-gyral temporal lobe		WHM	-	33, -6, -17	5.59	
Superior temporal gyrus	L	GM	38	-27, 10.5, -48	5.73	5389
Parahippocampal gyrus		WHM	-	-25.5, -25.5, -15	5.66	
Hippocampus		WHM	-	-17, -3, -11	5.39	
MCI v AD0.5						
n. s.						
MCI v AD1						
Inferior temporal gyrus	L	WHM	-	-37.5, -25.5, -24	6.15	3835
Superior temporal gyrus		GM	13	-51, -45, -18	5.98	
Inferior temporal gyrus		GM	-	-63, -39, -20	5.33	
MCI v AD2						
Inferior temporal gyrus	L	GM	17	-55.5, -43.5, -21	6.32	7720

Inferior temporal gyrus		WHM	-	-38, -29, -17	6.24	
Hippocampus		WHM	-	-30, -5, -30	5.82	
Hippocampus	R	WHM	-	24, -28.5, -9	4.92	3123
Parahippocampal gyrus		WHM	-	32, -8, -30	4.78	
Hippocampus		GM	-	20, -9, -17	4.61	
MCI v AD3						
n. s.						
AD0.5 v AD1						
Middle temporal lobe	L	GM	39	-46.5, -57, 21	5.49	1557
Middle temporal lobe		GM	21	-60, -62, 1	4.53	
Superior temporal gyrus		GM	-	-68, -48, 8	4.53	
AD0.5 v AD2						
Fusiform gyrus	L	GM	36	-37.5, -33, -22.5	5.03	2331
Inferior temporal gyrus		GM	-	-65, -35, -21	4.87	
Inferior temporal gyrus		GM	-	-65.5, -23, -23	4.59	
AD0.5 v AD3						
n. s.						
AD1 v AD2						
n. s.						
AD1 v AD3						
n. s.						
AD2 v AD3						
n. s.						

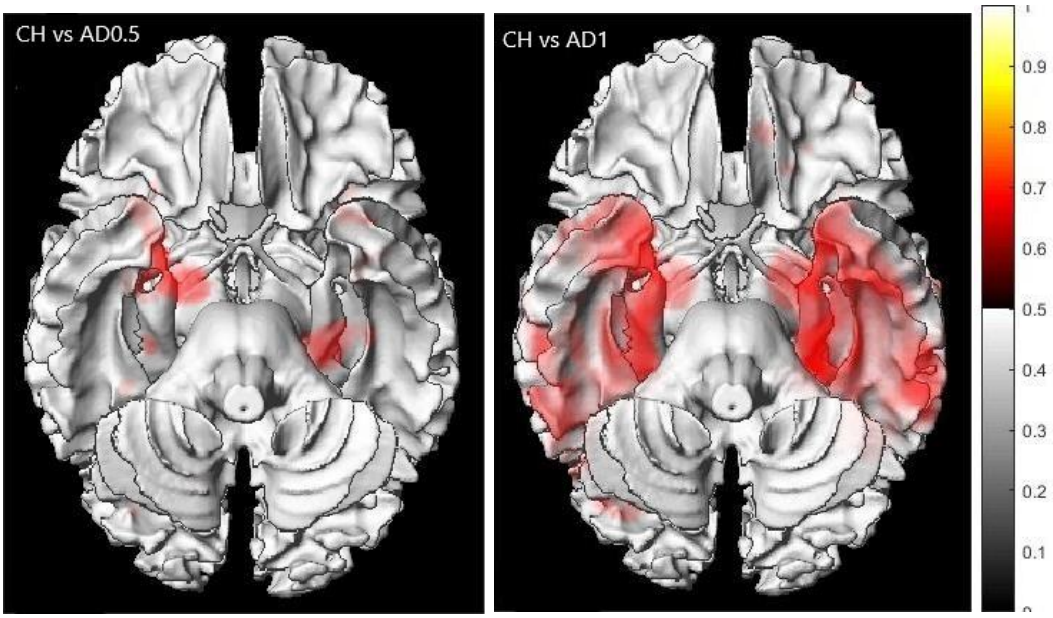
BA - Brodmann Area, CDR - Clinical Dementia Rating, GM - gray matter, WHM - white matter, R - right, L - left, MNI - Montreal Neurological Institute, n. s. - not significant.

As seen in the results presented in Table 6.5, the temporal lobes showed the most structural changes. No structural change in any PFC regions was observed. GM and WHM regions seem to be equally affected, as observed by the proportion of affected occurrences.

There were no significant structural changes between the CH and MCI participants, and between MCI and AD0.5 group. Thus, it may be concluded that structural changes at this stage (or these stages) are too subtle to detect, or at least with VBM analysis, or possibly the sample size may have been too small for any meaningful change to be shown.

In comparing CH with all the various AD stages, large cluster regions, especially in the WHM of the parahippocampal gyrus were heavily affected. Similarly, WHM in the left hemisphere of the inferior temporal lobe was shown to have undergone significant changes during the comparisons with the AD1 and AD2 groups. Involvement of GM in the left hemisphere of the superior temporal gyrus, and WHM of the right hemisphere of the sub-gyral temporal lobe, were seen with the comparison with the AD3 group. The progression of the structural change comparisons is shown in Figure 6.2.

Within the cluster of the CH versus AD2 and AD3 comparison, important areas of EF were observed. These included the amygdala, insula, the caudate (nucleus), putamen, and the anterior cingulate gyrus.



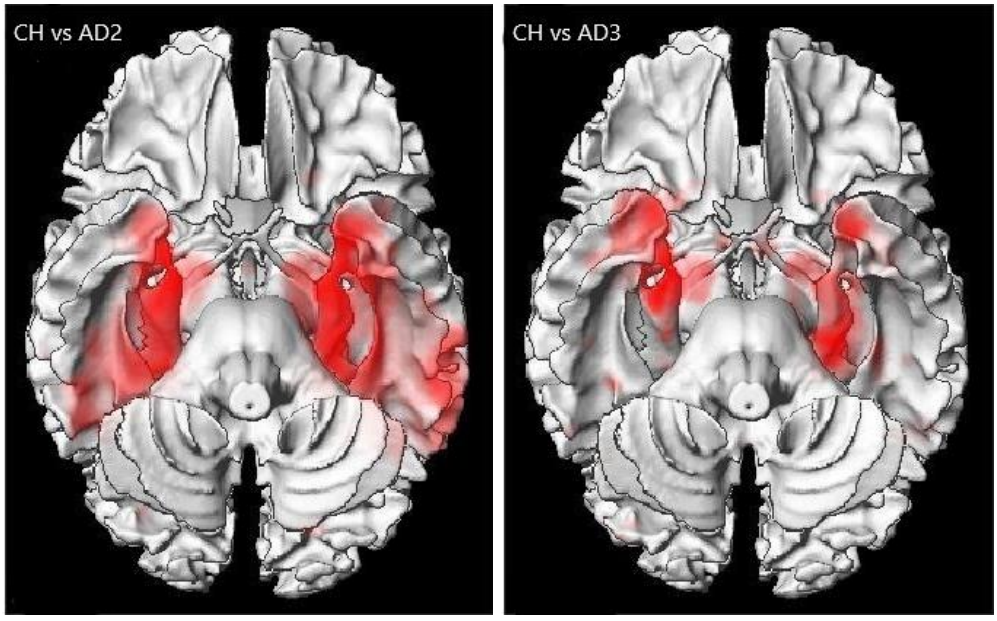


Figure 6.2. Significant Comparisons with the Cognitive Healthy group. Axial view.

Other significant EF areas were found in the WHM of the sub-lobar extra-nuclear and fusiform gyrus.

When comparing the MCI participants with the remaining AD participant groups, further changes in all these temporal lobe areas were seen. This included the GM of the inferior temporal gyrus, which was also seen with the CH participant comparisons, see Figure 6.3.

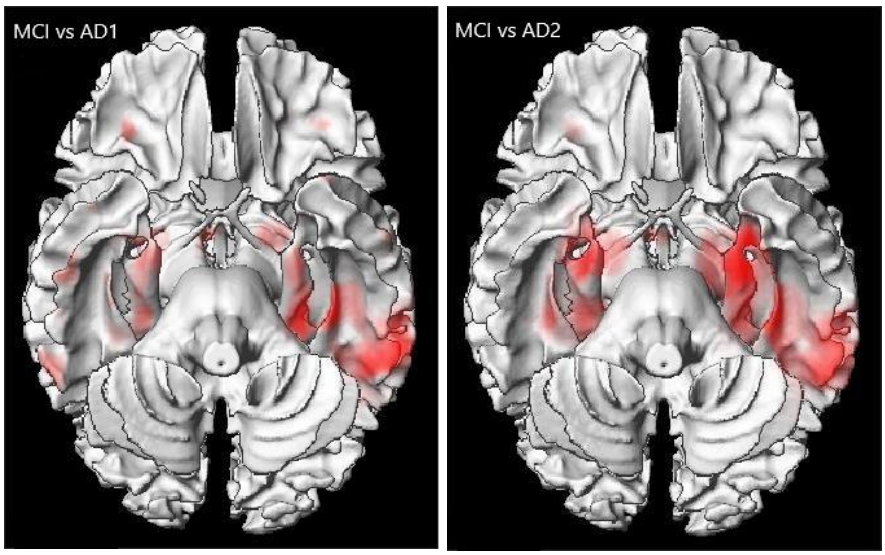


Figure 6.3. Significant Comparisons with the Mild Cognitive Impaired group. Axial view.

There was an insignificant difference in findings between the MCI and AD3.

The last two significant findings were between the AD0.5 and AD1, and between the AD0.5 and AD2 groups. Both identified large GM clusters in the left hemisphere, see Figure 6.4. The first in the middle temporal lobe and superior temporal gyrus, and the latter in the fusiform gyrus and inferior temporal gyrus.

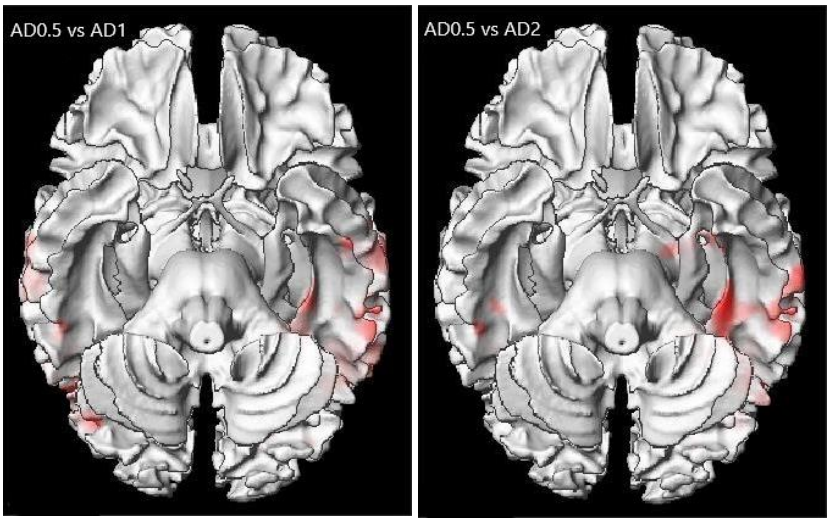


Figure 6.4. Significant Comparisons with the Alzheimer's disease CDR 0.5 group. Axial view.

As observed with the other comparisons with the AD3 group, no significant structural changes were observed.

No significant clusters were also not found during the AD0.5 versus AD3, AD1 versus AD2, AD1 versus AD3, and AD2 versus AD3 comparisons, which suggests no structural changes in GM and WHM had occurred.

In summary, increased structural change in the temporal lobes were observed. Greater changes in GM were seen between the later stages of AD, suggesting that the processing of information at designated areas was more specifically affected as AD progresses.

6.4. Discussion

The purpose of this VBM study was to examine how structural changes in the brain are related to an individuals' CDR score (C. P. Hughes et al., 1982) ranging from zero for CH in older adult participants, to 3 for severely cognitively impaired AD older individuals. Substantial changes were shown in the temporal lobes, which contains the parahippocampal gyrus, important in the encoding and retrieval of visuospatial processing

and episodic memory (Aminoff et al., 2013; Dundon et al., 2018) and the hippocampus, the primary region involved in long-term memory (LTM). The findings seemed to correlate with decline in the memory domain of the CDR scale, and the significant decline in the participant's performance in the Boston naming test, logical memory test, category fluency test, and digit span, particularly in the BDS. No structural change in any PFC regions was observed.

During the comparisons between the CH with all the various AD stages, large cluster regions, especially in the WHM of the parahippocampal gyrus, hippocampus and sub-lobar extra-nuclear areas were observed, a finding in agreement with previous research in MCI and AD individuals (J. P. Li et al., 2012; Liu et al., 2017; P. Wang et al., 2020; T. Wang et al., 2016; Yang et al., 2021). Reduction in WHM integrity is thought to be an early indicator of AD or various other dementias in CH and especially MCI (Luo et al., 2020; Zhuang et al., 2010). Such changes in WHM affect the processing speed of cognitive function (Turken et al., 2008). Thus, in this content, the performance loss in the TMT and WAIS-R Digit Symbol tests may be attributed to the brain changes.

The CDR scores of the MCI and AD participants indicated a slight decline in all but the personal care domain, revealing the initiation of cognitive decline. The changes in the striatum may account for the decline observed in the hobbies and orientation domain of the test, as it aids in physical movement. Particularly, the dorsal striatum which consist of the putamen and caudate, as the putamen is implicated in limb movement, and the caudate with attention, planning, emotional processing, and the execution of behaviour to achieve complex objectives (Robinson et al., 2012). Similarly, the decline seen in the judgement and community domains may be associated with the fusiform area, which is essential for facial and object recognition processing (Weinera & Zilles, 2016), and the insula. The region associated with an individuals' subjective emotional awareness such as empathy, disgust, fear and happiness (Critchley, 2008; Uddin et al., 2017). Also, the angular gyrus, important in the semantic processing of language, may be implicated (Seghier, 2013). Although the decline in any of the neuropsychological tests performed may be associated with any of these affected regions.

In the last stages of AD, the brain regions of the anterior cingulate gyrus, amygdala, as well as the parietal lobe were found to be significantly affected. These are all important regions

involved in cognitive processing, such as of attention, emotion, decision-making, judgement, execution of complex tasks, planning, visuospatial processing, as well as of episodic memory. Specifically, the amygdala is implicated in memory processing, and decision-making and emotional responses, i.e. fear, anxiety, and aggression (Gage & Baars, 2019). The anterior cingulate, an important area for EFs, implicated in the processing of several cognitive functions, including decision-making, the regulation of aggressive behaviour, emotional processing, communication, spatial memory, the control of attention, and error processing (Amanzio et al., 2011; Bubb et al., 2017; Kiehl et al., 2000; Nyberg & Eriksson, 2016; Tisserand & Jolles, 2003a; Martial Van der Linden et al., 2000). The parietal lobe with the processing of somatic sensation and visuospatial information (Lynch et al., 1977; Tisserand et al., 2004; Wagner et al., 2005). Thus, it may be concluded that the structural changes occurring in these regions may be involved in the decline observed in the non-memory domains of the CDR scale, i.e. in the community, hobbies, judgment, orientation, and/or personal care domains. Still, the precise areas involved in the tasks involved in some of the scale domains, i.e. community, cannot be accurately associated. Interestingly, it has been suggested that cortical thinning in the right anterior cingulate gyrus is a good predictor of progression of MCI to AD (Peters et al., 2014).

A surprising finding was the insignificant difference between the MCI and AD3, when the other comparisons between the MCI and other less severe AD participants showed substantial changes. This may be due to the cross-sectional comparison conducted in this study with the use of different participant groups, resulting in random variation between groups. Likewise, this result would be very unlikely with the employment of one set of participants in a longitudinal study. Nonetheless, this finding ultimately shows the limitations of how accurately the data may be interpreted.

Also, the lack of insignificant findings between the AD0.5 versus AD3, AD1 versus AD2, AD1 versus AD3, and AD2 versus AD3 comparisons may suggest that insignificant structural changes in GM and WHM had occurred. The gradual decline in cognition as AD severity increased suggests subtle changes may have been taking place that were not detected possibly due to the small sample sizes, particularly in the AD3 group (n = 10). Such changes may be non-structural, i.e. on the neural level such as decrease in the responsiveness of neurotransmitters, as described in Chapter 5, may possibly have occurred.

Finally, the lack of significant structural changes demonstrated in the frontal lobe may indicate the occurrence of minimal changes not detected by VBM. However, the large amount of WHM atrophy in other brain regions, including the midbrain, may suggest a disconnect to the neural activity between regions. This in turn could cause transmission deficits to the PFC. For example, the anterior cingulate gyrus is involved in many EFs, thus the structural changes observed in this area would interrupt the processing of abilities connected with it. The technique diffusion tensor imaging (DTI) (Arfanakis et al., 2002) would detect such a change. Nevertheless, this study only found extensive significant changes in the temporal lobes and not in the PFC. It may have been beneficial to have also assessed individuals living with frontotemporal dementia (FTD) to compare atrophy patterns between the conditions.

6.5. Conclusion

In conclusion, decrease in WHM was found to occur primarily in less cognitively impaired participants, whereas increased GM changes were evident in the more severe AD brain. This implies that deficits or a failure in the processing of neural activity at GM sites greatly impacts AD in the late stages of the condition.

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Chapter 7, General Discussion

7.1 Overview of Research and Aims

The research conducted in this thesis aimed to further our understanding into how cognitive ageing affects the executive functions (EFs) dual-tasking, inhibition, shifting, and updating (Miyake, Friedman, et al., 2000), and more specifically, the individual trajectory of their decline in older adults[1]. Disruption in the cognitive processing of one or more of these EFs may cause substantial interruption in an individual's life and in turn indicate the commencement of pathological cognitive decline, leading to a form of dementia, such as Alzheimer's disease (AD). As AD is a great public health issue due to the increasing rate of incidence there is an urgent requirement for an efficient way to effectively diagnose cognitive impairment at the earliest stage, such as mild cognitive impairment (MCI). Therefore, differentiating between pathological cognitive impairment and age-associated cognitive decline is particularly important.

In more detail, Chapter 2 provided a literature review of studies published between 2000 and 2019 evaluating the four mentioned EFs. A cross-sectional behavioural study assessing each of these EF abilities in young and older adults with a pair of tasks was presented in Chapters 3. Prior to the assessments, all participants were screened with an extensive battery of neuropsychological and functional tests, such as the mini-mental state examination (MMSE) (Folstein et al., 1975), Hopkins verbal learning test (Brandt, 1991), and spot-the-word test (Baddeley et al., 1993), to ensure an adequate cognitive profile. Most important to this thesis was the subsequent assessment of the individual trajectory of decline of the four named EFs in older adults (Chapter 3) using the z-scores of the task measures. The scores were statistically compared between the two age groups. The greatest decline rate observed in the older adults for each EF were then compared to determine how similar or dissimilar the rates of all four EFs were, based on the premise that EFs are simultaneously interrelated and independent (Miyake, Friedman, et al., 2000). Although this association has been found to change with increasing age, becoming less heterogenous due to changes in the PFC (Glisky et al., 2020). The rate of decline was found to be dependent on

[1] The research originally aimed to also assess individuals living with mild cognitive impairment and Alzheimer's disease and to complete an own MRI study.

the EF task employed in the examination of the specific EF ability, as the behavioural study observed different levels of decline with different tasks (Chapter 3).

A secondary aim of the research was to determine to what extent the outcome measures from the pair of tasks used for all the EFs correlated with each other in each group (Chapter 4) through correlation analysis. In addition, confirmatory factor analysis (CFA) was further employed to examine the consequence of ageing on the unity and diversity of the four by examining the loading factors of the task measures in each group.

The final study aimed to explore how the cognitive status, as assessed with the Montreal cognitive assessment (MoCA) (Nasreddine et al., 2005) and MMSE, together with performance in an array of EF tasks of cognitively healthy to advance AD older adults, associated with neuroanatomical changes. This was investigated utilising secondary neuroimaging data provided by the OASIS-3 database (LaMontagne et al., 2019), in a voxel-based morphometry (VBM) study (Chapter 6).

The following sections will discuss the main findings of these studies, before outlining limitations of the research completed, and areas for future development.

7.2 Summary and Discussion of Main Findings

EF have been examined with the employment of several tasks. The literature review presented in Chapter 2 highlighted the methodological challenges involved in the assessment of EFs which may impact the evaluation of findings across studies as there is no consensus on which tasks to use for the examination of EF abilities. Factors discussed included the type of stimuli used in a task, the task demand, outcome measure and the number of tasks utilised to assess an EF ability.

Emphasis was placed on the abilities dual-task (DT), inhibition, shifting, and updating as these were to be assessed in the behavioral studies presented in Chapter 3. The most frequently used tasks were identified in cognitively healthy ageing studies to be the psychological refractory period (PRP) paradigm (Pashler, 1984; Welford, 1952) for DT, the Stroop task (Golden, 1978) for inhibition, the trail making test (TMT) (Reitan, 1992) for shifting, and the n-back task (Kirchner, 1958) for updating (Jaeggi et al., 2010; Kirchner, 1958). In the studies assessing individuals living with MCI and AD, DT was frequently

evaluated with the (Baddeley's) digit recall and tracking (Baddeley et al., 1986) and Della Sala DT (Baddeley et al., 1986; Della Sala et al., 1995a), inhibition with the Stroop task, shifting with the TMT, and updating with the backward digit span (BDS) task (P. T. Griffin & Heffernan, 1983).

In accordance with these findings, two tasks were chosen for the behavioural studies. For DT, a modified version of the test for everyday attention (TEA) DT (Robertson et al., 2001) and a computerised PRP paradigm were employed, for inhibition, the Stroop task and Hayling sentence completion task (HSCT) (Burgess & Shallice, 1997), for shifting, the TMT and task switching paradigm (Rogers & Monsell, 1995), and for updating, the BDS and n-back tasks. However, despite these choices, in reflection of the DT choices, it would have been better to have used either the (Baddeley's) digit recall and tracking (Baddeley et al., 1986) or the Della Sala DT, as they have been more widely employed in EF studies, if not in cognitive ageing studies. The remaining tasks have been used frequently across studies researching a variety of conditions providing a good foundation and so were good choices.

Nevertheless, to reduce the possibility of erroneously collecting data and to increase the accuracy and ease of analysis of the task outcome measures, some of the pen-and-paper tasks, such as the Stroop task and TMT, could have been computerised. Also, in regard to the difference in the type of inhibition assessed by the Stroop task and HSCT, it would have been more beneficial to have used tasks that assess identical or similar inhibition abilities, such as the go/no-go task (Newman & Kosson, 1986), or stop signal task (Logan et al., 1984; Williams et al., 1999). This might have aided in finding an association between the task measures during the correlation analysis.

The cross-sectional behavioural studies presented in Chapter 3 investigated the rate of decline of the four EF abilities between young and older adults. These four abilities were chosen based on the premise that they are fundamental to the functioning of many other cognitive functions. The DT assessment results showed the older adults generated a significantly larger RT PRP effect in comparison to the young adults in the visual task. This finding in older adults has been consistently reported (Allen et al., 1998; Glass et al., 2000; Hartley, 2001; Hartley et al., 1999; Hein & Schubert, 2004; Verhaeghen et al., 2003), and has been attributed to an increase in the information-processing rate of the central bottleneck at the response-selection stage (Allen et al., 1998, 2002; Glass et al., 2000; Pashler, 1984,

1992, 1993, 1994; Schubert, 2008; Schubert et al., 2008; Tsang, 2013). The older adults have been suggested to be more cautious in their performance by taking their time before performing or resume performance of the second task (Allen et al., 2002), which also accounts for the insignificant difference in the accuracy performance. This further implies that the older adults engaged in a compensatory task-coordination strategy upon the introduction of the lag in presentation between the two tasks, as comparable performance was observed during the simultaneous presentations of two tasks as observed with the PRP DT and TEA DT.

For inhibition ability, age effects were observed with both tasks used. The Stroop task results revealed that the older participants were significantly less efficient at completing the incongruent section as compared to their younger counteracts, indicating intact but deteriorated inhibitory ability. A finding that has been frequently reported in studies (Albinet et al., 2012; Amer & Hasher, 2014; Andrés et al., 2008; Bherer et al., 2006; Boucard et al., 2012; Clarys et al., 2009; Damoiseaux et al., 2008; Keightley et al., 2006; Laguë-Beauvais et al., 2015; Langenecker et al., 2004; Mayas et al., 2012; Morrone et al., 2010; Z. Wang & Su, 2013). Similarly, with the HSCT, the older adults attained higher RT costs, signifying decline in inhibition ability, a finding commonly reported in literature (Bielak et al., 2006; Borella et al., 2011; Cervera-Crespo & González-Alvarez, 2017; Tournier et al., 2014; Zimmermann et al., 2017).

However, inhibitory control is a multi-dimensional construct (Dempster & Vegas, 1992; Diamond, 2013; Friedman & Miyake, 2004), and these tasks measure different constructs. The Stroop task is understood to assess the disruptiveness of a stimulus which is not required for the active suppression of thought (Borella et al., 2009; Diamond, 2013; Friedman & Miyake, 2004). Whereas the HSCT requires response inhibition and cognitive inhibition for the suppression of active processes to stop or limit irrelevant information from entering WM (Borella et al., 2009; Diamond, 2013; Friedman & Miyake, 2004). Thus, highlighting one of the issues that may be encountered with EF tasks, i.e. the assessment of a different type of the same EF.

Despite this, these were the only tasks to both show age effects for the same EF, indicating that inhibition was the most affected ability due to healthy ageing. Thus, it seems the

inhibition-deficit hypothesis (Hasher & Zacks, 1988; Lustig et al., 2007) may be accurate in stating that impairment in inhibition is the primary source of age-associated deficits reported in the performance of numerous cognitive tasks, especially those involving WM (Campbell et al., 2020; Hasher et al., 2008; Koch et al., 2010; Persad et al., 2002). Also, Gilsoul et al, (2019) found inhibition partly mediated the effect of ageing of the three other EFs.

For the assessment of shifting ability, no age effect was observed with the global cost measures of the TMT. However, considering only good performers were analysed, this is understandable. Thus, these remaining older participants were considered to have intact shifting ability, not affected by ageing. Reports from previous cognitive ageing studies have presented conflicting results (Damoiseaux et al., 2008; Keightley et al., 2006; Laguë-Beauvais et al., 2015; Laguë-Beauvais, Brunet, et al., 2013; Maquestiaux et al., 2010; L. D. Müller et al., 2014; Rhodes & Kelley, 2005; Skinner & Fernandes, 2008; Tournier et al., 2014; Waring et al., 2019). Although this may be linked to differences in the task requirements of these studies as some reported error rate, which was only used to eliminate bad performers in this study.

With the task switching paradigm (Rogers & Monsell, 1995), the older adults produced a larger mean RT global cost, a higher mean RT local shift cost, and a larger mean mixing task error rate shift cost. These findings are believed to be the result of the older adult's inability to effectively recruit the cognitive processes, hypothesised as difficulty in retrieving the task rules from long-term memory, and adeptly maintain and coordinate two tasks in working memory (WM) (Bopp & Verhaeghen, 2009; Gajewski, Ferdinand, et al., 2018; Kray et al., 2002; Kray & Lindenberger, 2000; Wasylyshyn et al., 2011).

Global shift costs are understood to measure the set-up cost associated with the maintenance and scheduling of the two mental task sets, in addition to the load on WM (Kray & Lindenberger, 2000; K. Z. H. Li et al., 2019; Mayr, 2001). Whereas local shift costs are believed to reflect the cognitive processes needed to deactivate the previous task set used in the previous trial to activate the newly presented task set (Monsell, 2003). Thus, the results suggest the older adults spend longer mentally arranging their thought process during completion of the global and local shift task conditions. Age effects in global shift costs are typically reported in literature, however local shift costs are thought to be

unaffected (Hartley et al., 1990; Huff et al., 2015; A. F. Kramer et al., 1999; Kray & Lindenberger, 2000; Mayr, 2001; Meiran et al., 2001; Salthouse et al., 1998). Nevertheless, Hillman et al, (2006) also reported these same RT cost findings.

Mixing task cost has been attributed to the control processes required for the maintenance of the two task sets during the shifting condition (Kray & Lindenberger, 2000). The larger error rate cost indicates this older group were not as efficient as the young adults at shifting between the tasks, therefore leading to more inaccuracies during performance. A finding that has been observed in several studies (Kray & Lindenberger, 2000; Mayr, 2001; Meiran et al., 2001; Reimers & Maylor, 2005; Van Asselen & Ridderinkhof, 2000; Verhaeghen & Cerella, 2002; Wasylyshyn et al., 2011), and proposed to be the result of deficits in selective attention (Meiran & Gotler, 2001), which is in line with the executive attention framework (Engle, 2002; Engle & Kane, 2004).

These age-related differences in task preparation, interference and shifting processes of the task switching task present its advantage over the TMT, as these separate cost measures tap into distinct components of the shifting process.

In the examination of WM updating ability, comparable performance between the age groups was observed with the BDS task although results from previous studies have been conflicting (Bherer et al., 2006; Chee et al., 2006; Damoiseaux et al., 2008; Ford et al., 2014; Gutchess et al., 2005; Isaacowitz et al., 2006; Pettigrew & Martin, 2014; Schroeder, 2014).

With the computerised spatial n-back task, the older adults produced more errors resulting in a higher cost value in comparison to the younger adults, a common finding (Albinet et al., 2012; Amer & Hasher, 2014; Berger et al., 2017; Clarys et al., 2009; Daffner et al., 2011; J. McCabe & Hartman, 2008; Missonnier et al., 2011; Nagel et al., 2011; Salat et al., 2002; Vaughan et al., 2008). It is theorised to be due to the increase in task demand, particularly during the 2-back and 3-back conditions (Bopp & Verhaeghen, 2018; Qin & Basak, 2020; Verhaeghen & Basak, 2005), and attributed to decrease in attentional control (Kane et al., 2007; Verhaeghen & Cerella, 2002). Further to this, older adults have been proposed to be slower at organising and managing new incoming information, and the processing of outgoing information, increasing the opportunity for inaccuracies (Kirchner, 1958). No age effect was found with the mean RT results.

Interestingly, there is evidence that ageing negatively affects spatial WM task performance greater than verbal WM task performance (Hale et al., 2011), which could account for the results seen here. Additionally, n-back task performance across the age groups has been reported to use different functions (Gajewski, Hanisch, et al., 2018). Young adults are alleged to use EFs such as interference control, shifting and updating. Whilst older adults are believed to rely more on attention, and to a smaller degree, shifting and updating (Gajewski, Hanisch, et al., 2018), indicating a change in processing strategy between the ages.

Neurally, the older adults' comparable performance with the young adults during performance of the TEA DT, PRP DT SOA 0ms, BDS task, and possibly the TMT, supports the theory of this group using an efficient task coordination strategy. Such a strategy includes the Scaffolding Theory of Ageing and Cognition (STAC) (Park & Reuter-Lorenz, 2009; Reuter-Lorenz & Park, 2014), which states older adults develop alternative and complementary neural networks to accomplish cognitive goals, such as the upregulation, delocalisation, or reorganisation of neural networks (Cabeza et al., 2018; Grady et al., 2016; Phillips & Andrés, 2010).

With the DT tasks, it is thought that as no age effect was observed with the performance of the TEA DT and PRP DT SOA 0ms but a PRP effect was found with the RT, the process of upregulation may have been used, as there must have been a lower asymptote point. Specifically, the compensatory process reached a threshold during the TEA and PRP DT SOA 0ms performances. Likewise, the process is suggested to have been used during performance of the updating tasks, as an age effect was only detected with the n-back task. The asymptote threshold was possibly sufficient enough to complete the BDS test.

Reorganisation is proposed for the TMT performance in the good performing older adults that completed the task properly. The processes for the Stroop task and HSCT are not postulated as it is hard to speculate which of the three might have been used. Even so, it is not known how compensatory mechanisms are selected or used by the brain, therefore the proposed mechanisms thought to be used during the DTs, TMT, BDS, and n-back by the older adults are theorised.

Nevertheless, as the older participants were able to successfully complete all the tasks, it is presumed the recruitment of the central executive (CE) for task processing is maintained

and without substantial impairment (Reuter-Lorenz & Park, 2014). Although decrease in cognitive control due to advance age resulted in slowness and/or reduced accuracy in some performances. Furthermore, in accordance with the frontal lobe hypothesis of neurocognitive ageing (Dempster & Vegas, 1992; West, 1996), the findings of the behavioural studies may provide evidence that decline of older individuals' cognitive ability is the result of age-associated structural changes in prefrontal brain regions which increases with age (Raz, 2000; Raz et al., 1997, 2005; Raz & Rodrigue, 2006; Salat et al., 1999, 2004; Tisserand & Jolles, 2003a, 2003b).

In the assessment of the individual trajectory of decline of the four EFs using the behavioural study outcome measures, shifting was observed to have the highest rate in the older adults. Next was inhibition, then updating, and DT the least. However, as the first three EFs had comparable high rates of decline that were not significantly different in comparison to DT, it can be speculated that there were two rates, one high and one low. Suggesting decline of these EF abilities is not uniform. This is in line with the findings of Miyake, Friedman, et al (2000), which found the three EFs with the high decline rates loaded similarly during a factorial analysis study, indicating they may share a common underlying cognitive component. Therefore, demonstrating the theory of the "unity" of EFs. As DT loaded independently, it was suggested to have its own underlying component and, as such, different from the other EFs, indicating the "diversity" of EFs. Thus, it would seem that DT ability is not as affected by the ageing process as much as the other three EFs.

The comparison of the trajectory of decline of these four EFs collectively has not been extensively researched in cognitive ageing, or pathological conditions. Therefore, these novel findings are promising and may offer further contribution into understanding how these EFs are affected by ageing. The trajectory of decline of these EFs due to MCI and early-stage AD were also originally planned to be investigated to gain further insight into the mechanisms involved in the transition from normal to pathological ageing, however this was not possible. It was hoped that by recognising a pattern of decline between these EFs, and possibly others, through consistent monitoring of decline rates in healthy individuals, deviations from it may signal the clinical presentation of a form of pathological cognitive impairment. Identifying early deficits is important as it facilitates early detection and possible treatment of a condition.

Nevertheless, this specific trajectory of decline was only observed with the use of the task measure with the largest decline rate for each EF in this research, i.e. the RT PRP effect, incongruent score of the Stroop task, local RT shifting cost of the task switching test, and error rate cost of the n-back. Therefore, this trajectory might not be observed with other EF task measures for these same four abilities. CFA studies in older adults have revealed several models of factor loading (Bettcher et al., 2016; Hedden & Yoon, 2006; Hull et al., 2008; Vaughan & Giovanello, 2010), which have been suggested to be the result of the different tasks used. Moreover, during the review of EF studies in Chapter 2, different outcomes, i.e. no performance deficit with one task verses deficit with another, were reported in some studies (Albinet et al., 2012; Boucard et al., 2012) that had employed multiple tasks to assess the same EF on the same group of participants.

Chapter 4 presented two different analyses of the task measures from Chapter 3. The first study assessed to what extent that task pair measures correlated in their result for each of the EFs. A significant positive correlation was only observed in the older adults between the DT error rate measures of the TEA telephone code search and the PRP DT SOA 0ms visual task. This association may provide evidence to support the change of the structure of EFs with increasing age due to neural reorganisation and the dedifferentiation hypothesis (Koen & Rugg, 2019; Tucker-Drob, 2009). It suggests stronger correlations between cognitive abilities in older adults than in their younger counterparts.

The lack of correlation in the young adults does not however, imply that the task pairs were not assessing the same EF, as different characteristics of the same EF may actually have been assessed, as with the inhibition tasks employed in Chapter 3.

In the second study, CFA was conducted to seek to what degree the cognitive processes underlying the construct of the EFs in the four task pairs EFs where independent and interrelated, i.e. examine the relations between the latent variables. Latent variables reflect the common factor shared by the tasks employed to assess a particular EF, and thus provide purer measures of the process they are intended to tap into.

The common EF factor loading analysis in the young adults proved inadequate and thus was not considered. In the older adults, the common Ef factor loading model was adequate,

suggest the four task pairs loaded to a common factor. The DT measures loaded the best, and while the inhibition measures loaded the worst. Surprisingly, as discussed earlier, inhibition is thought account for age-associated cognitive deficits. However, as the sample used in the CFA was smaller and not the same as that used in the behavioural and correlation studies, it may be assumed that inhibitory control was not as impaired in these group of participants as they performed all eight tasks correctly. Even so, Hull et al, (2008) similarly reported inhibition loading weakly in the CFA of task measures in older adults.

In the correlation factor loading analysis between the four EF task pair measures, a weak insignificant four-factor model was found in the young. However, in older adults, an insignificant two-factor model was observed, as a strong association between DT and updating was observed, resulting in a *DT/updating-shifting* model following removal of inhibition. Following application of Miyake, Friedman, et al (2000)'s proposed three-factor model, *inhibition-shifting-updating*, with the older adults, analysis proved it to be more adequate, hence this model was considered.

These results are in accordance with the findings reported by Bock et al, (2019) and Glisky et al, (2020), who described stronger associations between EFs with advancing age. Further providing evidence for the structural changes of EFs that takes place with advance age. Significant loading models may have been produced with larger participant numbers, as factor studies usually employ over 40 participants (Bettcher et al., 2016; Bock et al., 2019; Hedden & Yoon, 2006; Hull et al., 2008; Miyake, Friedman, et al., 2000; Vaughan & Giovanello, 2010).

Collectively, the behavioural studies and analyses performed on the task pair measures demonstrate that EFs are indeed diverse and independent through the observation of the different trajectories of decline. Although inhibition, shifting, and updating were shown to possess a similar higher rate of trajectory in comparison to DT. Furthermore, increased age was shown to change the structure of EF, particularly with the correlation analysis and CFA of the EF task measures. The EFs were observed to be more distinct in younger individuals, whereas in the older generation, the EFs loaded more strongly to each other.

The PFC is widely known to be essential for numerous higher-order cognitive functions. Therefore, a literature review was conducted in Chapter 5, describing the brain structures

and neural networks important for EF processing, especially the dorsolateral PFC (DLPFC), ventrolateral PFC (VLPFC), and the fronto-parietal neural network (Dixon et al., 2018; Marek & Dosenbach, 2018; Mezzacappa, 2011). All have been observed to be associated with task performance of the abilities DT, inhibition, shifting, and updating (Chmielewski et al., 2014; Hartley et al., 2011; Kaufmann et al., 2008; L. D. Müller et al., 2014; Sun et al., 2005; Talwar et al., 2020).

As a consequence of the neuroanatomical structural changes that occur due to ageing, neural activity associated with these abilities have been observed to be less lateralised in older individuals in comparison to their younger individuals (Cabeza et al., 2002). A process believed to be involved in compensatory processes. Such activity was found in the review of the neuroanatomical correlates of the task performance of several of the tasks employed in Chapter 3 as my own MRI study could not be conducted. For example, older adults' performance in the task switching task, has been associated with bilateral activity in the DLPFC, right insula and ventral visual cortex.

Other compensatory processes observed in the older adults included enhanced activity of the same regions used by younger adults and/or activity of additional brain regions not normally used by younger individuals. In line with this, performance in the PRP was associated with increased activity in the anterior PFC and occipital region (Chmielewski et al., 2014; Hartley et al., 2011). Stroop task with increased activity in the anterior inferior prefrontal cortices, particularly, the IFG, MFG, pre-SMA, and precuneus (Kaufmann et al., 2008). TMT with additional activity in the left medial and lateral PFC (L. D. Müller et al., 2014; Talwar et al., 2020). The BDS task with greater activity in the right IFG (BAs 44/45) (Sun et al., 2005), and with n-back task performance with additional activity in the parietal and cingulate cortices (Yaple et al., 2019).

To complement the behavioural study, the last study presented in Chapter 6 explored the structural changes that occur in older adults, from cognitively healthy to MCI to severe AD, through VBM analysis, with the utilisation of data from the OASIS-3 database (LaMontagne et al., 2019). Results showed significant volume loss bilaterally in gray (GM) and white matter (WHM) throughout the medial temporal lobes (MTLs) but not in the PFC. In accordance with AD deterioration, this finding was observed to correlate with decline in performance of the memory domain of the MoCA test, and the logical memory task.

A greater proportion of the clusters identified between the healthy and less severe AD groups were located in WHM, areas implicated in the transmission of neural activity. Whilst greater GM atrophy was observed between the more severe AD groups, indicating decreased neural processing in advance AD. Accordingly, WHM degeneration is understood to be significantly involved in AD progression (Caso et al., 2015; Migliaccio et al., 2012).

Other brain regions which showed significant loss, particularly of WHM, included the midbrain regions, the anterior cingulate gyrus, amygdala, striatum (more precisely, the caudate nucleus of the striatum), as well as the parietal lobe. These are all widely acknowledged to be important in the processing of EFs (Amanzio et al., 2011; Bush et al., 2000; Collette, Van Der Linden, et al., 2005; Elshafey et al., 2014; Laakso et al., 1995; Pini et al., 2016; Poulin et al., 2011; Seger & Cincotta, 2005; Stevens et al., 2011; Yildiz & Beste, 2015). The worsened performance of the participants in the MoCA domains (including community, hobbies, judgment, orientation, and personal care), and in the Boston naming test, category fluency, and digit span (BDS and forward digit span), TMT, WAIS-R Digit Symbol tests, is thought to associate with the increased loss of volume in these regions.

There were no substantial atrophy differences observed between the healthy and MCI participants, or between many of the moderate to late-stage AD severities, perhaps suggesting minuscule changes not detected during the analysis.

In summary, the findings of all the studies discussed further our understanding into the structure and processing of the EF abilities DT, inhibition, shifting, and updating in cognitively healthy young and older adults, and processes involved in the performance. Furthermore, the neuroanatomical and neuronal changes that occur from cognitively healthy older adults to MCI and severe AD was explored and associated with changes in cognitive status and performance in a group of EF tasks.

7.3 Study Implications

The research conducted in this thesis presented the differential process of how the EF abilities DT, inhibition, shifting, and updating are affected by the process of ageing, which was found to be in agreement with the prefrontal-executive theory proposed by Dempster & Vegas (1992) and further defined by West (1996). In turn, the performance deficits

observed in older adults are proposed to be due to a decrease in the efficiency to maintain cognitive control, especially during high demand task situations. This is said to be the consequence of structural changes in the PFC, as described by the executive attention framework by Engle (2002) and Engle & Kane (2004). Nonetheless, as a result, the older adults were shown to have recruited strategies to complete the tasks, in some cases as well as their younger counterparts, as described by the strategy-deficit hypothesis (Bailey et al., 2009).

In accordance with the Miyake, Friedman, et al (2000) concept of the unity and diversity of EFs, was the finding of the two distinct trajectory rates of decline of EFs, one high and one low. This may also be linked to the central executive system (CES) of the working memory model proposed by Baddeley & Hitch (1974). This system controls, coordinates, regulates, and integrates new information into and between the phonological loop (PL), visuospatial sketchpad (VSSP), and the episodic buffer slave systems (Baddeley, 2000). So, it may be concluded that the unity of EFs is a result of this underlying component. More specifically, as this singular system allocates cognitive resources in response to external information, these hypothetically independent systems may overlap in the processing of EFs, particularly of the WM domains, inhibition, shifting, and updating. While the diversity of EFs may relate to the primary source of information inputted into the CES.

The thesis findings have thus extended our understanding into the nature of cognitive decline, where with the exception of DT, decline was relatively homogenous. In light of this, potential clinical implications and uses of the findings may be considered. For example, to offset the effects of cognitive ageing, cognitive training programs should be implemented in order to minimise age performance deficits, which may in turn reduce the transition to neuropathological impairment (Iordan et al., 2020; Karbach & Schubert, 2013; Mowszowski et al., 2016; Penning et al., 2021; Zinke et al., 2014).

7.4 Limitations and Considerations

The studies presented in this thesis must be interpreted in consideration of a number of limitations. Firstly, the study samples and their composition. The sample sizes for both the young and older adult groups were relatively small which introduces potential difficulties in generalising the study results to the general population. Therefore, indicating the need for a

future replication study with larger samples to increase statistical power of the studies. Also, a smaller percentage of male participants were recruited into the study, particularly in the young adult group. This may further limit the generalisability of the present results to other populations. Researchers have reported increased variability in the DT cognitive performance of female participants (Kaur et al., 2014; Mäntylä, 2013; Poromaa & Gingnell, 2014; Wong-Goodrich et al., 2020; Wozniak et al., 2014), due to hormonal changes that transpire during menstruation. Hence, this may have occurred in this study and influenced the results of the DT group performances due to the larger number of female participants. This may have also extended to the other EF performances.

Additionally, the older participants were well educated as well as highly experienced professionals, which may suggest their level of cognitive reserve may have slowed their cognitive decline (Barulli et al., 2013; Cabeza et al., 2018; Meng & D'Arcy, 2012). Accordingly, it may be speculated that this group of older individuals, and the university educated young adult participants were not a true representation of the general population. Resulting in an underestimation of age effects, although the age effects could have balanced out, as the groups were similarly intellectually matched. However, the degree of education attained affects cognitive performance in young and older adults differently. Testing performance in well and low educated young adults does not seem to differ whereas better educated and intelligent older adults perform better than their less educated counterparts (Kaufman et al., 2016; Lövdén et al., 2020; McKoon & Ratcliff, 2012).

Secondly, there is the study design and procedure. Chronological age may play a more significant role among even older groups, for example in those over 80 years of age. Therefore, the inclusion of additional age groups such as middle-aged and particularly old-old (> 80 years of age) participants to further increase our understanding into trajectory of decline of EFs due to healthy ageing would be beneficial.

Regarding improvement of the study method, the use of different tasks to measure the cognitive processes of interest is suggested as the results attained in the behavioural studies were dependent on the specificity of the neuropsychological tests employed (Pettigrew & Martin, 2014; Schroeder, 2014; Sung et al., 2012; Sylvain-Roy et al., 2015; Waring et al., 2019). Other tasks may generate different age-related results to those reported in the studies presented. Similarly, employing additional tasks for the assessment of each EF, i.e.

more than two, would increase the accuracy of the study results as some of the task pairs reported dissimilar levels of cognitive decline. This would also aid in the examination of the factor loadings of the EFs through CFA, as tasks load differently, and with the correlation analysis of task measures assessing the same EF.

Furthermore, there is the issue regarding task familiarity. A number of participants of both age groups, but particularly the young adults, mentioned prior knowledge and experience with a few tasks such as the Stroop test, either from a university course or through a previous study participation. Many had participated in other academic, healthcare, and/or scientific research trials and studies. This may have potentially caused bias as these participants may have possibly performed better in these tests than a fully naïve participant sample due to being more experienced and so more trained in the task requirements. This may in turn affect the assessment of age effects. For instance, more experienced young adult performers in a cross-sectional comparison with less experienced older adults would result in an overestimation of age effects due to a type I error. Thus, to avoid such a problem, including a questionnaire regarding prior task experience and/or knowledge during participant screening would allow for this to be formally accounted for and assessed. Possibly by having the less experienced participants complete tasks twice, or a more feasible solution, include prior task experience as a co-variate.

Therefore, in light of these limitations, future studies addressing these issues are needed for a better understanding of EF decline due to healthy cognitive ageing.

7.5 Directions for Future Research

The studies presented in this thesis aimed to broaden our understanding of the decline of EF abilities as a consequence of 'normal' ageing, as well as the concept of the unity and diversity of EFs. However, a number of potential directions for future research can be undertaken to expand on the work presented.

Performing the described behavioural studies, as was originally planned in this thesis, on cognitively impaired individuals, such as those living with MCI and/or established groups of individuals living with dementia, particularly early-stage AD would be highly advantageous. This would allow for further insight into the trajectory of decline of the four EFs in these

neurodegenerative conditions and thus, the tracking and comparison of decline of individual EFs by detecting deviations from 'normal' decline rates. Such research could have profound clinical implications by allowing for the identification of potential MCI and/or dementia patients who might benefit from early cognitive training.

In addition, investigation into a vaster variety of EFs, including visuospatial and planning abilities, must be researched for a thorough understanding of decline of cognitive abilities, as EFs coordinate and collaborate with each other to bring about an action. This will further assess the concept of the unity and diversity of EFs. Tasks including the Tower of London (Shallice, 1982), or Tower of Hanoi tasks (Humes et al., 1997), or the Six Elements test (Wilson et al., 1996) may be employed for such assessments.

Moreover, manipulating and comparing of the stimulus used in the PRP, task switching, and n-back tasks, should be considered. For example, the use of picture/symbol, letter, or word stimuli can be explored to determine what effect is made on performance outcomes, in comparison to what was observed with the use of digits. Particularly in older adults, as they have been reported to perform better with lexicon stimuli in comparison to non-lexicon stimuli (Balota, 1996). Importantly, research has shown these various types of stimuli use different brain networks for their processing, hence task performance may differ depending on the extent at which such networks are affected by brain ageing (Azizian et al., 2006; Carreiras, Monahan, et al., 2015; Carreiras, Quiñones, et al., 2015; Kahlaoui et al., 2007; Seifert, 1997). Thus, differences in age effects may be observed.

Regarding the findings presented in Chapter 6, a possible area of research should be to undertake a functional MRI study to explore the neuroanatomical correlates of the four EFs presented in the behavioural studies on the cognitively healthy young and older adults. Such a study would ideally also include the cognitively impaired participant populations, such as MCI and/or AD and/or frontotemporal dementia (FTD), in an effort to determine the underlying neural activity of their cognitive abilities. FTD affects the PFC more extensively than AD, so a more comprehensive comparison of decline in cognitive abilities with structural involvement may be made.

Finally, comparing the performance of low and highly educated participants across the age groups to gain additional knowledge on the concept of cognitive reserve and cognitive ageing would be interested.

7.6 Conclusion

The primary aim of this thesis was to assess the EF abilities dual-tasking, inhibition, shifting, and updating, in young and older adults, and to determine the trajectory of cognitive decline as a consequence of ageing, through the behavioural studies. The exact pattern of deterioration may allow for a proper understanding of the mental processes involved in healthy ageing.

With an increasing proportion of older individuals, a firm understanding of normal cognitive ageing is necessary, as it presents a framework against which pathological ageing can be compared. Moreover, the neuroanatomical change from healthy to pathological impairment through VBM analysis provided insight into the precise route of structural change occurring during the onset and progression of AD with respect to cognitive decline.

Thus, this research may aid as a means to monitor cognitive transition and/or an approach for cognitive intervention(s) in order to avert additional cognitive decline through the development of cognitive training programs to improve specific cognitive domains. Furthermore, it may allow for the development of a low cost, non-invasive preclinical dementia diagnostic tool, as age-associated decline in these EFs will serve as a baseline for healthy aged cognition. In this manner, preventing further deficits and/or cognitive decline, as well as decreasing financial, medical and carer burden on the general public of therapeutically approaches.

Supplementary Chapter, Executive Function Abilities in Cognitively Healthy Young Adults

S. Introduction

Executive functions (EFs) are critical for routine cognitive processes, as they facilitate complex behaviours such as planning, reasoning, maintaining goals, flexibly coordinating actions, suppression of competing actions or thoughts, and more. These are abilities important for completing everyday activities and as such, for living independently (Deary et al., 2009; Diamond, 2013; Harada et al., 2013). These EFs are stated to be most developed in early adulthood, specifically in the early twenties (Salthouse, 2009), as this is when the brain, particularly the prefrontal cortex (PFC), the region of its association (P. Yuan & Raz, 2014), has completely developed. Following this, it starts to steadily deteriorate with age (Salthouse et al., 2003; P. Yuan & Raz, 2014).

Of particular interest are the EFs, dual-tasking, inhibition, shifting and updating, which are thought to be most essential for performing complex cognitive activities and frequently correlate with the activities of daily living and instrumental activities of daily living (Diamond, 2013; Miyake, Friedman, et al., 2000). These EFs heavily rely on attention, i.e. divided, selective and focused attention, and short-term memory (STM), which are especially optimal in early adulthood (Diamond, 2013). Accordingly, cognitively healthy (CH) young adults are considered to be most proficient at performing and completing tasks of various complexities, possessing better response times (RTs), obtaining minimum error rates, and attaining faster completion times in comparison to older adults (Salthouse, 1995, 1996; Salthouse & Meinz, 1995). For this reason, adult participant studies typically use this population as a control or baseline group for performance comparison (Salthouse, 2005; Salthouse et al., 2003).

In this behavioural study, the objective was to investigate the EF abilities of the CH young adult population on a battery of tasks assessing the cognitive domains, dual-tasking, inhibition, shifting and updating, in order to serve as a baseline group. This study was part of a cross-sectional study for comparison with a CH, non-demented, older adult population presented in Chapter 3. A further group of older cognitively impaired individuals, specifically, those living with mild cognitive impairment (MCI) and early-stage Alzheimer's

disease (AD), were originally planned to be included in this study. However, due to the COVID-19 pandemic, this was not accomplished. Thus, this chapter presents a descriptive characterisation of a young CH sample.

As a consequence of the study design, a number of assessments normally utilised in older and/or cognitively impaired individuals were recruited for use in the cross-sectional study, with the purpose of undertaking a fair as possible comparison of the participant groups. Additionally, in the assessments of EFs, many tasks have been employed in clinical and research settings, as there is no single universal method for their examination. So, the issue of consistency in task results is seen as tasks intended to measure a particular EF regularly depend on the involvement of other EFs, but the extent which these other functions are being used is unclear. Moreover, some tasks were created to assess specific EFs, whilst others were not, thus there may be issues in effectively correlating task measures.

Nevertheless, a number of traditional neuropsychological tests are frequently used in the evaluation of EFs, including the trail making test (Reitan, 1992) for shifting, the Stroop task (Stroop, 1935) for inhibition, and numerous subtests of the Wechsler Adult Intelligence Scale (Wechsler, 1955), including the backward digit recall span, for updating. All of which will be utilised in this study, with the addition of five more, as two EF tasks were employed to assess each of the four EFs being researched. Thus, a secondary aim of this study was to explore the correlation of each of the EF task pair results, as they should ideally provide a similar estimate of EF abilities if they are truly assessing the same element. This is presented in Chapter 4.

S. Methods

S. Participants

A total of 32 (7M/25F) young adult participants were initially recruited into the study, three (2M/1F) withdrew after the first (screening) session and two (2F) after the second. The data for the two individuals who completed only two of the three sessions was used in the study. The data of one female participants (aged 47) was withdrawn due to being an age outlier. Thus, 26 participants (5M/21F) completed all study sessions, aged 18 to 33 years (mean of 21.18, SD 4.43).

All had normal (or corrected to normal) vision and hearing.

S. Procedure

Participants were recruited through poster and online advertisement at Brunel University London. Individuals were provided with the participant information sheet (PIS) for their review prior to the first screening session. Once agreement to participate was confirmed, the participant completed the online study recruitment questionnaire (Appendix 2) to determine study participation suitability. Data collected included demographic information, level of education, profession, medical history of severe auditory or visual abnormalities, psychiatric, neurological, or systemic diseases which could cause cognitive impairments. In addition, severe physical disability, a history of epilepsy or other conditions that may cause uncontrolled movements or tremours were all considered exclusion criteria. Once accepted for participation, all individuals were invited to the screening visit.

Participants completed three sessions, a screening and two EF visits, each lasting approximately 60 minutes in duration at the Uxbridge campus of Brunel University London. Once written informed consent was obtained, all the screening assessments were completed. The participants completed the tests, the geriatric anxiety scale (GAS) and geriatric depression scale (GDS) (Yesavage et al., 1983), activities of daily living scale (ADL) and instrumental activities of daily living scale (IADL) (Lawton et al., 1969), and the spot-the-word test (Baddeley et al., 1993) online via a Qualtrics link. As well as the Hopkins verbal learning test (HVLT) (Brandt, 1991) in person.

In the first EF session, the assessments were completed in the following order: test for everyday attention (TEA) DT telephone search subtest, computerised task switching test, backward digit recall span (BDS)**,** and the Hayling sentence completion test (HSCT). In the second EF session, the assessments were always completed in the following order: trail making test (TMT), computerised n-back, Stroop task, and the computerised psychological refractory period paradigm task (PRP) tasks. All the tasks except the BDS and Stroop task, included a practice run prior to beginning the actual study task. All assessments are described in sections 3.2.3, and 3.2.4. Following completion of all study sessions, all participants were presented with the study debrief form and compensated with either 12 course credits or a £20 Amazon voucher.

All study documents, including the PIS, study consent form and debrief sheet can be viewed in the Appendix (2a, 3a, and 4a, respectively). This study was approved by Brunel University's Department of Life Sciences Ethics Committee.

S. Screening Assessments

Please refer to section 3.2.3.

S. Executive Function Assessments

Please refer to section 3.2.4.

S. Statistical Analysis

The data was assessed by using the Statistical Package for Social Sciences (SPSS), version 26.0.0.0 (IBM SPSS Statistics, IBM Corp, Armonk, NY). Participants were excluded from analysis on each task if they performed above or below 3 standard deviations (SDs) from the rest of the groups' mean performance. Descriptive data and the study behavioural data were collected. Chi-squared, χ^2, test was further used to assess gender and handedness.

Paired-samples t-tests and one-way repeated measures analysis of variance (ANOVA) were used to assess congruent and incongruent performance of the same tasks. In addition, the n-back pairwise comparison *p*-values were Bonferroni corrected due to the numerous pairwise assessments conducted using an online calculate, https://www.easycalculation.com/statistics/bonferroni-correction-calculator.php, to reveal the new (corrected) alpha level needed to be passed, i.e. 6 (number of comparisons). The Bonferroni corrected alpha was taken as 0.00851. The significant effects for all the tests were reported at $p < 0.05$, unless stated otherwise.

S. Results

S. Demographics and Screening data

The group demographic data and the descriptive summary of the results can be viewed in Table S1.1.

Table S1.1. Demographic Data of the Young Participants

Characteristic	**Young Adults** (Mean/SD)
Age, years	21.18 (4.43)
Gender (M/F)	5/23
Education, years	14.46 (1.32)
Handedness (L/R)	2/26
Mini-Mental State Examination	28.46 (1.29)
Montreal Cognitive Assessment	26.71 (2.27)
Geriatric Anxiety Scale	19.75 (9.99)
Geriatric Depression Scale	12.32 (3.40)
Activities of daily living scale	6.00 (0.00)
Instrumental activities of daily living scale	7.18 (1.28)
Hopkins Verbal Learning Test, Part A	7.38 (1.63)
Hopkins Verbal Learning Test, Part B	11.07 (1.18)
Hopkins Verbal Learning Test, Discrimination index	18.45 (2.23)
Spot-the-word test	28.96 (3.11)

The group was deemed cognitive healthy following assessment. Though, a mild level of depression was observed, no participant reported that they had been clinically diagnosed with depression (e.g. by a medical profession). Minimal anxiety was indicated. Furthermore, both the GAS and GDS are designed to be used on older adult individuals, so the questions asked may not be suited for this younger group, as evident by participants probing some of the questions asked especially in the GDS, i.e. regarding spouse, children, etc. However, because the overall study aimed at assessing older adults and performing a cross-sectional analysis between the groups, these two scales were included. Additionally, the group was concluded to be functional independent and capable of completing everyday tasks effectively from their scores in the activities of daily living scale and instrumental activities of daily living scale.

Verbal learning and memory were examined with the HVLT. A significant difference was found between the performance in both parts of the test, $t(27) = -10.97$, $p < 0.001$, accounting for the delay in recall demand of second test section.

Lastly, the groups' premorbid IQ was assessed to be normal with assessment with the spot-the-word test.

S. Executive Functions Abilities in the Young Adults

S. Dual-Tasking

Dual-tasking was examined using the TEA telephone search subtest and PRP paradigm. The groups' performance results can be viewed in Table S1.2 below.

Table S1.2. Dual-tasking Results of the Young Adult Participants

Task	**n**	**Young Adults** (Mean/SD)
Test for Everyday Attention, telephone auditory DT, code count accuracy (%)	24	90.41 (13.34)
Test for Everyday Attention, telephone count DT, code count accuracy (%)	24	79.17 (15.12)
Psychological Refractory Period paradigm, auditory ST RT (ms)	24	616.97 (199.59)
Psychological Refractory Period paradigm, auditory ST error rate (%)	24	7.33 (7.91)
Psychological Refractory Period paradigm, auditory DT (SOA 0ms) RT1 (ms)	24	1079.62 (365.27)
Psychological Refractory Period paradigm, auditory RT1 DT cost (SOA 0ms), RT (ms)	24	462.65 (323.27)
Psychological Refractory Period paradigm, auditory DT (SOA 0ms) RT1 error rate (%)	24	10.75 (9.81)
Psychological Refractory Period paradigm, auditory DT (SOA 0ms RT2) error rate cost (%)	24	3.42 (6.92)
Psychological Refractory Period paradigm, visual ST RT (ms)	24	503.54 (109.17)
Psychological Refractory Period paradigm, visual ST error rate (%)	24	3.42 (4.55)
Psychological Refractory Period paradigm, visual DT (SOA 0ms) RT2 (ms)	24	1312.99 (418.22)
Psychological Refractory Period paradigm, visual RT2 DT cost (SOA 0ms), RT (ms)	24	809.45 (381.28)
Psychological Refractory Period paradigm, visual DT (SOA 0ms) RT2 error rate (%)	24	7.75 (7.13)

Psychological Refractory Period paradigm, visual DT (SOA 0ms) RT2, error rate cost (%)	24	4.33 (5.71)
PRP paradigm, DT (SOA 0ms) RT2-RT1, RT cost (ms)	24	233.37 (134.72)
PRP paradigm, DT (SOA 0ms) RT2-RT1, error rate cost (%)	24	-0.03 (0.08)
Psychological Refractory Period paradigm, visual DT RT2 (SOA 1000ms) (ms)	24	743.43 (360.35)
Psychological Refractory Period paradigm effect, SOA 0 – 1000ms, visual task, RT2 (ms)	24	569.56 (254.83)
Psychological Refractory Period paradigm, visual DT RT2 (SOA 1000ms) rate (%)	24	9.08 (11.25)
Psychological Refractory Period paradigm effect, SOA 0 – 1000ms, RT2 error rate (%)	24	-1.33 (9.60)
Psychological Refractory Period ANOVA, RT2, SOA 0ms, SOA 1000ms	-	< 0.001
Psychological Refractory Period ANOVA, RT2, error SOA 0ms, SOA 1000ms	-	0.503

RT - Response time, SOA - Stimulus Onset Asynchrony, * - one-way repeated measures.

In the TEA test, a paired-samples t-test between the auditory and telephone code search tasks revealed a significant difference in accuracy performance between the two, $t(23) = 2.541$, $p = 0.018$.

In the second DT, the first condition of the PRP task at SOA 0ms, the visual and auditory stimuli were presented at the same time. A paired-samples t-test between the ST and DT at SOA 0ms showed significance for the auditory task (RT1) RT, $t(23) = -7.01$, $p < 0.001$, and error rate, $t(23) = -2.42$, $p = 0.024$, and the visual task (RT2) RT, $t(23) = -10.40$, $p < 0.001$, and error rate, $t(23) = -3.72$, $p = 0.001$.

Analysis of the performance between the two tasks at SOA 0ms showed there to be a difference in the performance for RT, $t(23) = -8.49$, $p < 0.001$, but not error rate, $t(23) = 1.96$. $p < 0.062$.

The second PRP DT ability was assessed at SOA 1000ms. Here only the visual stimuli, RT2, was considered as this was the task presented at 1000ms (Pashler, 1994; Schubert & Szameitat, 2003a; Szameitat et al., 2011). A paired-samples t-test confirmed the difference between the performance at SOA 0ms and 1000ms was significant for RT only, $t(23) = 10.95$, $p < 0.001$. Thus, no difference in accuracy, $t(23) = -0.68$, $p = 0.503$.

In summary, both tasks demonstrated the groups' capability in completing tasks simultaneously, although at a cost, in comparison to the completion of two tasks individually.

S. Inhibition

Inhibition was examined using the HSCT and the Stroop task. The groups' performance results can be viewed in Table S1.3 below.

Table S1.3. Inhibition Results of the Young Adult Participants

Task	**n**	**Young Adults** (Mean/SD)
Hayling sentence completion test, Part A RT (s)	26	22.27 (8.22)
Hayling sentence completion test, Part A RT completion score	26	4.73 (1.08)
Hayling sentence completion test, Part B RT (s)	26	29.04 (18.53)
Hayling sentence completion test, Part B RT score	26	5.92 (0.84)
Hayling sentence completion test, inhibition RT cost (s)	26	6.77 (17.80)
Hayling sentence completion test, Part C, Error score	26	6.00 (1.98)
Hayling sentence completion test, overall score	26	5.38 (1.36)
Stroop, Word (no. out of 100)	26	93.19 (10.00)
Stroop, Colour (no. out of 100)	26	71.54 (13.97)
Stroop, Colour-Word (no. out of 100)	26	47.04 (10.92)
Stroop, Colour-Word' (no. out of 100)	26	39.69 (5.39)
Stroop, CW-W	26	-46.15 (14.71)
Stroop, CW-C	26	-24.50 (14.19)
Stroop, ANOVA	-	< 0.001*
Stroop, Inhibitory control	26	6.92 (10.48)

* - one-way repeated measures.

Please note one participant was removed from analysis due to audio recording issues. In the HSCT, a paired-samples t-test showed there to be no difference in the groups' performance between parts A and B, $t(25) = -1.94$, $p = 0.064$. The test's scoring system categorised part A performance as 'moderately average', part B as 'average', the error rate performance in part B as 'moderately average', and the overall test score collectively classified to be 'moderately average'. Though, individual participant performances ranged from 'poor' to 'high average'. This is in line with a study reported by Borella et al (2011), as a result individual differences.

A one-way repeated measures ANOVA [conditions (C, W, CW)] was calculated $F(2, 50) = 124.78$, $p < 0.001$, $\eta_p^2 = 0.83$, which revealed a significant difference in the accuracy performance between the three Stroop conditions. Thus, the Stroop effect was observed as expected in the CW section.

However, the positive value of the interference score [6.92 (10.48)] indicates that the group possessed adequate ability in inhibiting interfering information (Scarpina & Tagini, 2017; Stroop, 1935).

To compare the difference in the costs between performance in the CW and C (CW-C), and W (CW-W), a paired-samples t-test was conducted. Significance was found, $t(25) = 7.00$, $p < 0.001$, indicating the performance of the two congruent tasks was difference.

In conclusion, both tasks attained the desired outcome when assessing inhibition. The group were able to successfully control their inhibitory capacity, though their performance was not as efficient as in the non-inhibitory conditions.

S. Shifting

Shifting was examined using the task switching test and TMT. The groups' performance results can be viewed in Table S1.4 below.

Table S1.4. Shifting Results of the Young Adult Participants

Task	**n**	**Young Adults** (Mean/SD)
Task Switching, local shift repetition RT (ms)	26	1253.00 (350.88)
Task Switching, local shift repetition error rate (%)	26	3.69 (4.22)
Task Switching, local shift shifting RT (ms)	26	1328.95 (340.29)
Task Switching, local shift shifting error rate (%)	26	8.42 (7.72)
Task Switching, local shift cost (RT)	26	75.96 (84.29)
Task Switching, local shift error rate cost (%)	26	4.77 (5.92)
Task Switching, mixing task repetition RT (ms)	26	966.32 (179.70)
Task Switching, mixing task repetition error rate (%)	26	2.85 (2.74)
Task Switching, mixing task shifting RT (ms)	26	1253.00 (350.88)
Task Switching, mixing task shifting error rate (%)	26	3.69 (4.22)
Task Switching, mixing task cost (RT)	26	286.67 (222.77)
Task Switching, mixing task error rate cost (%)	26	0.88 (3.71)
Task Switching, global shift repetition RT (ms)	27	963.08 (177.01)
Task Switching, global shift repetition error rate (%)	27	3.04 (2.86)
Task Switching, global shift shifting RT (ms)	27	1312.44 (349.75)
Task Switching, global shift shifting error rate (%)	27	8.96 (7.94)

Task Switching, global shift cost (RT)	27	349.36 (219.29)
Task Switching, global shift error rate cost (%)	27	5.85 (5.72)
Task Switching, RT cost ANOVA	-	< 0.001
Task Switching, error rate ANOVA	-	< 0.001
Trail Making Test, Part A RT (s)	24	32.29 (10.80)
Trail Making Test, Part A error rate (%)	24	2.08 (10.21)
Trail Making Test, Part B RT (s)	19	64.11 (19.54)
Trail Making Test, Part B error rate (%)	19	15.79 (33.55)
Trail Making Test, RT Shifting cost (s)	19	31.00 (17.68)
Trail Making Test, Error rate shifting cost (%)	19	13.16 (36.67)

Three shifting types were assessed with the task switching task, local shift, mixing task, and global shift.

Paired-samples t-test comparing performance between the repetition and shifting conditions revealed significance in all the RTs, and all but one of the error rates. For the local shift, RT, $t(25) = -4.60$, $p < 0.001$, and the error rate, $t(25) = -4.08$, $p < 0.001$. For mixing task, RT, $t(25) = -6.56$, $p < 0.001$, and the error rate, $t(25) = -1.19$, $p = 0.247$. For global shift, RT, $t(26) = -8.28$, $p < 0.001$, and the error rate, $t(26) = -5.26$, $p < 0.001$.

The shift types were compared with ANOVA analysis (local shift, mixing task, global shift), revealing a significance difference for both the RTs and error rates, $F(2, 24) = 43.50$, $p < 0.001$, $\eta_p^2 = 0.78$, and $F(2, 24) = 11.95$, $p < 0.001$, $\eta_p^2 = 0.50$, respectively.

Hence, participants presented with the characteristic task-shifting costs associated with this task by producing longer RTs, more errors, in two of the shifting types assessed, indicating the demand on the shifting EF.

In the TMT, a significant difference with the RT was also shown between the task conditions, $t(18) = -7.64$, $p < 0.001$. Although, an insignificant difference in shifting error rate was found, $t(18) = -1.56$, $p = 0.135$, which is understandable as only the good performers were included in the task analysis.

To conclude, shifting ability assessment with the task switching task resulted in prolonged RTs, and increased error rates with the local and global shift analysis. From the participants that successfully completed the entire TMT, there was no difference in error rate performance between the repetition and shifting conditions, only with the RT.

S. Updating

Updating was examined using the BDS test and n-back task. The groups' performance results can be viewed in Table S1.5 below.

Table S1.5. Updating Results of the Young Adult Participants

Task	**n**	**Young Adults** (Mean/SD)
Backward Digit Span Test (no. out of 14 spans)	28	7.86 (2.16)
N-back, RT, ANOVA*	-	0.392
N-back, error rate, ANOVA*	-	< 0.001
N-back, 0-, RT	26	536.86 (89.89)
N-back, 0-, error rate (%)	26	2.40 (2.32)
N-back, 1-, RT	26	525.91 (153.08)
N-back, 1-, error rate (%)	26	14.90 (8.13)
N-back, 2-, RT	26	573.06 (186.48)
N-back, 2-, error rate (%)	26	40.05 (18.65)
N-back, 3-, RT	26	562.74 (189.19)
N-back, 3-, error rate (%)	26	52.84 (14.81)
N-back, RT updating cost (ms)	26	25.88 (186.22)
N-back, error rate updating cost (%)	26	50.43 (14.34)

The group averaged a score equated to a span length of 5. However, all participants were able to successfully recall up to 4 digits backwards. Only two participants were able to correctly recall the longest span of 8 digits, one doing so in both trials, see Table S1.6 for more detail. No participant scored the maximum test score of 14, i.e. correctly recall all the spans in reverse order.

Table S1.6. Young Adults Backward Digit Span Performance. The test involves the completion of seven spans (lengths 2 to 8), twice. The highest span length achieved by a participant is presented.

Span Length	**Highest Span Achieved**
2	0
3	0
4	6
5	5
6	12
7	3
8	2

With the n-back task, a one-way repeated measures ANOVA test [conditions (0-, 1-, 2-, and 3-back)] indicated an insignificant main effect between the RTs of the n-back conditions, $F(3, 75) = 1.01$, $p = 0.392$, $\eta_p^2 = 0.04$. Another one-way repeated measures ANOVA [conditions

(0-, 1-, 2-, and 3-back)] test on the error rates showed a significant main effect, $F(3, 75) = 140.01$, $p < 0.000$, $\eta_p^2 = 0.85$, as seen with the increase in errors produced with task difficulty.

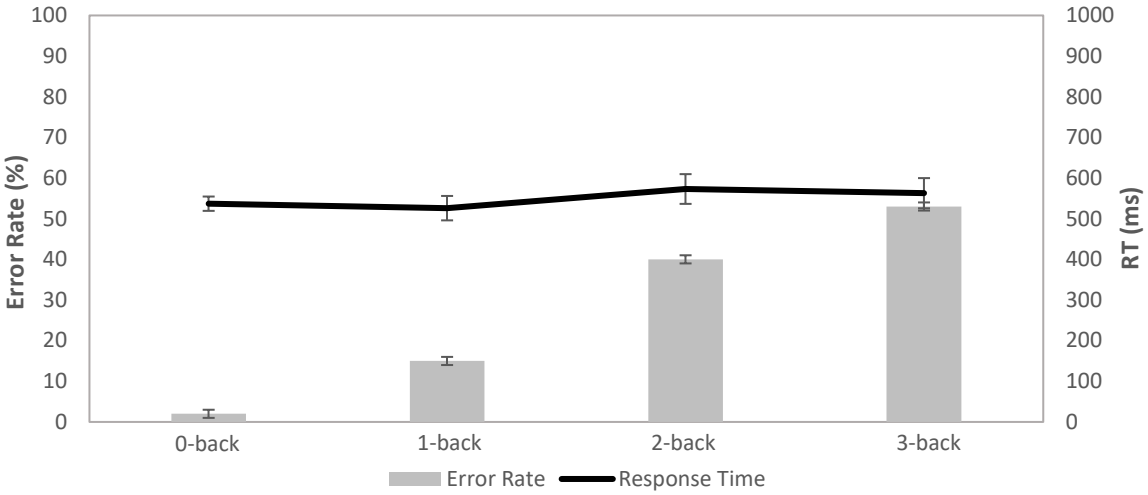

Figure S1.1. Young Adult Group N-Back task performance. This figure presents the relationship between the mean n-back RT in ms (line and right axis) and the error rates in % (bars and left axis) at 0-, 1-, 2-, and 3-back in the young adult group. Error bars denote SEM (standard error mean).

The combined performances are seen in Figure S1.1. The fastest RTs were observed at the 1-back and largest error rate at 3-back.

To further examine the groups' performance, a series of pairwise paired-samples t-tests was conducted between the n-back conditions for RTs and error rates. Based on the Bonferroni correction, the alpha was taken as 0.00851. Significance was only found between all the error rate pair comparisons, confirming that there were indeed differences in the accuracy performance of all the n-back task condition performances. The participants spent approximately the same amount of time completing each n-back condition.

Finally, the updating cost (difference between the 3-back and 0-back conditions) further demonstrated the large difference in error rate between the easiest and hardest n-back condition, 50.43% (14.34), and the rather small increase in RT 25.88ms (186.22).

In sum, the assessment of updating was confirmed with both tasks. As the task demand increased, the participants produced more errors during performance of both tasks.

S. Discussion

This study forms the basis for a cross-sectional study on the assessment of the four EF abilities. The data gathered here sets the reference point for comparison with an older adult group. Thus, the CH young adults were characterised for their abilities in dual-tasking, inhibition, shifting and updating, with two separate tasks each. The results demonstrated that these individuals did not encounter any problems in performing the tasks and the tasks were sensitive enough to not show ceiling effects. Furthermore, EFs are usually assessed by comparing a baseline condition with low demands, i.e. ST, congruent, task repetition, 0-back, etc, with the higher demand condition, i.e. DT, incongruent, task shifting, 3-back, etc. By comparing the two conditions, for instance DT vs ST, congruent vs incongruent, shifting vs repetition, 0- vs 3-back, an estimation of the respective EF ability is determined. In other words, the 'cost' measures (i.e. DT, inhibition, shifting, updating costs) is taken as reflecting the demands on the EF. Thus, this study confirmed that all paradigms worked sufficiently, and the costs may be observed as a 'proof of concept'. Consequently, the cost measures for the young adult controls were determined.

S. Dual-tasking

In the examination of dual-tasking capability, a modified TEA telephone search subtest and the PRP task were used. The findings from the TEA test suggest that the participants were better at completing the auditory task in comparison to the visual telephone code search task during the DT condition. This could be due to the participants not being able to maintain simultaneous performance in each task of the ST condition, therefore sacrificing the visual task over the auditory, as a strategic choice. However, it could be that the visual task was more demanding than the auditory task and hence the participants preferred to complete the easier auditory task. Accordingly, it has been suggested that task context, characteristic, as well as the use of technology may factor into how individuals strategise undertaking a DT (Israel & Cohen, 2011; Janssen & Brumby, 2010).

In the PRP, the DT costs and the PRP effect for the RTs and error rates were considered. Firstly, significant DT costs, i.e. the difference in the RT and error rate of the auditory task (RT1) and visual task (RT2) during ST and at SOA 0ms were observed. Specifically increased RTs and errors rates during dual-tasking. However, since RT1 was responded to first, there

was a significant difference between their RT DT costs but not the error rates. Therefore, demonstrating interference of the two tasks with each other during such performance is caused by competition for controlled-attention resources (Pashler, 1992; Schubert, 2008). Notably, STs are simple and less demanding to complete, whereas the cognitive process of dual-tasking demands additional functions, for example, the recruitment of supplementary EFs for coordinating and resolving the interference, such as divided attention. Accordingly, the occurrence of such costs confirms this task as an assessment of dual-tasking and its validation for use in this research with other participant groups.

The second assessment of the PRP task was the PRP effect indicating the inability to process two tasks simultaneously by the bottleneck (Laguë-Beauvais, Gagnon, et al., 2013; Pashler, 1984, 1994; Schubert et al., 2008). This was evident with this young adult groups' performance during the visual task at SOA 0 and 1000ms by the difference in RT and error rates produced. It revealed the increased occurrence of a delay during the processing of the visual task at SOA 0ms, when the auditory and visual tasks are simultaneously presented, in comparison to at 1000ms, when the visual task is presented 1000ms after the auditory task. Similarly, as with DT costs, the interference at the bottleneck shows the demand for additional EFs for its resolution. However, there is a difference in these assessments. DT cost is a broader assessment in that it compares performance in ST, where there is only one requirement of a stimulus-response mapping in WM for its completion, to dual-tasking, which entails two. In the PRP effect, two DT conditions are compared with each other, making it is a more specific measure. Still, both measures showed significant DT costs and will be considered in the cross-sectional study.

S. Inhibition

Inhibitory control was assessed with the Stroop task and the HSCT. The Stroop task's measure of inhibition is mainly based on performance in its incongruent, CW condition, where participants are required to suppress their automated reading response in favour of the less automated naming the ink colour response. This interference is referred to as the Stroop effect and calculated as a score of the overall task, including performance in the congruent word and colour only sections (Adólfsdóttir et al., 2017), which was evident with this young adult population. The task requires participants to have sufficient availability of

resources and effective flexible allocation of attention to successfully complete the sections, as well as the ability to efficiently maintain the active goal state, in order to successfully account for the task demands (D. P. McCabe et al., 2005). Thus, in addition to assessing inhibition, it is known to also measure other cognitive processes, including attention, processing speed, cognitive flexibility, and WM, and so may be employed for measuring several cognitive functions (Scarpina & Tagini, 2017).

The ability to inhibit was further observed with the HSCT through the evaluation of the participants RT and error made during completion of its second condition, where the participants had to produce a word to create a non-meaningful sentence, the interference. This requires the cognitive process of controlled attention to inhibit interference from the highly activated, automated, connected word, for the sentence. However, cognitive processes such as language, and semantic memory, and the ability to initiate and generate a response are fundamental and basic necessities to effectively understand and process the task, overall (Cervera-Crespo & González-Alvarez, 2017). The observation of an increase in RTs in the condition in comparison to the first, non-inhibition condition, as well as a reduced number of correct responses, reflects inhibition failures. An overall test score is calculated based on these RTs, and the errors produced in the inhibition condition (Bielak et al., 2006; Borella et al., 2011). A disadvantage of this test is that it fails to consider errors that may be generated in the non-inhibition condition. Even so, this task is regarded as a better measure of inhibition than the Stroop task because it seems to resemble inhibitory demands of actual life, since the capacity to suppress inappropriate words and/or behaviours forms part of numerous regular social interactions (Burgess et al., 2006). Nevertheless, both tasks were successful in assessing the EF inhibition in this young adult group.

S. Shifting

The ability to shift was evaluated with a computerised task switching test and the TMT through the measure of shifting cost. In the TMT, shifting capacity was tested in the second section of the assessment. The participants produced longer RTs, due to the increase in task demands, as a consequence of alternating between connecting a number to a letter and back to a number, etc, in ascending order, as observed by the significant difference reported in the RT shifting cost. The cognitive processes, inhibition/interference control, attention,

episodic memory, and WM are all thought to contribute to its performance, in addition to semantic memory, as prior knowledge of the alphabet and ascending number sequence is required for its successfully completion (Oosterman et al., 2010; Salthouse, 2011b; Sánchez-Cubillo et al., 2009). A shortcoming of the task is that shifting cost is calculated from only one performance of a non-shifting and shifting trial, however as this single performance consists of repeated actions, each move to the next number or letter may be considered a trial. Still, the change in task demand can be observed by the number of participants who successfully completed part A, approximately 96%, in comparison to part B, 77%, of the task, where those who produced more than two errors in either part of the task were excluded from use in the final analysis. So, it can be concluded that this task was successful in assessing shifting ability, and no floor or ceiling effects were produced.

Significance in RT and error rate of the local shift and global shift shifting cost, including the RT of the mixing shifting cost, with the task switching was further observed. The shifting costs indicated the successfulness of this task in this young adult group. These costs are derived from the average performances in blocks from a non-shifting condition and a shifting condition, and so represent difficulty in maintaining and selecting between the two possible response sets (Reimers & Maylor, 2005). Hence, the global shift cost is understood to be associated with the maintenance of numerous task configurations in WM (Huff et al., 2015; Wasylyshyn et al., 2011). Whereas local shift cost measures the ability to inhibit the thought process of the previous trial to complete the current trial (Monsell, 2003). The mixing cost is thought to reflect the ability to maintain executive control in completing multiple task conditions (Braver et al., 2003; W. P. Chang et al., 2020).

Therefore, the attentional and shifting demands may be considered to be higher than with the TMT. Furthermore, it has been found that participants respond significantly slower and typically with less accuracy directly following completion of a shifting trial. Thus, as the task conditions are randomly cued in this task, i.e. one shifting trail may be followed by a non-shifting trial, and then the other non-shifting trial, this may contribute further to the shifting cost. Even so, this may be reduced through adequate preparation, as with this task and usually in computerised task switching tasks, a cue was presented prior to each trial (Hirsch et al., 2016; Monsell, 2003). Regardless, this task demonstrated efficacy is assessing the EF

shifting. Hence, it can be seen that both shifting paradigms worked well in this young adult group through the production of costs.

S. Updating

WM updating capability was studied with the verbal BDS test and a spatial n-back task. With the BDS task, all participants managed to average a span length of four, a length suggested to be an average for this population by Woods et al (2011) who observed a span of 4 to 6 in their study assessing young and middle-aged healthy adults. This task, as well as other span tasks, is alleged to be dependent on several cognitive factors, including chunking and rehearsal. A domain general ability for the allowance of cognitive control and executive attention, particularly in verbal skills but especially in the facilitation of WM storage (Conway et al., 2005). The demand on WM storage is shown through the decreased number of participants successfully recalling the longer span lengths backwards. Hence, this task was effective in assessing updating ability in this group.

Likewise, in the n-back task, accuracy in task performance was greatly affected with increase in WM memory demands. A significance in updating error rate cost was reported, in comparison to relatively small RT updating cost. The increase in n-back difficulty resulted in increased task demands on WM as shown by the gradual increase in error rates from 0- to 3-back, whereas RTs were roughly constant for the group. Collectively, it requires the cognitive processes, attention, selection, decision-making, spatial awareness, the encoding of the incoming stimuli, WM, along with inhibition and interference of the previous trial and/or task condition (Jaeggi et al., 2010; Owen et al., 2005; Redick & Lindsey, 2013). Thus, as the n-back condition increases, the demands on spatial awareness, and especially encoding of new information and updating of WM are demonstrated with the increased error rate. Evidently, this and the BDS test proved sufficient in the examination of updating capability.

The EF findings of this young adult group will be referred to in the behavioural study of CH older adult group for a cross-sectional analysis of performance, presented in Chapter 3.

S. Conclusion

These results provide the basis for the analysis of how EFs are affected by ageing and/or neurodegenerative conditions. As discussed in the introductory section, CH young adults are suggested to be better performers than other adult groups in a range of EFs, and thus constitute a good foundation for comparison studies with other adult populations, including CH older adults.

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Appendix

1. Task Descriptions

Task	Description
Dual-Tasking	
Alphanumeric equation task and a visual detection DT (Compton & Logan, 1991; Logan, 1988)	Participants are required to perform an alphanumeric equation while simultaneously responding to a colour change on a computer screen.
Auditory discrimination and visual identification task (Bherer et al., 2006)	Participants are required to distinguish between low and high pitch tones whilst identifying which of the two letters (B or C) is presented on a computer screen.
Baddeley's digit recall and tracking task and its variant (Baddeley et al., 1986)	In the recall condition participants must verbally repeat (i.e. recall) a span of digits immediately following their presentation, in the same order heard. Spans started with a one-digit length which was increased by a digit after the participant had completed three trials at that length. In the tracking condition, participants tracked the path of a white square on a computer screen. Both task conditions were performed separately and simultaneously.
Digit recall and tracking task (Foley et al., 2013)	In the recall condition, a fixed span length for the participant is used. This is previously established as the maximum span length recalled during a 90 second single-task practice session. In the tracking condition, participants are required to draw a line in successive order through a series of 319 circles arranged along an irregular path across a sheet of A3 paper with a pencil, as fast as they can, from start to finish in 90 seconds. The tasks are performed separately and simultaneously.
Della Sala DT (Della Sala et al., 1995a)	Pen and paper version of Baddeley's digit recall and tracking task and its variant (Baddeley et al., 1986).
Psychological Refractory paradigm (PRP) (Pashler, 1994; Welford, 1952)	Participants perform two speeded choice-response tasks, e.g. an auditory and visual task or two visual tasks, etc at different stimulus onset asynchronies (SOA, the time between the presentation of the two task). Numerous SOAs may be used in a task, i.e. SOA of 0ms, 100ms, 200ms, etc.
The colour and letter dual-task (Laguë-Beauvais et al., 2015)	Participants are instructed to prioritise responding to the letter task over the colour task during one block of trials. In another block, both tasks are prioritised.
Test for Everyday Attention (TEA) dual-task telephone search subtest (Robertson et al., 1994, 2001)	Participants are required to perform a visual scanning task where they searched for a specific telephone code with a matching symbol, and an auditory task, where they counted the number of low frequency tones heard, in an audio of combined high and low frequency tones. The tasks are normally performed separately and simultaneously.
Visual and auditory processing paradigm (Dannhauser et al., 2005)	Two stimuli, a visual and auditory, are presented in alternating ON and OFF periods. The visual stimulus consisted of a square black and white chequerboard pattern that filled up the entire screen. The squares were reversed at three distinct frequencies (2, 4, 8 Hz) for fixed periods of 16s alternating with 16s of cross-hair fixation (OFF). The order of reversal frequencies was randomized

	within each set of three consecutive stimulation–fixation cycles. The auditory stimulus consisted of a male voice reading a list of nouns presented at three randomized word rates (30, 60, 90 words/min) for fixed epochs of 24s, alternating with 24 s of silence (OFF).
Visual stimulus and cognitive DT Makizako et al (2013)	In the visual stimulus, participants are instructed to push a button on the presentation of a bright red light, and in the cognitive test, count backward to 1, where the starting point for counting was selected randomly (from the numbers 100, 90, 80, 70, 60, 50, 40, 30 and 20) by the examiner.
DT word span task (Beni et al., 1998)	Participants must verbally read the words presented aloud and to press the animal key whenever they read an animal name. There are three trials for each span size from two to eight.
Inhibition	
Antisaccade task (Hallett, 1978; R. J. Roberts et al., 1994).	In Sylvain-Roy et al (2015)'s version a visual cue was presented on either the left or right of the screen followed immediately by a target arrow, on the opposite side. The participants were required to indicate the direction the arrow pointed. In Crawford et al (2017)'s version, participants are required to gaze in the opposite direction to a presented red dot. In the first modified version, a memory-guided antisaccade task, participants were presented with a randomly placed red dot as the target, along with four adjacently placed green dots as distractors. Firstly, they were instructed to gaze at the target in the first condition, then secondly, they had to gaze at the location of the previously presented target on a blank screen. In the second version of the task, a go/no-go antisaccade task was used. The presentation of a centrally placed red cross denoted a 'no-go' response, while a green cross required a 'go' response.
Flanker task (Eriksen & Eriken, 1974)	Participants requires to respond to a centrally placed stimulus "flanked" by concurrently presented irrelevant stimuli (that can be congruent or incongruent with the central stimuli), e.g. <<< **<** <<< or <<< **>** <<<.
Go/no-go task (Newman & Kosson, 1986)	Participants are required to respond to the appearance of a specific stimulus ('go' condition) but withhold responses on the presentation of a different stimulus ('no-go' condition).
Emotional go/no-go task (Waring et al., 2019)	The go/no-go task with the use of various facial expressions, i.e. happy, sad, as stimuli.
Hayling Sentence Completion Test (HSCT) (Burgess & Shallice, 1997)	requires participants to complete a high cloze sentence with a missing last word. In part A, the initiation section, the congruent condition of the test, a related, expected word should be provided. In part B, the inhibition section, the incongruent condition, an unrelated, unexpected word should be provided.
Emotional HSCT (Dupart et al., 2018)	Analog of the HSCT using emotionally charged sentences and compared the words the participants produced as either emotionally neutral, positive, or negative.
Stroop task (Stroop, 1935)	Participants must complete three sections each consisting of 100 items, a word naming (congruent), an ink colour naming (congruent), and naming of the ink colour of the word (incongruent). Participants perform these tasks as quickly as

	possible, usually within a specific timeframe, e.g. within 45 seconds per section.
Modified Stroop (Bohnen et al., 1992)	Stroop task with an added a fourth condition where participants were required to switch between naming the colour of the ink and naming of ink colour of the word, i.e. the incongruent condition.
Delis–Kaplan Executive Function System Colour-Word Interference test (D-KES CWIT) (Delis et al., 2001)	Stroop task with an added a fourth condition, where participants instead switch between word naming (not colour naming) and naming of the ink colour of the word.
Math Stroop (Zamarian, Semenza, et al., 2007)	Participants must complete two mixed blocks of addition and multiplication problems. With the addition sign they had to solve as multiplication and vice versa.
Interference and Reverse Stroop (Amieva, Lafont, et al., 2004)	Briefer version of the Stroop, consisting of cards with colour names (BLUE, RED, YELLOW, GREEN) printed in a contrasting ink. In the Interference version, participants must identify the word, and the Reverse version, participants must identify the ink colour.
Victoria Stroop (Spreen & Strauss, 1998)	This is a briefer version of the traditional Stroop task, consisting of three stimulus cards comprised of 24 items, where participants are required to quickly name either the, 1) colour of dots (Dot condition—Card, 1), 2) colour of the ink of the neutral words printed (Word condition—Card 2), and 3) colour of the ink in which the words (names) are printed (Interference condition—Card 3).
Nonverbal Stroop task (Pettigrew & Martin, 2014)	Task comprises three conditions, a neutral condition, where participants were presented with a stimulus in the centre of a computer screen, e.g. left-pointing arrow. In the congruent condition, the stimulus is on the same side the arrow is pointing, e.g. left-pointing arrow on the left side of the screen. In incongruent condition, the stimulus is on the opposite size the arrow is pointing, e.g. a left-pointing arrow on the right side of the screen. The participants were required to respond with the direction the arrow was pointing, right or left.
Picture-word interference task (Lupker, 1979; Schriefers et al., 1990)	This task involves the completion of two conditions, an interference condition, where a picture is superimposed with a distractor word from the same semantic category, and a non-interference condition, where a picture is superimposed with a distractor word from a different semantic category. Participants were required to respond with what was seen in the picture, while ignoring the word.
Negative priming (Tipper, 1985)	Participants are required to respond to a stimulus that was previously presented as a distractor in trial (n), so becoming the target.
Random number generation task (Audiffren et al., 2009)	Participants are required to produce a number between 1 and 9 verbally every time a computer-generated tone is heard, approximately every second, such that a string of numbers is generated randomly. 100 responses are recorded, usually within 100 seconds. The total adjacency score (%), i.e. the distribution of adjacent digits (in ascending or descending series) from the ordinal sequence of alternatives (i.e. 1–2; or 8–7–6) is measured.

	Successful performance requires the efficiency of two EFs, the correct inhibition of overlearned schemas (i.e. counting) and correct updating of WM.
Simon task (Simon, 1969)	Similar to the nonverbal Stroop minus the neutral condition, where in response to the colour of the shape of a stimulus, i.e. a red or green circle or square, participants had to respond left or right.
Stop-signal task (Logan et al., 1984; Williams et al., 1999)	Participants must perform a specific task as quickly as they can following the presentation of a 'go' signal and stop following a 'stop' signal during the duration of a trial.
Shifting	
Behavioural Assessment of the Dysexecutive Syndrome rule shift cards task (Wilson et al., 1996)	The task consists of 21 nonpictorial playing cards. In part 1, participants are required to respond with "Yes" to a red card and "No" to a black card. In the second part, a new rule is provided, respond "Yes" if the presented card is the same color as the previous turned card and "No" if the colour is different. Therefore, participants had to modify their responses, inhibiting their original response set and shift their thought process.
Design fluency test (Harter et al., 1999; Jones-Gotman & Milner, 1977)	Participants are to complete three test conditions to create different designs in 'n' number of squares by using four straight lines to connect. The first condition requires connecting filled unnumbered dots within 60 seconds, 2) unfilled dots, and 3) the shifting condition, alternate between connecting filled and unfilled dots.
Dimension-switching task (Albinet et al., 2012; Monsell & Mizon, 2006; Rogers & Monsell, 1995)	Participants are presented with the word, LEFT or RIGHT, enclosed in a left or right arrow, presented above or below the centre of a white screen. Depending on the location of the presented stimulus, participants are required to respond with the direction either printed in text (the word) or the direction of the arrow. Participants completed word and arrow only task blocks, as well as blocks of pseudo-randomly mixed word and arrow trial.
Trail making test (Reitan, 1992; Reitan & Wolfson, 1986)	This test encompasses two parts, in part A, the participant is required to connect 25 numbered (1, 2, 3, etc) dots or circles, in sequential order, and in part B, alternate between letters and numbers in ascending order (1, A, 2, B, etc).
Alternating trail making version (Schmitter-Edgecombe & Sanders, 2009)	Analogous of the traditional trail making test part B.
Modified TMT part B test (Chen et al., 2013)	Entails alternating connecting lines between numbers and weekday circles, within 120 seconds.
Oral trail making test (Bastug et al., 2013)	In part A, participants are instructed to verbally count from 1 to 25, and in part B, to alternate between counting numbers and letters as seen in the paper version, 1-A-2-B, etc
Colour trails test (D'Elia et al., 1996)	Analogous of the trial making test, was utilised by two studies, Huang et al (2017) and McGuinness et al (2010), in AD participants. It requires participants to complete two parts, in part 1, the participants connect circles numbered 1 to 25 in ascending order, and part 2, connect the numbers 1 to 25 in order, but alternate between two colours (i.e. 1-pink-2-blue-3-pink-, etc).

Left–right shifting task (Belleville et al., 2008)	Participants are required to identify one of two digits presented on the left side of a screen in the first block, and on the right side of a screen in the second block. In the shifting block, the target number is randomly placed on either side of the screen and indicated by a visual cue.
More-odd shifting task (Salthouse et al., 1998; Zheng et al., 2012)	Participants complete three task conditions, 1) respond either "greater" or "less" if a red number presented on a screen is larger or smaller then a five, respectively, 2) respond with "odd" or "even" when the number is coloured green, and 3) a combination of the conditions 1) and 2) in one block, where the participant is cued to the task to perform.
Number-letter task (Rogers & Monsell, 1995)	Participants are required to classify whether a number-letter pair presented in one of four boxes in the centre of a computer screen are either odd or even, or a vowel or consonant. More precisely, whether the number is odd or even when the pair is seen in one of the top two boxes, during the number task, or if the letter is a vowel or consonant when the pair is seen in one of the bottom two boxes, during the letter task.
Plus-minus task (Jersild, 1927; Miyake, Friedman, et al., 2000; Spector & Biederman, 1976)	Participants are required to complete three conditions, 1) to add a specific number to every number presented, 2) subtracts a specific number from every number presented, and 3) alternate between adding and subtracting a specific number.
S-R compatibility switching task (Albinet et al., 2012; Monsell & Mizon, 2006; Rogers & Monsell, 1995)	Participants are presented with a screen containing a white frame. At the start of each trial, the white frame changes colour to red or green. After a duration of 250ms or 1750ms, a left or right pointing arrow is presented at a random location within the frame. Participants are required to respond by pressing a button located either on the side indicated by the arrow, when the frame is green, or the opposite side, when the red frame. Participants complete single blocks of one frame colour, and then mixed blocks with both frame colour occurring pseudo-randomly.
Task switching paradigm (Rogers & Monsell, 1995)	Participants are required to perform two conditions, a repetition condition, where participants complete the same task repeatedly in a block (two different tasks are completed), and a shifting condition, where the completion of the two repetition tasks presented pseudo randomly within the same block is required.
Visual elevator (Robertson et al., 2001)	Part of the TEA, participants are required to count upwards or downwards as they follow a series of visually presented numbers corresponding to floors in an elevator. The task demands the participants shift the direction of counting.
Wisconsin card sorting task (Berg, 1948; Nelson, 1976)	Participants are presented with a number of stimulus cards with sets of symbols that vary in colour, shape, and number (e.g. 3 green triangles or 2 yellow squares). They are instructed to categorise them according to a particular dimension (i.e. colour, shape or number). The category rule changes every time 10 (out of a maximum of 128) response cards have been sorted correctly, but the participants are unaware of this pattern.
Updating	
(Alpha)bet span task (Belleville et al., 1998;	Participants must either repeat a list of words in the same serial order presented to them or mentally rearrange them into alphabetical order.

Craik, Bialystok, et al., 2018)	
Backward digit recall span test (WAIS-R or WAIS-III) (Egeland, 2015; P. T. Griffin & Heffernan, 1983; Wechsler, 2012)	Participants must immediately recall a list of digits previously presented in reverse order. The span length ranges from two to eight, and each length is completed twice.
Backward spatial span (Wechsler, 1987)	Participants are required to recall various sequence spans presented on a screen in reverse order.
Keep track task (Yntema, 1963)	Participants are required to keep track of 15 words presented in sequential order and remember the last (most recent) word from one of 'n' categories presented, e.g. colours or animals. They must respond with the last word at the end of the trial. Sylvain-Roy et al (2015)'s version, participants read a series of semantically correct or anomalous sentences, and judge each, i.e. with 'yes' or 'no', for semantic plausibility, in addition to remembering the last word of the sentence. They must recall all the words verbally at the end of each series, which varies from two to five sentences of four blocks per series length.
Letter-number sequencing (Egeland, 2015; Wechsler, 2012)	Participants must recall a sequence of previously presented randomly mixed letters and numbers in sequential order, i.e. letters alphabetically ordered first (A, B, C, etc), and then numbers in ascending numerical order (1, 2, 3, etc).
Letter updating task was employed by (Sylvain-Roy et al., 2015)	Participants orally recalling the last consonant seen in a series of consonants visually presented. The number of consonants to be recalled is determined individually for the participant prior to the start of the actual task, minus one item, during a practice session. The participants are presented with a series of four different lengths, 1) the participant's span minus one, 2) the participant's span plus one, 3) the participant's span plus three, and 4) the participant's span plus five items, randomly
N-back task (Jaeggi et al., 2010; Kirchner, 1958)	Participants respond with the position of a stimulus presented on a screen 'n' position(s) prior. In the non-spatial version, participants are required to recognise a stimulus presented at 'n' screen positions prior. In the spatial version, the position on the screen the stimulus is presented is required. For example, at 0-back trial, the position of the stimulus at 0 position (the present) screen is required. During 1-back, the position a screen prior to the present screen is required, and so on. The higher the n-back position, the greater the WM demand. Thus, a 3-back task will consist of the completion of the 0-, 1-, 2- and 3-back conditions.
Operation span (Turner & Engle, 1989)	A mathematical operation, and an item (word or letter) are presented to the participant. They must verbally say if the operation is correct (i.e. true or false) and remember the item presented. At the end of each trial, the participant must recall the items in serial order. After three consecutive errors the task is terminated. Typically, the task consists of 15 trials with two to six operation-word pairs, 3 trials per length.
Random number generation task (Baddeley, 1998)	Previously described under inhibition. It also assesses updating ability by measuring the Redundancy score (%), which is based on the rate on which individual digits are utilised. A score of 0%

	suggests no redundancy, i.e. good randomness, and no repetitiveness of digits (e.g. 5, 1, 7, 9, 3, 6, 2, 4, 8), whilst a score of 100% equates to complete redundancy, i.e. repeated use of the same response choice, throughout (e.g. 1, 1, 1, 1, 1, 1, 1, 1, 1, 1).
Reading span (Daneman & A.Carpenter, 1980)	typically involves participants verbally read sentences and remember the last word of each sentence in a set or block. They must recall all the last words verbally in the order of each set. The sentences get increasingly longer in a set until the participant fails three in a row.
Spatial running span task (Albinet et al., 2012; Boucard et al., 2012; Morris & Jones, 1990)	Participants are presented with an empty 4 x 4 matrix on a computer screen, where sequences of six, eight, ten, or twelve black dots are presented randomly in one of the 16 squares of the matrix, at a rate of a dot every two seconds. No location is repeated in the sequence, and the sequence length is never known. Participants are required to recall the last four dot locations at the end of each sequence in strict forward serial recall order using a computer mouse. They must complete twelve sequences, three for each length.
Tone-monitoring task (Larson et al., 1988; Miyake, Friedman, et al., 2000)	requires participants to keep track of the number of a series low, medium, high pitch tones presented randomly. The participants are instructed to press an appropriate keyboard button when they heard three tones of the same pitch.
Verbal running span task (Albinet et al., 2012; Boucard et al., 2012; Morris & Jones, 1990)	Participants are presented with a list of six, eight, ten, and twelve consonants on a computer screen, every two seconds. Participants are instructed to recall the last four consonants at the end of each sequence, strict forward serial recall. The sequence length is never known. They must complete twelve sequences, three for each length.
Word backward span (Yeom et al., 1992)	Essentially the same as the backward digit span but with words instead of digits. Participants are read various increasing span lengths of words and required to immediately verbally recall the span of words in reverse order.

2. Cognitive Abilities Study Recruitment Questionnaire

Q1 Who is completing this questionnaire?

- ○ Myself
- ○ Individual on the volunteer's behalf. Please specify e.g. spouse, friend, sibling, and note that all responses to the following questions refer to the study recruitment volunteer only.
  _____

Q2 What is your title?

- ○ Ms
- ○ Miss
- ○ Mrs
- ○ Mr
- ○ Dr
- ○ Other, please specify _____

Q3 Full name (first, last)_____

Q4 Address_____

Q5 Email address_____

Q6 Contact number_____

Q7 What borough do you reside in?

- ○ Ealing
- ○ Harrow
- ○ Hillingdon
- ○ South Bucks
- ○ Other, please specify _____

Q8 Date of Birth (day, month, year)_____

Q9 Age_____

Q10 City, Country of birth_____

Q11 Gender

- ○ Male
- ○ Female

Q12 Nationality

- ○ British
- ○ Other, please specify _____

Q13 Ethnicity

- ○ Asian, Indian
- ○ Asian, Pakistani
- ○ Asian, other, please specify _____
- ○ Biracial, please specify _____
- ○ Black, African
- ○ Black, Caribbean
- ○ Black, other, please specify _____
- ○ White, British
- ○ White, other, please specify _____
- ○ Other, please specify _____

Q14 Marital Status

- ○ Single
- ○ Civil Partnership
- ○ Married
- ○ Divorced
- ○ Widow(er)
- ○ Other, please specify _____

Q15 Do you have children?

- ○ No
- ○ Yes, how many? _____

Q16 How tall are you? (In feet and inches, where 1 foot = 30cm and 1 inch = 2.54cm)

_____

Q17 How much do you weigh? (In stones and pounds, where 1 stone = 6.35kg)

_____

Q18 What is your native/first language?

- ○ English
- ○ Other, please specify _____

Q19 Are you fluent in another language?

- ○ No
- ○ Yes, please give details of language(s) and level of fluency, i.e. verbally fluent in Welsh

_____

Q20 Do you have any difficulty reading or writing (dyslexia, dyspraxia, etc.)?

- ○ No
- ○ Yes, please specify _____

Q21 What is your highest level of education?

- ○ O-Levels/GCSEs or equivalent (Secondary/High School leaver)
- ○ Vocational qualification, please specify _____
- ○ A-Levels or equivalent (Sixth Form/College leaver)
- ○ Higher National Diploma (HND)/No degree but attended university
- ○ Bachelor's degree
- ○ Master's degree
- ○ Doctorate degree
- ○ Professional degree, please specify _____

Q22 What is your current job? (If retired, last job before retirement, if studying, write 'student' and give details of area of study, i.e. BSc Psychology student, etc)

_____
_____

Q23 Are you right or left handed, or both?

- ○ Right
- ○ Left
- ○ Both

Q24 Do you exercise regularly?

- ○ No
- ○ Yes. Please give details; type of exercise and average hours per week

_____

Q25 What is your average number of hours of sleep per night?

_____

Q26 Do you or have you ever smoked nicotine (cigarettes)?

- ○ No
- ○ Yes, currently. Please give the following details: For how many years?, how many cigarettes/per day? _____
- ○ Yes, previously. Please give the following details: How long ago?, for how many years?, how many cigarettes/per day? _____

Q27 Have you used any recreational drugs in the last 30 days? e.g. cocaine, marijuana, ecstasy etc.

- ○ No
- ○ Yes

Q28 Do you or have you ever regularly consumed caffeine, e.g. coffee, tea, soft drinks/soda, sports drinks?

- ○ No
- ○ Yes, currently. Please give the following details: How much and how often in a week? _____
- ○ Yes, previously. Please give the following details: How long ago?, for how many years?, how much and how often in a week? _____

Q29 Do you or have you ever regularly consumed alcohol?

- ○ No
- ○ Yes, currently. Please give the following details: How much?, how often? _____
- ○ Yes, previously. Please give the following details: How long ago?, for how many years?, how much?, how often? _____

Q30a Do you suffer from any of the following?

	Yes	No
Anxiety	○	○
Blackouts or dizzy spells	○	○
Claustrophobia	○	○
Colour blindness	○	○
Depression	○	○
Hearing problems	○	○
Vision problems	○	○

Q30b If you answered yes to any condition in Q30a, please give details with dates, medication(s).

_____
_____

Q31a Have you ever suffered or been diagnosed/treated for the following?

	Yes	No
Memory problems	○	○
Mild Cognitive Impairment	○	○
Alzheimer's Disease	○	○
Lewy Body Disease	○	○
Parkinson's Disease	○	○

Q31b If you answered yes to any condition in Q31a, please give details with dates, medication(s).

_____
_____

Q31c In regards to Q31a, do you have a family history of any of these conditions? please give details

_____
_____

Q32a Have you ever suffered from or been diagnosed/treated for the following?

	Yes	No
A psychiatric condition	○	○
Cancer	○	○
Diabetes	○	○
Epilepsy	○	○
Hypertension	○	○
Rheumatoid Arthritis	○	○
Stroke	○	○
Traumatic brain injury	○	○

Q32b If you answered yes to any condition in Q32a, please give details with dates, medication(s).

_____
_____

Q33 Do you any other condition or disability not already mentioned?

_____
_____

College of Health and Life Sciences
Department of Life Sciences

PARTICIPANT INFORMATION SHEET

Study title
Executive Function and Dual-task Abilities.

Invitation Paragraph
You are being invited to participate in a research study to be conducted at Brunel University. Before you make your decision to take part, it is important for you to understand why the research is being done and what it will involve.

Please take time to read the following information carefully and discuss it with your relatives and/or friends if you wish.

Please let us know if there is anything that is unclear or if you would like more information. Thank you for reading this. You will be given a copy of this information to keep.

What is the purpose of the study?
The aim of this study is to investigate a certain type of cognitive processes called executive functions (EFs) in different populations, i.e. in young adults and elderly individuals.

Why have I been invited to participate?
Across the different populations, we aim to test 120 participants. You have been invited to take part because you meet the study inclusion criteria, such as being in a certain age group.

Do I have to take part?
No, study participation is completely voluntarily and you can withdraw from participation at any time without giving a reason. If you decide to take part then you will be asked to sign a consent form.

What will happen to me if I take part?
The study will consist of one to three sessions.

In the first session, the screening visit, you will be asked to fill out some questionnaires and to perform some paper-and-pencil and verbal tasks and tests.

Depending on the outcome of this session, you might be invited to a second and third session where you again will be asked to complete some paper-and-pencil and verbal tasks and tests. In addition, you will be asked to perform some tasks and tests on a standard computer, using a computer keyboard to respond.

Finally, we might invite you to participate in a further study involving brain imaging (magnetic resonance imaging, MRI). However, this would constitute a separate study, in which participation is voluntary again. If you agree to participate in the brain imaging study, you will be given further information.

What do I have to do?

You do not have to do anything to prepare for this study.

What are the possible disadvantages and risks of taking part?

There are no known risks or disadvantages in completing any of the tasks and questionnaires in the study.

What if something goes wrong?

In the unfortunate event of something going wrong, you can withdraw from the study at any time and/or seek advice from Dr Andre Szameitat, Reader in Psychology, Senior Tutor (Division of Psychology), andre.szameitat@brunel.ac.uk or submit a complaint to Professor Christina Victor, Chair College of Health and Life Sciences Research Ethics Committee christina.victor@brunel.ac.uk.

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the University will be anonymised, which means it will have personal information such as your name and address removed so that you cannot be identified from it.

What will happen to the results of the research study?

The research data will be coded (for anonymity) and analysed by the researcher(s) before being reported. The results will be disseminated, for instance at public talks, conferences, in scientific journals, and/or social media. The anonymised research data may be analysed and reported for purposes not related to this study. The anonymised research data may also be shared with other researchers, and/or made available as “open data”. This means the data will be publicly available and may be used for purposes not related to this study. However, it will not be possible to identify you from these data, which means

that at no point will any uniquely identifiable data be shared. The data will be stored by the lead researcher for a period of at least ten years from completion of the project (subject to any legal, ethical or other requirements of the funding body). If you take part in this research, you can obtain a copy of the publication by contacting the researcher. You may withdraw your data, without giving a reason, until the point at which your data is anonymised, the results of the study are published in any form, and/or until the point at which your data is made publicly available in an anonymised form.

Who is organising and funding the research?

The research is organised by Ms Mojitola Idowu, PhD student at Brunel University London, mojitola.idowu@brunel.ac.uk). This research does not receive any external funding.

What are the indemnity arrangements?

Brunel University London holds insurance policies which apply to this study. If you can demonstrate that you experienced harm as a result of your participation in this study, you may be able to claim compensation. Please contact Prof Peter Hobson, the Chair of the University Research Ethics committee (peter.hobson@brunel.ac.uk) if you would like further information about the insurance arrangements which apply to this study.

Who has reviewed the study?

This study has been reviewed by the College Research Ethics Committee.

Brunel University's commitment to the UK Concordat on Research Integrity

Brunel University is committed to compliance with the Universities UK Research Integrity Concordat. You are entitled to expect the highest level of integrity from our researchers during the course of their research.

Contact for further information and complaints

For general information

Ms Mojitola Idowu (PhD Student), mojitola.idowu@brunel.ac.uk and
Dr Andre Szameitat (Supervisor), Reader in Psychology, Senior Tutor (Division of Psychology), andre.szameitat@brunel.ac.uk, 01895 267387.

For complaints and questions about the conduct of the Research

Professor Christina Victor, Chair College of Health and Life Sciences Research Ethics Committee christina.victor@brunel.ac.uk.

Thank you very much for your participation!

b. Study 2, Older Adults

College of Health and Life Sciences
Department of Life Sciences

PARTICIPANT INFORMATION SHEET

Study title
Executive Function and Dual-task Abilities in the Elderly.

Invitation Paragraph
You are being invited to participate in a research study organised by Brunel University. Before you make your decision to take part, it is important for you to understand why the research is being done and what it will involve.

Please take time to read the following information carefully and discuss it with your relatives and/or friends if you wish.

Please let us know if there is anything that is unclear or if you would like more information. Thank you for reading this. You will be given a copy of this information to keep.

What is the purpose of the study?
The aim of this study is to investigate a certain type of cognitive processes called executive functions (EFs) in different populations, i.e. in young and elderly individuals.

Why have I been invited to participate?
Across the different populations, we aim to test 120 participants. You have been invited to take part because you meet the study inclusion criteria, such as being in a certain age group.

Do I have to take part?
No, study participation is completely voluntarily and you can withdraw from participation at any time without giving a reason. If you decide to take part then you will be asked to sign a consent form.

What will happen to me if I take part?
The study will consist of one to three sessions.

In the first session, the screening visit, you will be asked to fill out some questionnaires and to perform some paper-and-pencil and verbal tasks and tests.

Depending on the outcome of this session, you might be invited to a second (and third) session where you again will be asked to complete some paper-and-pencil and verbal tasks and tests. In addition, you will be asked to perform some tasks and tests on a standard computer, using a computer keyboard to respond.

Finally, we might invite you to participate in a further study involving brain imaging (magnetic resonance imaging, MRI). However, this would constitute a separate study, in which participation is voluntary again. If you agree to participate in the brain imaging study, you will be given further information.

What do I have to do?

You do not have to do anything to prepare for this study.

What are the possible disadvantages and risks of taking part?

There are no known risks or disadvantages in completing any of the tasks and questionnaires in the study.

What if something goes wrong?

In the unfortunate event of something going wrong, you can withdraw from the study at any time and/or seek advice from Dr Andre Szameitat, Reader in Psychology, andre.szameitat@brunel.ac.uk or submit a complaint to Professor Christina Victor, Chair College of Health and Life Sciences Research Ethics Committee christina.victor@brunel.ac.uk.

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the University will be anonymised, which means it will have personal information such as your name and address removed so that you cannot be identified from it.

What will happen to the results of the research study?

The research data will be coded (for anonymity) and analysed by the researcher(s) before being reported. The results will be disseminated, for instance at public talks, conferences, in scientific journals, and/or social media. The anonymised research data may be analysed and reported for purposes not related to this study. The anonymised research data may also be shared with other researchers, and/or made available as “open data”. This means the data will be publicly available and may be used for purposes not related to this study. However, it will not be possible to identify you from these data, which means

that at no point will any uniquely identifiable data be shared. The data will be stored by the lead researcher for a period of at least ten years from completion of the project (subject to any legal, ethical or other requirements of the funding body). If you take part in this research, you can obtain a copy of the publication by contacting the researcher. You may withdraw your data, without giving a reason, until the point at which your data is anonymised, the results of the study are published in any form, and/or until the point at which your data is made publicly available in an anonymised form.

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Who has reviewed the study?

This study has been reviewed by the Brunel University, College of Health and Life Sciences Research Ethics Committee.

Brunel University's commitment to the UK Concordat on Research Integrity

Brunel University is committed to compliance with the Universities UK Research Integrity Concordat. You are entitled to expect the highest level of integrity from our researchers during the course of their research.

Contact for further information and complaints

For general information

Ms Mojitola Idowu (PhD Student), mojitola.idowu@brunel.ac.uk and
Dr Andre Szameitat (Supervisor), Reader in Psychology,
andre.szameitat@brunel.ac.uk, 01895 267387.

For complaints and questions about the conduct of the Research

Professor Christina Victor, Chair College of Health and Life Sciences Research Ethics Committee christina.victor@brunel.ac.uk.

Thank you very much for your participation!

4. Consent form
    a. Study 1, Young Adults

College of Health and Life Sciences
Department of Life Sciences

CONSENT FORM

Executive Function and Dual-task Abilities

The participant should complete the whole of this sheet		
	Please tick the appropriate box	
	YES	NO
Have you read the Research Participant Information Sheet?		
Have you had an opportunity to ask questions and discuss this study?		
Have you received satisfactory answers to all your questions?		
Who have you spoken to?		
Do you understand that you will not be referred to by name in any report concerning the study?		
Do you understand that you are free to withdraw from the study:		
• at any time?		
• without having to give a reason for withdrawing?		
Do you agree to take part in this study?		
Do you agree that we may contact you in the future to participate in related follow-up studies?		
Signature of Research Participant:		

Date:
Name in capitals:
I am satisfied that the above-named has given informed consent.
Witnessed by:
Date:
Name in capitals:

Researcher name:	**Ms Mojitola Idowu**	Signature:
Supervisor name:	**Dr Andre Szameitat**	Signature:

b. Study 2, Older Adults

College of Health and Life Sciences
Department of Life Sciences

CONSENT FORM

Executive Function and Dual-task Abilities in the Elderly.

The participant should complete the whole of this sheet		
	Please tick the appropriate box	
	YES	NO
Have you read the Research Participant Information Sheet?		
Have you had an opportunity to ask questions and discuss this study?		
Have you received satisfactory answers to all your questions?		
Who have you spoken to?		
Do you understand that you will not be referred to by name in any report concerning the study?		
Do you understand that you are free to withdraw from the study:		
• at any time?		
• without having to give a reason for withdrawing?		
Do you agree to take part in this study?		
Do you agree that we may contact you in the future to participate in related follow-up studies?		
Signature of Research Participant:		

Date:
Name in capitals:
I am satisfied that the above-named has given informed consent.
Witnessed by:
Date:
Name in capitals:

Researcher name:	**Ms Mojitola Idowu**	Signature:
Supervisor name:	**Dr Andre Szameitat**	Signature:

5. Debrief form
    a. Study 1, Young Adults

College of Health and Life Sciences
Department of Life Sciences
Division of Psychology

Debrief form

Executive Function and Dual-task Abilities

We would like to take this opportunity to say **Thank You** for taking the time to participate in this study.

Please be assured, all data collected will be treated in the strictest confidence. You are free to withdraw your data from the research at any time by contacting
Ms Mojitola Idowu, Mojitola.Idowu@brunel.ac.uk or
Dr Andre Szameitat, Andre.Szameitat@brunel.ac.uk.

You may withdraw your data, without giving a reason, until the point at which your data is anonymised, the results of the study are published in any form, and/or until the point at which your data is made publicly available in an anonymised form.

The completed research will help to gain an understanding of cognitive capacity in the cognitively healthy young and elderly populations, and the cognitively impaired elderly population. Specifically, how certain executive functions, i.e. inhibition, shifting and working memory updating, as well as dual-task ability is affected in the mild cognitive impaired (MCI) and Alzheimer's disease (AD) populations. You were chosen to take part in this study because you are aged 18 years or older, and are either cognitively healthy or a sufferer of MCI or AD.

If you were unduly or unexpectedly affected by taking part in the study please feel free to feed it back to the researcher. If you feel unable for whatever reason what-so-ever to talk with the researcher then please contact either Dr Andre Szameitat (Andre.Szameitat@brunel.ac.uk 01895 267387), Dr Janine Spencer (Janine.Spencer@brunel.ac.uk 01895 265474) or the Division of Psychology Research ethics coordinators Achim.Schuetzwohl@brunel.ac.uk 01895 266367, or Noam.Sagiv@brunel.ac.uk 01895 265341.

The following support services may be of interest to you:

SEN Learning Support Services
London Borough of Hillingdon
Civic Centre
Uxbridge
Middlesex
UB8 1UW
T: 01895 812164

Samaritans of Hillingdon
2 Press Road
Uxbridge
Middlesex
UB8 1AT
T: 01895 253355

Teacher Support
https://www.teachersupport.info/facts-sheets/coping-stress
24/7T: 08000 562 561

The Education Union
http://www.atl.org.uk/

b. Study 2, Older Adults

College of Health and Life Sciences
Department of Life Sciences
Division of Psychology

Debrief form

Executive Function and Dual-task Abilities

We would like to take this opportunity to say **Thank You** for taking the time to participate in this study.

Please be assured, all data collected will be treated in the strictest confidence. You are free to withdraw your data from the research by contacting
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The completed research will help to gain an understanding of cognitive capacity in the cognitively healthy young and elderly populations, and the cognitively impaired elderly population. Specifically, how certain executive functions, i.e. inhibition, shifting and working memory updating, as well as dual-task ability is affected in the mild cognitive impaired (MCI) and Alzheimer's disease (AD) populations. You were chosen to take part in this study because you are aged 18 years or older, and are either cognitively healthy or a sufferer of MCI or AD.

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