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Non-Invasive Techniques for the Detection and Diagnosis of Dementia

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NON-INVASIVE TECHNIQUES FOR THE DETECTION AND DIAGNOSIS OF DEMENTIA

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Non-Invasive Techniques for the Detection and Diagnosis of Dementia

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Abstract

Non-Invasive Techniques for the Detection and Diagnosis of Dementia

Joseph Alexander Blount

Key Words: Dementia, Alzheimer's, Cognition, Non-Invasive Diagnosis

It is estimated that there are currently fifty million people living with dementia worldwide. An accurate and early diagnosis of dementia is important in order to initiate appropriate treatment programs as soon as possible. Common methods of neuropsychological assessment can be sensitive to external factors which may compromise accuracy. The aim of this thesis was to investigate techniques that have the potential for the detection of dementia that avoid some of the external influences.

The thesis looked at measurements of (i) postural stability (ii) facial analysis and (iii) fully-immersive virtual reality in cognitively-healthy individuals. These techniques were chosen as postural stability and facial analysis change in dementia and whilst virtual reality has previously been used in dementia research, fully-immersive virtual reality measures have not been established. To see if the measurements were associated with cognitive function, participants completed a series of cognitive tests.

Results indicate that all techniques explored shared a relationship with memory performance, with lower anteroposterior postural sway ($F(1,22) = 17.76$, $p < 0.01$), number of activities participated in that involve a posture element ($F(2, 39) = 3.77$, $p < .05$; Wilk's $\Lambda = 0.84$, partial $\eta 2 = 0.16$), the greater the frequency of negative facial expressions ($F(2, 18) = 4.49$, $p < .05$; Wilk's $\Lambda = 0.67$, partial $\eta 2 = 0.33$.), and low blink rate ($t(11.02) = 2.62$ $p < .05$) all showing better scores on memory tests. Moreover, better scores on the fully-immersive virtual reality task predicted better scores on with short-term memory ($F(1,22) = 20.20$ $p < 0.01$), LTM ($F(1,22) = 09.10$ $p < .01$), associative learning ($F(1,22) = 08.75$ $p < .01$), and a dual–task test ($F(1,22) = 04.64$ $p < .05$).

The novel findings that elements such as postural stability, participation in sports, facial expressions of emotion, blink rates, and spatial memory as assessed in fully-immersive virtual reality highlight that non-invasive techniques can provide measurements that correspond to cognitive ability. This may hold implications for dementia diagnoses. Future research should assess whether these relationships can also be found in an older adult population. If this relationship is found in older adults, it could justify further research into how these techniques could be applied in a clinical context.

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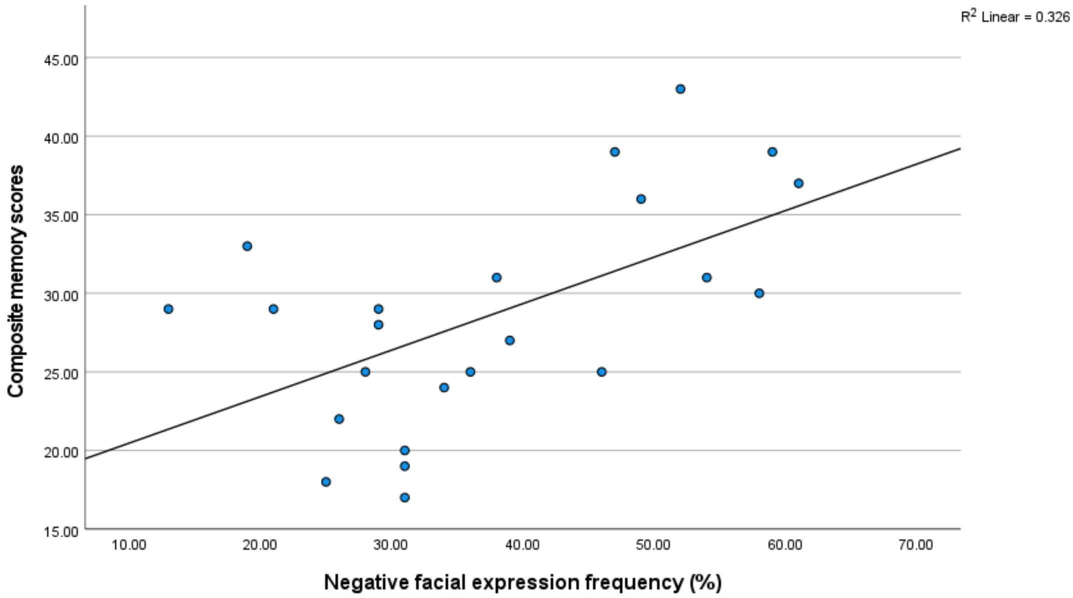


List of Abbreviations

Acetylcholine (Ach)

Acetylcholinesterase Inhibitors (Achei)

Alzheimer's Disease (AD)

Amyloid Precursor Protein (APP)

Amyloid B40 (Aβ)

Analysis Of Covariance (ANCOVA)

Animal-Assisted Therapy (AAT)

Anteroposterior (AP)

Backwards Working Memory (BWM)

Behavioural And Psychological Symptoms of Dementia (BPSD)

Behavioural Therapy (BT)

Cambridge Neuropsychological Test Automated Battery (CANTAB)

Centre Of Pressure (COP)

Cerebrospinal Fluid (CSF)

Cognitive Abilities Screening Instrument (CASI)

Cognitive Stimulation Therapy (CST)

Computerised Tomography (CT)

Dementia With Lewy Bodies (DLB)

Electroencephalogram (EEG)

Electromyographic (EMG)

Entorhinal Cortex (EC)

Facial Action Coding System (FACS)

Force Platform (FP)

Frontotemporal Dementia (FTD)

General Data Protection Regulation (GDPR)

General Practitioner (GP)

Global Deterioration Scale' (GDS)

Graded Naming Test (GNT)

Interactive Music Therapy (IMT)

Long-Term Memory (LTM)

Magnetic Resonance Imagining (MRI)

Massage Therapy (MT)

Mediolateral (ML)

Memantine Hydrochloride (MH)

Microtubule Associated Protein Tau (MAPT)

Mild Cognitive Impairment (MCI)

Mini Mental-State Examination (MMSE)

Montreal Cognitive Assessment (MoCA)

Multivariate Analysis of Covariance (MANCOVA)

Multivariate Analysis of Variance (MANOVA)

National Health Service (NHS)

National Institute for Clinical Excellence (NICE)

National Institute on Aging (NIA)

N-Methyl-D-Aspartate (NMDA)

Non-Spatial WM (NWM)

Organic Light-Emitting Diode (OLED)

Personal Computer (PC)

Positron Emission Tomography (PET)

Reality Orientation Therapy (ROT)

Receptive Music Therapy (RMT)

Reminiscence Therapy (RT)

Rowland Universal Dementia Assessment Scale (RUDAS)

Short-Term Memory (STM)

Single-Photon Emission Computed Tomography (SPECT)

Spatial WM (SWM)

Standard Deviation (SD)

The Mini Cognitive Assessment (Mini-Cog)

Three-Dimensional (3D)

Time Of Day (ToD)

United States (US)

United States Food and Drug Association (FDA)

Useful Field of View (UFOV)

Validation Therapy (VT)

Virtual Action Planning Supermarket' (VAP-S)

Virtual Cognitive Stimulation Therapy (Vcst)

Virtual Reality (VR)

Virtual Route Learning Test (VRLT)

Wii Balance Board (WBB)

Working Memory (WM)

World Health Organisation (WHO)

List of Publications

Blount, J. A., Ugail, H., & Lesk, V. E. (Manuscript in preparation). Exploring the Relationship between Postural Sway and Cognitive Functioning.

Blount, J. A., Ugail, H., & Lesk, V. E. (Manuscript in preparation). Assessing the Relationship between Spatial Memory and Cognitive Functioning in a Fully-Immersive Virtual Reality World.

Blount, J. A., Ugail, H., & Lesk, V. E. (Manuscript in preparation). Using Machine Learning to Analyse Facial Expressions of Emotion and Cognitive Functioning.

Chapter One

Thesis Aims and Overview

1.1 Introduction and Aims

Empirically informed neuropsychological observations are crucial for determining cognitive deficits (Sherman et al., 2020). The primary purpose of neuropsychological assessments is to draw inferences about the structural and functional characteristics of the brain by evaluating behaviour in controlled stimulus-response situations (Trepp et al., 2020). Neuropsychological assessments can take many forms, though often standardised tests are used in order to generate an objective diagnosis of cognitive impairment (Chapman et al., 2010). These tests can assess cognitive functioning in a wide range of cognitive domains including language, learning, and memory, but they can also assess subdomains such as long-term memory, or recognition memory (Battista et al., 2017).

Neuropsychological assessments are routinely used diagnostic tools in assessing cognitive functioning in ageing populations, and are important for the identification of neurodegenerative conditions (Anderson et al., 2017). However, they are not perfect. Most neuropsychological tests were developed for use within educated western populations (Franzen et al., 2020). Furthermore, neuropsychological assessments have been found to be sensitive to demographic variables such as age, gender, and education (Jacova et al., 2007; Fields et al., 2011; Morais et al., 2018), as well as being affected by dietary factors such as caffeine intake (Walters and Lesk, 2015; 2016), and even the time of day (ToD) that testing takes place (Walters and Lesk, 2015).

The neuropsychological battery which is most often used to diagnose dementia, the Mini Mental-State Examination (MMSE), has been criticised for being strongly influenced by non-cognitive domains such as quality of life, ethnocentricity and overdependence on language ability (Devenney and Hodges, 2017). Furthermore, the results on the MMSE can be affected by levels of literacy (Devenney and Hodges, 2017). The discussed limitations of neuropsychological assessments reflect a number of weaknesses in their methodology which must be addressed in order to strengthen the accuracy and reliability in their generated data. There are a range of non-invasive factors that warrant investigation in order to explore their potential to be assessed or considered in tandem with currently used diagnostic methods in order to bolster the accuracy of a diagnosis achieved with the use of neuropsychological assessments.

This thesis aims to explore some non-invasive techniques for the detection and diagnosis of dementia which hold the potential to be utilised alongside neuropsychological assessments in order to strengthen the accuracy of a dementia diagnosis. In this thesis, postural stability, the influence of posture-related activity, the relationship between facial cues, such as facial expressions of emotion and blink rates on cognition were assessed in cognitively-healthy individuals in order to assess the feasibility of their inclusion into diagnostic practice in future. The findings are discussed in the context of their potential to be utilised in a diagnostic capacity, particularly relating to dementia. The findings reported within this thesis were generated from cognitively-healthy populations, this is a salient starting point due to the need for normative data generated from young, cognitively-healthy populations, in order to assess the feasibility of utilising these explored factors in a diagnostic context. As such, the findings reported in this thesis hold implications for improving the accuracy and reliability of dementia diagnoses.

Each experimental chapter considers an exploration of a single non-invasive psychological or physiological factor. Following the experimental chapters there is an overall discussion chapter, which summarises the main findings of the study, suggests implications and applications of the findings, and provides a conclusion to the thesis.

1.2 Overview of Thesis Structure

This thesis is composed of ten chapters; what follows is a brief overview of the contents of each chapter:

Chapter One, the current chapter offers an introduction to the thesis, discussing the idea of neuropsychological assessments as well as the aims of the thesis. Following this there is an overview of the thesis structure.

Chapter Two contains an in-depth overview of dementia and Alzheimer's Disease (AD). Including a discussion of the nature of degenerative illnesses and the different subtypes of dementia. This chapter closes by discussing the importance of an early diagnosis of dementia, the impetus of researchers to diagnose AD in the earlier stages, and what this would mean in practice.

Chapter Three contains a discussion and review of the currently used methods of diagnosing dementia, both invasive and non-invasive methods, as well as factors which are known to be related to dementia yet are not utilised in a diagnostic capacity. This chapter discusses the benefits and limitations of each, as well as their practicality, appropriateness, and readiness to be implemented within a clinical context.

Chapter Four contextualises the importance of an early diagnosis of dementia by exploring the benefits and limitations of different forms of dementia treatments. This includes pharmacological interventions and non-pharmacological therapies for dementia as well as typical and atypical interventions.

Chapter Five investigates the relationship between postural stability and cognitive functioning. Difficulty in controlling postural stability has been found to be a prominent feature in both dementia (Visser, 1983) and in Mild Cognitive Impairment (MCI) (Shin et al., 2011), which is often regarded as a transitionary stage between normal aging and AD (Sullivan et al., 2019). Yet the relationship between postural stability and cognitive functioning within healthy populations was previously unexplored. This study reported findings that standard deviations in anteroposterior (AP) sway was significantly, negatively related with scores on tests of Short-Term Memory (STM), Long-Term Memory (LTM), Working memory (WM), and associative learning. It was concluded that these findings have to potential to justify the integration of postural stability assessments into clinical practice.

Chapter Six aims to further the findings of Chapter Five by exploring the relationship between an individual's proclivity to participate in posture-related sporting activity and scores on cognitive assessments. This was an online study using self-report questionnaires and cognitive tests of memory and reasoning. Results reported that individuals who participated in a greater number of posture-related sporting activities performed better on assessments of memory than those who participated in fewer. It was concluded that these findings expanded the results witnessed in Chapter Five by providing ecological validity which cannot be afforded by lab-based experimental research.

Chapter Seven investigates facial expressions of emotion and whether they share a relationship with cognitive functioning. This is another factor which has found to be related to cognition in individuals suffering from dementia (Seidl et al., 2008; 2012; Asplund, et al., 1991), yet previously had an unclear relationship within young, cognitively-healthy populations. This study utilised machine-learning technology in order to assess the facial expressions of emotion in cognitively-heathy individuals. Results reported that individuals who demonstrated an increased frequency of negative facial expressions performed better on memory assessments than individuals who demonstrated respectively greater proportions of neutral or positive expressions. This was an unexpected finding as previous literature has stated that AD patients demonstrate a greater frequency of negative expressions of emotions (Asplund et al., 1995; Smith, 1995) or fewer recognisable emotions at all (Seidl et al., 2008; 2012). It was concluded that if this relationship can be witnessed across various age groups and cultures, that evaluation of clinical expressions of emotions could be utilised in a diagnostic context, although more research is warranted to understand the relationship in more detail.

Chapter Eight builds on the findings of Chapter Seven by exploring the relationship between cognitive functioning and blink rates. Prior research has demonstrated a relationship between blink rates and cognitive functioning in dementia patients (Bonanni et al., 2007; Anzellotti et al., 2008; Mohammadian et al., 2015), as well as MCI patients (Ladas et al., 2014), but this relationship within healthy populations is less clear. This study utilised the same participant cohort as Chapter Seven. Findings showed that individuals who produced the lowest 25% of blink rates performed better on a series of memory assessments than the remaining 75%. These results were surprising, as previous contemporary research has reported a positive relationship between blink rates and cognition (Kuwamizu et al., 2020; Ortega et al., 2021).

Chapter Nine utilises fully-immersive Virtual Reality (VR) to assess spatial memory, and explores the relationship between spatial memory and cognitive functioning, while also reflecting on whether novel technologies which afford a greater capacity for naturalism may offer distinct and separate findings than previous studies which used less naturalistic methods. Results reported that, on the hardest trial, there was a significant negative relationship between time taken to complete the trial, and scores on tests of STM, LTM, and associative learning, whereas a significant positive relationship was witnessed between time taken to complete the final trial and the difference of scores between the two components of a dual-task assessment. It was concluded from this study that results generated from fully-immersive VR were similar, yet distinct from previous findings reported using on-screen VR.

Chapter Ten summarises the main findings of the thesis, while exploring the implication and applications of the findings, in both clinical and academic contexts. This chapter then presents ideas for possible future research, before providing a conclusion to the thesis.

Chapter Two

Dementia and Alzheimer's Disease

2.1 Introduction

The purpose of this chapter is to introduce dementia and AD, including definitions, prevalence, symptoms, prognosis, and information on diagnoses. An understanding of these conditions is pertinent to this present thesis as the findings from the experimental chapters (See Chapters Five-Nine) are discussed in the context of bolstering the accuracy of a dementia/AD diagnosis.

2.2 Dementia

2.2.1 Prevalence and Incidence of Dementia

The global population is aging (Khow and Visvanathan, 2017). As individuals live longer, there is an increased prevalence of age-related illnesses such as dementia (Ragin, 2017). Dementia has been identified as a major challenge facing the world at this time (Treadaway et al., 2019). 850,000 Britons are currently estimated to be living with dementia, costing individuals and the government a combined £34.7 billion annually (Alzheimer's Society, 2020). It is thought that over one million individuals in the UK will be suffering from dementia by the year 2025 (Prince et al., 2015). The annual cost of dementia in the UK is set to rise sharply over the next two decades, to £94.1 billion by 2040 (Alzheimer's Society, 2020); whereas worldwide, there are currently around fifty million people suffering from dementia (WHO, 2020), costing individuals and the government a combined total of $818 billion annually (Prince et al., 2015; Livingston et al., 2020). Although, exact estimates are difficult to achieve, due to the difficulty of diagnosing young-onset dementia (Lambert et al., 2014).

2.2.2 What is Dementia?

Dementia is not one, single, specific illness (Fymat, 2019); it is an umbrella term which encompasses a series of distinct and separate subtypes (see Figure 1). Dementia is a progressive, neurodegenerative condition which is life-limiting (Mataqi and Aslanpour, 2020). It has been defined as acquired deficits of cognitive functions, including deficits in complex attention, executive ability, learning and memory, language, visuospatial-perceptual ability, and social cognition (Sorbi et al., 2012). It is further stated that the cognitive deficits may be accompanied by behavioural disorders and must be significant enough as to interfere with the functional independence of the individual (Sorbi et al., 2012). All dementias are characterised by deficits in memory, reasoning, behaviour, and communication (Clark et al., 2018) and currently has no known cure (Ashby-Mitchell et al., 2017).

2.2.3 Dementia Subtypes

As mentioned above, dementia is not a single illness (Fymat, 2019). The umbrella term of dementia encompasses over 100 different conditions (Khattak et al., 2018). The most common forms of dementia, calculated over a 30-year retrospective study conducted by Brunnström et al. (2009) are displayed within the graph below:

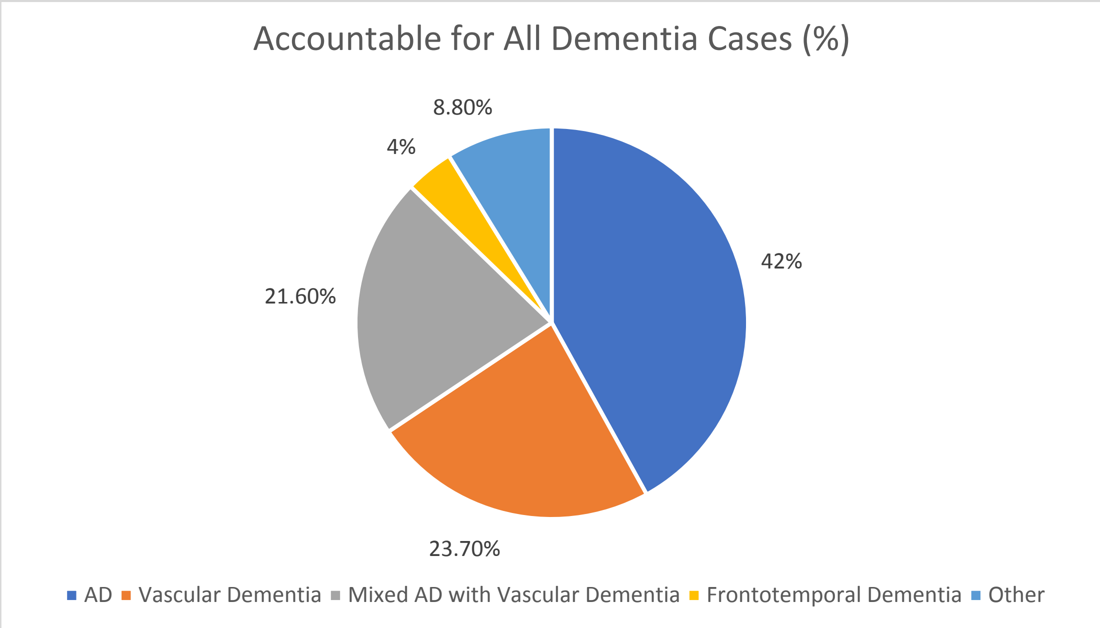


Figure 1 Dementia Subtypes

'Other' includes combinations other than combined AD mixed with vascular dementia (Brunnström et al., 2009). As can be seen above, there exists a diverse set of dementia subtypes. However, the most common subtype of dementia by far is AD (Lee et al., 2017).

2.3 Alzheimer's Disease

2.3.1 AD Background and History

November 3rd, 1906, at the 37th meeting of the Society of Southwest German Psychiatrists in Tübingen, Germany, Alois Alzheimer presented the findings of his research, describing the clinical and neuropsychological characteristics of the disease which was to be named for him (Alzheimer, 1907; Kraepelin, 1913). Today, AD is not only the most common subtype of dementia, but the most common neurodegenerative disease in the world (Santiago and Potashkin, 2021), affecting 25% of individuals over the age of eighty-five (Carrera et al., 2012).

As a subtype of dementia, AD can also be defined as a chronic, complex neurodegenerative disease (Ikonomovic and Abrahamson, 2017), characterised by deficits in memory, reasoning, behaviour, and communication (Clark et al., 2018) with no known cure (Ashby-Mitchell et al., 2017).

There are two common categorisations of AD: early onset, and late onset (or sporadic) (Mendez, 2019). Early onset AD occurs sooner in life, wherein symptoms begin to present themselves between the ages of thirty and sixty (Berkis et al., 2010). This is a less common form of AD, accounting for between 1-6% of cases (Berkis et al., 2010). There appears to be a strong genetic component to early onset AD, as 60% of cases show a familial history of developing AD (Bird, 2008). Late onset AD is the much more common category of AD, accounting for around 90% of cases (Bature et al., 2017). Although most cases of AD are thought to be sporadic, there are four main risk factors for AD which are (i) increasing age, (ii) familial association, (iii) Down syndrome, and (iv) carrying the apolipoprotein E4 allele (Brown et al., 2005).

2.3.2 AD Symptoms

Regardless of the cause, as with all dementias, AD is characterised by deficits in memory, communication, behaviour, and reasoning (Clark et al., 2018). However, the most pronounced of these deficits can be seen in memory (Rabipour et al., 2021). This complicates the diagnostic process, as memory can be influenced by several factors including age (Jacova et al., 2007), gender (Fields et al., 2011), and education level (Morais et al., 2018). While AD diagnoses assess accelerated cognitive decline, the extent to which memory loss is accelerated in the individual can be difficult to ascertain, however, as proportionality of memory loss is relative to the individual. Similarly, other symptoms of AD, such as spatial disorientation, anxiety and confusion, and changes in personality are not uniformly witnessed in every patient (Dubois et al., 2007). The difficulties in achieving an early and accurate diagnosis are discussed in greater detail in Chapter Three. As a progressive illness, AD is often subdivided into three states: mild, moderate, and severe (NIA, 2017). The United States (US) National Institute on Aging (NIA) (2017) has provided information on the symptoms of mild, moderate, and severe AD Which are as follows:

Mild AD:

- Memory loss
- Poor judgment leading to bad decisions
- Loss of spontaneity and sense of initiative
- Taking longer to complete normal daily tasks
- Repeating questions
- Trouble handling money and paying bills
- Wandering and getting lost
- Losing things or misplacing them in odd places
- Mood and personality changes
- Increased anxiety
- Increased aggression

Moderate AD:

- Increased memory loss and confusion
- Inability to learn new things
- Difficulty with language and problems with reading, writing, and working with numbers
- Difficulty organizing thoughts and thinking logically
- Shortened attention span
- Problems coping with new situations
- Difficulty carrying out multistep tasks, such as getting dressed
- Problems recognising family and friends
- Hallucinations, delusions, and paranoia
- Impulsive behaviour such as undressing at inappropriate times or places or using vulgar language
- Inappropriate outbursts of anger
- Restlessness, agitation, anxiety, tearfulness, wandering—especially in the late afternoon or evening
- Repetitive statements or movement, occasional muscle twitches

Severe AD:

- Inability to communicate
- Weight loss
- Seizures
- Skin infections
- Difficulty swallowing
- Groaning, moaning, or grunting
- Increased sleeping
- Loss of bowel and bladder control

While it is common for AD to be measured using the terms mild, moderate, and severe (NIA, 2017), it is also often the case that the condition is regarded as a series of seven stages.

2.3.3 The Seven Stages of AD

As previously discussed, AD is a neurodegenerative disease (Ikonomovic and Abrahamson, 2017). This means that over time the symptoms worsen (Forlenza et al., 2010). Reisberg et al. (1982) devised a seven-stage ‘Global Deterioration Scale’ (GDS) which chronicles the cognitive and behavioural decline that one can expect to witness in an individual suffering from AD (Reisberg et al., 1982). See below:

Table 1 The Seven Stages of AD

Stage	Designation	Characteristics
One	No cognitive decline	• Does not exhibit symptoms of cognitive decline
Two	Very mild cognitive decline	• Forgetting words • Misplacing objects • May go unnoticed by people around them • Can occur in normal aging
Three	Mild cognitive decline	• Forgetting recent information such as a passage they have just read, or the name of someone they were just told • Cannot make plans • Disorganised • Frequently starts misplacing/losing objects
Four	Moderate cognitive decline	• Loses interest in hobbies • Avoids meeting people • Avoids attending social events • Calculating expenses becomes difficult • Disoriented to time, place, or date • At this stage, signs become clear to see • A diagnosis is likely to be made at this point
Five	Moderately severe cognitive decline	• Major memory impairment, forgetting house address or phone number • Forgetting how to bathe • Difficulties getting dressed
Six	Severe cognitive decline	• Mistake close relatives for another • Fail to remember the names of close relatives • Suffer from severe confusion and anxiety • Need assistance using the bathroom
Seven	Very severe cognitive decline	• Completely dependent on assistance to eat, drink or sit. • Severely impacted mobility • Suffer from incontinence • Struggle with speaking

As can be seen from this table, as the patient suffering from AD continues to deteriorate, the symptoms become increasingly severe. The Seven Stage model of AD was revised in 1996, wherein it was argued that the seven stages should be considered as relative to the individual rather than a set-in-stone stepwise transition (Kraemer et al., 1996). Despite this, the seven-stage model is regarded, even today, as a useful tool to identify the progression of AD by the symptoms presented by the patient (Babu, 2021). As the degeneration worsens over time, there is a push to diagnose AD at increasingly earlier stages (Petersen et al., 2001). The following Chapter will discuss the importance of achieving an early diagnosis, as well as the currently used methods, and potential future methods, of achieving an early diagnosis.

2.3.4 Pathologies of AD

The exact cause of AD currently remains unclear (Suttisansanee and Kruawan, 2019). However, the presence of misfolded extracellular plaques comprised of amyloid β40 (Aβ) and an abnormal accumulation of intracellular neurofibrillary fibrils of tau protein defines the primary pathological conditions of AD (Filippi et al., 2018; Srivastava et al., 2021). This occurs in the medial temporal lobe of the brain (Tian et al., 2019). However, the link between these proteins and any neurodegenerative disorder is unclear due to pathological changes occurring long before any symptoms are apparent, and previous development of clinical techniques to reduce Aβ levels in AD patients has reported poor efficacy (Srivastava et al., 2021; Kim et al., 2019). Furthermore, improvements in neuroimaging techniques have allowed for more detailed and sophisticated evaluations of various manifestations of cerebrovascular diseases (Rizzi et al., 2021).

2.3.4.1 Cholinergic Hypothesis. The cholinergic hypothesis was developed by Bartus et al. (1982) and states that the cause of AD is that the neuronal and neuro-muscular regions are lacking sufficient levels of the neurotransmitter Acetylcholine (ACh). This hypothesis resulted from observations that the postmortem brains of AD patients presented pronounced cholinergic cell loss in the nucleus basalis of Meynert (Davies and Maloney, 1976) and has become the most widely accepted hypothesis for the cause of AD (Srivastava et al., 2021).

Early studies into this hypothesis conducted by Bierer et al. (1995) saw cholinergic antagonists administered to both human participants and rats, and reported a marked improvement on information processing, learning and memory after the administration of the antagonists (Bierer et al., 1995). One problem which has been identified with the research of Brier et al. (1995) was the lack of studies which compared aged-matched controls and AD groups with a young population control group, which is necessary in order to isolate dementia effects from age-related cognitive impairment (Contestabile, 2011). However, since this research was conducted, further studies have confirmed the vital role of cholinergic transmission in memory and attention encoding, as well as in cognitive functioning more generally (Hasselmo and Sarter, 2011).

Despite over four decades of research, research into the cholinergic hypothesis has slowed (Bohnen et al., 2011). This could be due in part to the limited efficacy of cholinesterase inhibitors used in clinical practice (Zemek et al., 2014); However, four of the five most common drugs for treating AD are based on the cholinergic hypothesis (Bortolami et al., 2020; Zhu et al., 2019). For a more detailed discussion on dementia treatments, see Chapter Four.

2.3.4.2 Genetics and Amyloid β. According to Srivastava et al. (2021), the genetic component of AD can be attributed to the autosomal dominance of one of three genes:

PSEN1- responsible for the protein Presenillins 1

PSEN2- responsible for the protein Presenillins 2

APP Gene- responsible for the Amyloid Precursor Protein (APP)

Mutations in any of these genes can result in an incorrect cleavage in APP, causing the protein to misfold, forming Aβ42 protein, instead of Aβ40 (Zhang et al., 2020). The accumulation of Aβ42 results in the formation of senile plaques, which is regarded as one of the primary pathological conditions of AD (Filippi et al., 2018; Srivastava et al., 2021).

Previously, genetic studies have determined that mutations on genes which encode APP were associated with enhanced production of Aβ and an increased ratio of Aβ42 being produced compared to Aβ40 (Mayeux and Stern, 2012). Further research has demonstrated that an increased ratio of Aβ42 protein can act as a predictor for the development of AD, whereas a shift in ratio favouring Aβ40 protein can reduce toxicity (Findeis, 2007). Furthermore, it has also been reported that an overabundance of APP in individuals suffering from Downs syndrome during their teenage years resulted in a build-up of neurofibrillary fibrils typically seen in AD which correlated with onset of mid-life cognitive decline (Faustino et al., 2017). It has been argued that these discussed findings contribute to the amyloid cascade hypothesis of AD which states that gradual accumulation of Aβ proteins trigger the pathogenesis of AD (Faustino et al., 2017).

Since the genesis of this theory, there has been much research on the precise role of Aβ proteins in AD. If the gradual build-up of Aβ proteins is considered as the trigger event to developing AD, it stands to reason that if one were to undo this accumulation of Aβ proteins then the development of AD may cease (Hardy and Higgins, 1992). However, the findings of research thus far have been less than promising. It appears as though the amount of plaque does not correlate with cognition (Karran et al., 2011) and further, that cognitively-healthy older adult participants also presented a heavy build-up of Aβ plaques (Gómez-Isla et al., 1996).

2.3.4.3 Tao Proteins. Another protein which is considered as a primary pathological condition of AD is the tao protein (Srivastava et al., 2021). The Microtubule Associated Protein Tau (MAPT) gene, located on chromosome 17, is responsible for encoding the tao protein (Andreadis, 2006) and is phosphorylated in three different positions (Srivastava et al., 2021). In a healthy human brain, tao proteins are responsible for attaching to microtubules to aid in their maintenance and stability (Matus, 1988); however, in AD the protein becomes hyperphosphorylated, wherein the protein forms paired helical filaments (Iqbal et al., 2010) causing the protein to lose its ability to attach to microtubules, and thereby forms into neurofibrillary tangles (Liu et al., 2019). Neurofibrillary tangles which are formed via the accumulation of hyperphosphorylated tau proteins disintegrate the network of microtubules within nerve cells, resulting in a breakdown of biomechanical communication between the cells, causing the destruction of its cytoskeleton (Srivastava et al., 2021).

While previous research has highlighted a correlation between neurofibrillary tangles and cognitive decline (Tian et al., 2019; Selkoe and Schenk, 2003), it cannot be targeted as a cause of AD alone, as previous research has reported that treating various tau species in mice was ineffective in improving cognition (Congdon et al., 2016; Srivastava et al., 2021). For this reason, any treatments which target tau proteins also target Aβ as well (Lane et al., 2018).

2.3.4.4 Neural Atrophy. Section 2.3.4 mentioned that neuroimaging technologies have revealed abnormalities in neural processes. Postmortem examinations of AD patients have consistently revealed atrophy of the temporal, frontal, parietal and hippocampal areas of the brain (Whitwell et al., 2007). More recently, a strong link has been identified between atrophy of the insular cortex and AD: Firstly, general cognitive performance has found to be negatively correlated with insular atrophy (Pan et al., 2021). Furthermore, other studies have shown that insular atrophy is positively related to psychotic tendencies such as hallucinations and delusions (Blanc et al., 2014; Kwan-Chun Ting, 2015). Whereas other studies have revealed a negative relationship between insular atrophy and difficulties in identifying emotions in AD patients (Li et al., 2016).

Atrophy is a particularly important area of concern, as previous research has shown that synaptic loss is closely correlated to the degree of cognitive impairment presented by the individual suffering from AD (Spires et al., 2005), therefore making it a reliable indicator of the progression of AD (Ten Kate et al., 2017).

2.3.4.5 Other Pathologies. There are numerous pathologies of AD which have not yet been touched upon in this section. What follows is a collection of other pathologies of AD which have seen less research than other pathologies. The first of these to consider is glutamate excitotoxicity. Glutamate is a neurotransmitter; an overabundance of which may lead to cell death (Srivastava et al., 2021). There are treatment drugs available which target the glutaminergic systems in order to reduce excess glutamate (Kaur et al., 2020) therefore this pathology of AD is manageable.

The next pathology to consider is vitamin B5 deficiency. Previous research has reported a marked reduction in vitamin B5 in individuals suffering from AD (Ismail et al., 2020). Moreover, it has been reported that reduced levels of vitamin B5 may be a causal factor of neurodegeneration in AD (Srivastava et al., 2021), and that suitable oral doses of vitamin B5 can reverse neurodegeneration in its initial stages (Xu et al., 2020).

The third pathology considered in this section is mitochondrial deficits. Mitochondria are essential in the process of neurotransmission (Gazit et al., 2016). It has been reported that a variety of functions associated with mitochondria decline in normal aging (Srivastava et al., 2021). This has been associated with the initial stages of neurodegeneration, although the timeline of events is unclear (Swerdlow, 2020). A low mitochondrial count, as well as mitochondrial mutation and oxidation have been previously associated with AD (Butterfield and Halliwell, 2019; Wang et al., 2006). The final pathology to be considered in this section is brain micro-ribonucleic acid which simply responsible for inhibiting the over-production of Aβ plaques and has also been found to hold some responsibility in inhibiting tau hyperphosphorylation (Wang et al., 2019). There are other pathologies which could be addressed or discussed in this section, but the discussion of every pathology is not the purview of this thesis. The following section will reflect on the most important pathologies regarding AD:

2.3.4.6 Pathology Reflection. Aβ plaques and tau fibrils are regarded as the primary pathological conditions of AD (Filippi et al., 2018; Srivastava et al., 2021), the cholinergic hypothesis is regarded as the most widely accepted hypothesis for the cause of AD (Srivastava et al., 2021), and the loss of synaptic structure due to atrophy is regarded as an important area of research (Herrup, 2010). The primary focus of this thesis is to assess potential non-invasive techniques for the detection and diagnosis of dementia to be utilised alongside previously established diagnostic criteria to improve the accuracy of a dementia diagnosis, and in order to support the diagnostic process, we must consider the symptoms.

2.4 Chapter Summary

This chapter has been an introduction to dementia and AD. It has highlighted the difference between these two conditions while providing information on a variety of kinds of dementias. In particular this chapter explored AD, the most common form of dementia (Lee et al., 2017), and discussed the stages of degeneration, pathologies, symptoms, and prognoses. The following chapter summarises the process that an individual goes through in order to be diagnosed with dementia and the conditions in which each of the most commonly used diagnostic tools for dementia may be implemented, while highlighting the importance of an early diagnosis, and the difficulty of achieving such. The following chapter also reviews and explores factors which are known to be related to dementia, but are not currently utilised in a diagnostic capacity. It will explore these factors within the context of their readiness and applicability to be utilised in a diagnostic capacity.

2.5 Highlights

- An ageing global population results in and increased prevalence of dementia (Khow and Visvanathan, 2017; Ragin, 2017).
- There is currently estimated to be 850,000 Britons suffering with dementia, costing £34.7 billion annually (Alzheimer's Society, 2020).
- Dementia is an umbrella term comprised of over 100 different conditions (Khattak et al., 2018).
- Dementia has no known cure and is characterised by deficits in memory, reasoning, behaviour, and communication (Clark et al., 2018; Ashby-Mitchell et al., 2017).
- AD is the most common subtype of dementia (Lee et al., 2017).
- The cause of AD is unclear (Suttisansanee and Kruawan, 2019).
- Common pathologies of AD include a build-up Aβ plaques and an accumulation of tau protein tangles in the medial temporal lobes of the brain (Filippi et al., 2018; Srivastava et al., 2021; Tian et al., 2019).
- The most widely accepted hypothesis for the cause of AD is that the neuronal and neuro-muscular regions are lacking sufficient levels of ACh (Bartus et al., 1982; Srivastava et al., 2021).
- Diagnoses of AD can be influenced by a number of factors including age (Jacova et al., 2007), gender (Fields et al., 2011), and education level (Morais et al., 2018).
- AD is often divided into mild, moderate, and severe AD, but is still frequently regarded as a seven-stage model (NIA, 2017; Babu, 2021).
- There is a push to diagnose AD at earlier stages (Petersen et al., 2001).
- The following chapter discusses current and potential methods of diagnosing dementia, as well as the importance of an early diagnosis.

Chapter Three

Non-Invasive Methods of Diagnosing Dementia and Alzheimer's Disease

3.1 Introduction

The previous chapter, Chapter Two, introduced dementia and AD, including different types of dementia and their prevalence and incidence. Chapter Two mostly focussed on AD, as this is reported to be the most common form of dementia (Lee et al. 2017). Symptoms, pathologies, and speculative causes of AD were also discussed along with the seven-stage model of AD. This chapter will discuss the current methods which are used to generate a diagnosis of dementia and AD, and then discuss the importance of an early diagnosis. Following this, a review of potential diagnostic criteria will be conducted in order to assess factors which are known to be related to dementia but are not yet implemented in a diagnostic context.

3.1.1 Background to Dementia Diagnoses

Achieving a dementia diagnosis is a complex process, requiring screening assessments, neuroimaging and neuropsychological assessments (Wissing et al., 2021). Diagnoses, particularly in the early stages of cognitive decline, are not straightforward to achieve and variations within symptoms are commonplace (Eschweiler et al., 2010).

A true diagnosis of AD cannot be achieved until post mortem (Mosconi et al., 2008) due to the plaques and tangles that pathologise AD, which cannot be witnessed in a living patient (Mosconi et al., 2008) However, a clinical diagnosis of dementia typically follows a two-stage process – (i) identifying the presence of dementia and then (ii) determining the subtype (Eschweiler et al., 2010). According to the National Health Service (NHS) (2020), the process of achieving a dementia diagnosis begins with an individual booking an appointment with their General Practitioner (GP). In this appointment, the GP will ask the individual about any symptoms they might feel they have, about other aspects of their health, and about everyday tasks, such as:

- Personal care (washing and dressing, for example)
- Cooking
- Shopping
- Paying bills

It is advised that a close relation accompanies the individual to their GP appointment, so that they can also describe the changes that they have seen in the behaviour of the individual attending the appointment (NHS, 2020). During this appointment, the GP will administer a cognitive assessment, and may suggest a blood test (see section 2.4.2 for a detailed discussion on diagnostic methods). If the GP is able to rule out other causes for the cognitive decline, the patient will then be referred to a dementia specialist, who may conduct more tests, or run neuroimaging scans such as a Magnetic Resonance Imagining (MRI) scan or a Computerised Tomography (CT) scan to assess neural degeneration (NHS, 2020). The specialist is then capable of achieving a diagnosis of dementia (NHS, 2020).

However, dementia is not well understood in the general population (Alzheimer's Research UK 2016). A study has shown that 56% of individuals wait over one year to seek a dementia diagnosis due to fear of a diagnosis (Alzheimer's Society, 2016). Furthermore, it is difficult to discriminate between cognitive decline due to normal aging, or due to pathological abnormalities (Hedden and Gabrieli, 2004; Petersen, 2011). Consequently, individuals suffering from the less common forms of dementia may struggle to gain a diagnosis (La Fontaine Papadopoulos, 2016).

3.1.2 Diagnostic Tests

3.1.2.1 Neuroimaging One of the most common ways of diagnosing dementia is by using neuroimaging technology, such as an MRI scan, amyloid positron emission tomography (PET), or single-photon emission computed tomography (SPECT) (Ishii, 2020). Neuroimaging can provide biomarkers which are useful for supporting dementia diagnoses (Ishii, 2020). However, instead of being used alone to diagnose dementia, neuroimaging technology is used to rule out other possible causes for the symptoms of dementia, such as tumours, haemorrhages, or stroke (Marshall, 2018). An MRI/CT scan can also reveal the anatomical structure of the brain and in AD has shown that the hippocampus is significantly more atrophied than would normally be expected in healthy cognitive ageing (Marshall, 2018); although, upcoming advancements in neuroimaging technology means the methodology will likely offer an increase in the diagnostic accuracy of specific cognitive disorders (Frantellizzi et al., 2020).

As well as MRI and CT scans, single photon emission computerised SPECT or PET scans can be used. However, these are not employed as frequently as MRI or CT scans (Alzheimer's Society, 2020). PET and SPECT scans differ from MRI and CT scans as they provide images of brain activity based on blood flow, oxygen consumption, or glucose use (Marshall, 2018). This information can be used to reveal loss of brain mass, which is commonly associated with AD and other dementias, as well as revealing information which helps to discriminate between dementias, such as cortical blood flow (Marshall 2018).

3.1.2.2 Cerebrospinal Fluid Profiling The next method of diagnosing dementia to consider is the use of cerebrospinal fluid (CSF) profiling. CSF is a fluid which circulates through the ventricles of the brain (Bear et al., 2020). CSF serves two functions: firstly, the fluid submerges the brain, providing buoyancy in order to reduce the weight of the brain resting on the skull (Wright et al., 2012). Secondly, the fluid provides a medium to provide nutrients to, and remove waste products from the brain (Wright et al., 2012). Changes to the composition, flow, or pressure of CSF can be emblematic of the development of neurological conditions (Wright et al., 2012). Therefore, CSF can produce valuable information regarding neurological diagnoses (Wright et al., 2012).

Profiling CSF requires a procedure called a lumbar puncture (Wright et al., 2012). This is an invasive technique that involves introducing a needle below the termination of the spinal cord and passing through the dura mater of the spinal cord in order to access the subarachnoid space, allowing us to sample CSF (Wright et al., 2012).

Previous research has found that AD patients present significantly lower level of Aβ and higher level of tao protein in their CSF than healthy controls (Petersen, 2009; Olsson et al., 2016). However, there is a series of potentially damaging side-effects of a lumbar puncture, such as local infections, uncorrected bleeding diathesis, risk of herniation, and congenital abnormalities (Wright et al., 2012; Sinclair et al., 2009; Hasegawa and Yamamoto, 1999). As such, the National Institute for Clinical Excellence (NICE) only recommend the use of a lumbar puncture for a diagnosis of AD in people with MCI when the severity of progression is unclear (Leroi et al., 2020; NICE, 2018).

3.1.2.3 Blood Tests There are other tools which can be used in addition to neuroimaging or CSF profiling, such as blood tests (Harper and Suskind, 2019). Both fluctuating blood pressure and high blood glucose levels have been linked to cognitive dysfunction (Peters et al., 2020, Wilum-Anderson et al., 2020). Recent research has found specific protein biomarkers which can sensitively discriminate between AD and controls, providing useful information for AD diagnoses (Yao et al., 2019). Blood tests can also be used to rule out health issues which may present similar symptoms to dementia such as hormonal imbalances which produces high levels of thyroid hormones or low levels of vitamin B12, which have been shown to negatively impact cognitive functions (Mao et al, 2020, Jatoi et al., 2020).

3.1.2.4 Neuropsychological Assessments As discussed above, when an individual has a meeting with their GP regarding a dementia diagnosis, the GP may issue neuropsychological assessments to assess a battery of cognitive functions, including STM, LTM, concentration, attention, language, communication, orientation, or visuospatial abilities. (NHS, 2020). One such neuropsychological assessment is the MMSE

3.1.2.5 The Mini Mental-State Examination The MMSE is a five-ten minute examination which focuses on the cognitive aspects of mental function (Folstein et al.,1975), and is the most commonly used method of diagnosing dementia (Scheffels et al., 2020). However, there are concerns with the MMSE. Some argue that the MMSE should be retired due to issues with reliability, validity, and ethnocentricity (Carnero-Pardo, 2014; Devenney and Hodges, 2017). Moreover, it has been argued that the MMSE was never originally intended to be used as a diagnostic tool for dementia (Folstein et al., Helzer, 1983). Although the MMSE is the most widely used tool for diagnosing dementia, other tools have been developed which have been found to be able to detect dementia to some extent, but are not as clinically prevalent (Marshall, 2018).

Some neuropsychological tests which have been found to be able to diagnose a cognitive impairment include The Mini Cognitive Assessment (Mini-Cog) (Borson et al., 2000), the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005), and the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Sahakian et al., 1988).

3.1.2.6 The Mini Cognitive Assessment The Mini-Cog was developed in response to other assessments being overly-dependent on language ability or requiring specialist training to administer (Borson et al., 2000). The Mini-Cog is presented as an alternative to other methods as it is fast to administer, and is unaffected by age, education, and language ability (Borson et al., 2000).

3.1.2.7 The Cambridge Neuropsychological Test Automated Battery

The CANTAB is a technological battery of assessments which again attempt to move away from the language dependence of other dementia assessments, such as the MMSE. It is a technological, computer-based cognitive battery assessment which can test for a number of neuropsychological functions such as associative memory (Sahakian et al., 1988), i.e., associations between a visual stimulus and spatial location (Égerházi, et al., 2007), and semantic memory (McKenna and Warrington, 1980).

3.1.2.8 The Montreal Cognitive Assessment The MoCA was developed to be a quick test of general cognitive abilities (Nasreddine et al., 2005). Lasting only ten minutes, it aims to diagnose MCI rather than dementia (Nasreddine et al., 2005). Although, research has reported that AD patients also perform poorly on many of the cognitive domains assessed in the MoCA (Julayanont and Nasreddine, 2017).

3.1.3 Early Diagnosis

Section 3.1.2 discussed the different methods which are currently used to diagnose dementia, including neuroimaging, CSF profiling, blood tests, and neuropsychological assessments. These tools are used in order to generate a diagnosis of dementia. For context, this following section explores the importance of achieving an early diagnosis.

It is difficult to overstate the importance of achieving an early and accurate diagnosis of dementia. There are multiple factors which are to be considered when considering the importance of an early diagnosis, such as the incidence, economic considerations, implications for treatment options, and identifying cognitive decline which may be reversable.

3.1.3.1 Early Diagnosis Considerations: Incidence. As discussed in section 2.2.1, all over the world, people are living longer (Khow and Visvanathan, 2017) and age is a primary risk factor for developing dementia (Brown et al., 2005). Subsequently, the aging population is a driving factor for the increasing prevalence of dementia (Ragin, 2017). Previous research has estimated that there are around fifty million individuals around the world suffering from dementia, and by the year 2025, over one million people will be suffering from dementia in the UK alone (Prince et al., 2015; WHO, 2020). If dementia was diagnosed earlier, pharmacological treatments such as acetylcholinesterase inhibitors (AChEI) (See Chapter Four for an in-depth discussion regarding pharmacological treatments for dementia) could be administered earlier, which has the potential result of the individual maintaining a greater quality of life for longer (Luzny et al., 2014). This would also aid in reducing the economic burden of care costs, as care would not be necessary until later in life due to the individual remaining independent for longer (Petersen, 2009). However, this is speculative, as there is currently no evidence that earlier treatment will prolong the quality life long enough to influence the date of institutionalisation (Rountree et al., 2013). The economic considerations of dementia are discussed below.

3.1.3.2 Early Diagnosis Considerations: Monetary Costs. It has been reported that the incremental health care and nursing home costs for those with dementia were $28,501 per person per year in the US in 2010 (accounting for inflation, this is over $38,000 in today's money) (Alzheimer's Association 2021). In the US, total payments in 2021 for all individuals with dementia is estimated at $355 billion (Alzheimer's Association 2021). It is projected in the UK that the total annual cost of dementia will increase from its current level of £34.7 billion annually to £94.1 billion annually by 2040 (Alzheimer's Society, 2020). The currently estimated worldwide financial cost of dementia of is $818 billion (United States Dollars) annually (Prince et al., 2015; Livingston et al., 2020).

In 2018, the Alzheimer's Association commissioned a study of the potential cost savings that an early diagnosis of AD could achieve (Alzheimer's Association 2021). It was reported that, if 88% of individuals achieved a diagnosis in the MCI stage, rather than not at all, that around $7 trillion could be saved in medical and care costs (Mebane-Sims, 2018). Finally, regarding treatment, research has estimated that if there were a treatment introduced in 2025 that delays AD onset by five years, that this would reduce total health care payments by 33% and individual payment by 44% by 2050 (Alzheimer's Association, 2015). See below for other treatment implications that an early diagnosis of dementia could influence.

3.1.3.3 Early Diagnosis Considerations: Implications for Treatment Options. An early diagnosis of dementia would mean that dementia treatments could be initiated sooner. Initiating treatment early could help to reduce the acceleration of cognitive decline by increasing the levels of acetylcholine in the brain (Haake et al., 2020). Falling levels of acetylcholine has been linked with the symptoms of AD worsening, and previous research has reported that treating AD with cholinesterase inhibitors in the earlier stages assists in minimising the behavioural changes which can be witnessed in the later stages (Haake et al., 2020). This means that starting treatment earlier could result in the patient spending less time spent in a care home, with the associated costs (Markwick et al., 2012). Currently, dementia is often identified too late, where the cognitive decline that has currently taken place reduces the efficacy of treatment drugs (Pantel et al., 2004). An earlier diagnosis would assist in both starting the treatment sooner, and ensuring that the treatment drugs are operating at maximum efficacy (Alzheimer's Association, 2021). Furthermore, an early diagnostic assessment of dementia will assist in predicting the onset of disease, which aids in developing preventative therapies (Pandey and Ramakrishnan, 2020). There are many treatment options available for dementia, see Chapter Four for a discussion of the benefits and limitations of a variety of dementia treatments, both pharmacological and non-pharmacological in nature.

3.1.3.4 Early Diagnosis Considerations: Identifying Reversible Cognitive Decline. One of the main reasons that dementia is difficult to diagnose is due to the symptoms of dementia being shared by other illnesses (NHS, 2020). Cognitive decline may not be due to dementia, it may be due to other conditions, such as depression, anxiety, delirium caused by an infection, or hyperthyroidism (NHS, 2020) These conditions, such as depression, are treatable and manageable (Farías-Antúnez et al., 2018), and if treated, the cognitive decline seen could be reversed (Hu et al., 2018).

3.1.4 The Difficulties in Achieving an Early Diagnosis

The benefits of an early diagnosis of dementia as listed in section 3.1.3 raise the question of why earlier diagnoses are not taking place. The answer to this is that an early diagnosis of dementia is difficult to achieve (Ibanez et al., 2020). As a neurodegenerative illness (Ikonomovic and Abrahamson, 2017), the symptoms of dementia gradually become worse over time (Forlenza et al., 2010). Due to the nature of neurodegenerative illnesses, this means symptoms such as memory loss are less pronounced in the earlier stages (Pozzebon et al., 2018). This issue is compounded by the fact that the underlying pathological changes which cause the symptomatic onset occur decades before any symptoms can be seen (Forlenza et al., 2010). This means that it is often the case that a diagnosis of dementia is achieved too late (Pantel et al., 2004). By the point of achieving a diagnosis, structural damage to the brain may have reached an extent that treatments for the condition are not as effective as they could have been if a diagnosis had been achieved in a timelier manner (Pantel et al., 2004). As such, there is an ongoing push to diagnose AD at increasingly earlier stages (Petersen et al., 2001). Many of the tests described above could be considered invasive in nature. This chapter now looks at potential non-invasive measures to aid diagnosis that could be implemented in diagnostic contexts, in order to bolster the accuracy, reliability and allow for an earlier dementia diagnosis.

3.2 Meta-Analysis Introduction

The following section of this chapter is a review which explores and critiques the efficacy and applicability of non-invasive factors which are known to be related to dementia yet are not yet utilised in a diagnostic context. Methods reviewed here are (i) hearing loss, (ii) facial expression analysis, (iii) language production, (iv) assessments of neuropsychological functioning and (v) balance and posture. The evaluation will also discuss how these methods could potentially be used in conjunction with other non-invasive and invasive methods, and also how advancements in technology could be used to improve the reliability and accuracy of these methods.

3.3 Methods

3.3.1 Search Method

A literature review was conducted, focussing on English language papers written any year until 2021. No specific starting year was decided upon due to all articles written on the non-invasive diagnosis of dementia were considered relevant. The online databases used in this review were Web of Science, Science Direct, Psychinfo, PubMed, Cochrane, IEEE Xplore, Google Scholar, and Summon.

3.3.2 Study Selection

Papers were deemed to be relevant if they met the selection criteria, as follows: criterion 1: the study met the definition of non-invasive, criterion 2, the study had a focus on diagnosis, rather than rehabilitation, and criterion 3, the study had a focus on dementia of any type.

3.4 Results

What follows is a summary of the reviewed articles, placed into category by the area of study, which are assessments of neuropsychological functioning, hearing loss, facial expressions, and language production. These articles will be explored further in the discussion. Following the summary, Table 2 highlights the benefits and limitations of each area of dementia research.

3.4.1 Neuropsychological Functioning

The Entorhinal Cortex (EC) is the first region of the brain to show degeneration in AD (Howett et al., 2017). Among other cognitive functions, the EC is implicated in memory formation (Sekeres et al., 2018). This claim is supported by further research which found that participants in very early stages of AD show deficits in delayed recall tasks (Scheltens et al., 2018).

Research has also shown how all types of dementia impact executive functioning, where the ability to manipulate information has found to be impaired in patients suffering from dementia as compared to healthy controls (Yatawara et al., 2017). Whereas, specifically for AD, results show that participants suffering from AD perform poorly on cognitive tests, such as the Tower of London test, and tests of regional integration (Shafiee-Kandjani et al., 2020). Further findings demonstrate that AD affects attentional processing (Van Diepen et al., 2019). This has been shown by findings that in dual-task assessments, the greater the level of cognitive impairment displayed by the participant, the longer the tasks took to complete (Kayama et al., 2012; Kayama et al., 2013). With regards to the effects of cognitive impairment on processing speed, typically a standardised Stroop test is used as a measure (Coghe et al., 2018). It has been found that cognitively-healthy older participants perform worse on the Stroop test than younger participants; however, this performance is worse still in participants suffering from AD (Bélanger et al., 2010).

Given that the MMSE is the most commonly used method of diagnosis (Scheffels et al., 2020), it tends to be the focus of comparison studies against other clinical assessments of dementia. Meta-analysis studies of the MMSE criticise it as being used in many situations where other cognitive assessments would have yielded comparable or better results (Tsoi et al., 2015). However, these analyses also reported that the MMSE was the best tool for ruling out a diagnosis of dementia, but for everything else, it was concluded other assessments should be utilised (Mitchell, 2009).

Other studies have reported conflicting results. In a large-scale assessment of the sensitivity of the MMSE against the Mini-Cog, it was found that the Mini-Cog shows similar sensitivity and specificity as the MMSE (Borson, et al., 2003). However, other research has reported findings that the Mini-Cog has the highest sensitivity out of the Mini-Cog, MMSE, and the Cognitive Abilities Screening Instrument (CASI) (Borson et al., 2000). The Mini-Cog was praised further for being the assessment which is least reliant on language and is the least affected by education (Borson et al., 2000). This is important given that the Mini-Cog was found to have similar sensitivity to the MMSE. The participants in this study were a random sample of 1,119 older adults, whereas when the Mini-Cog was found to be more sensitive, the participants consisted of 129 participants who were deemed to have ‘probable dementia’. Borson et al. (2000) concluded that the Mini-Cog is ready to be incorporated into clinical analysis. And since then, NICE guidelines now recommend incorporating the Mini-Cog into a short screening process for dementia (NICE, 2018).

Next, the CANTAB battery was assessed. It has been reported that due to its computerised nature, the CANTAB battery offers substantial benefits in terms of precision, speed, and reliability over paper-based assessments of neuropsychological functioning (Day et al., 2019). The CANTAB battery has many potential applications, including diagnosis, assessment of cognitive development, and used to inform occupational health (Fray et al., 1992). It has been found to be sensitive in diagnosing a multitude of neurodegenerative illnesses such as AD, Parkinson's disease, Huntington's disease and AIDS (Fray et al., 1992).

These findings have been furthered by Égerházi et al. (2007) who tested participants with AD against an MCI group and healthy controls. They were tasked with completing tests of memory, attention and executive functions. Results indicated that the AD group performed significantly worse than both the MCI group and healthy controls (Égerházi et al., 2007). Furthermore, studies have found that when the CANTAB battery is used in conjunction with the MMSE and Mini-Cog it can be highly accurate, with the ability to predict with 100% accuracy whether or not forty individuals suffering from questionable dementia would go on to develop probable AD (Blackwell et al., 2004). Whereas when asked to discriminate between normal cognitive aging, MCI, and AD, the CANTAB battery alone has shown an accuracy of 81% in identifying which of these three groups an individual belongs to (Junkkila et al., 2012).

3.4.2 Hearing Loss

Previous research shown that there is an interaction between hearing loss and dementia. In a study of 100 individuals with AD, it was found that in a double-blind experiment, hearing loss was significantly and independently related to severity of cognitive dysfunction (Uhlmann et al., 1989). Later research furthered these results in a large-scale study of 639 individuals, finding that with mild, moderate, and severe hearing loss, the risk of all-cause dementia increased (Lin et al., 2011). It was concluded that hearing loss was a marker for all-cause dementia, but did not consider each form of dementia separately (Lin et al., 2011). Furthermore, it was concluded that further study is required to identify if hearing loss is a marker for pre-dementia (Lin et al., 2011). However, there may be a case for using hearing loss as a diagnostic tool as research has also demonstrated that in the case of 347 healthy older adults, poorer hearing was directly related to lower scores on tests of cognitive function (Lin, 2011). Therefore, it seems that hearing loss may interact with cognitive functioning. However, research has shown that even in older adults with appropriately fitted hearing-aid technology, scores on tests of cognitive function were significantly lower than normative data (Wong et al., 2014).

3.4.3 Language Production

Next, the literature surrounding how dementia interacts with an individual's ability to coherently produce language was assessed, which returned finding that dementia has a complex relationship with language production. This research was built from Kemper et al. (2001) who found that a decline in grammatical and syntactical complexity is accelerated in the case of AD. These results have been furthered by the findings that dementia affects the syntactic complexity and sentence structure produced by individuals suffering from the disease (Meteyard et al., 2014).

Furthermore, it has been found that in conversations with an interviewer, participants suffering from dementia showed a significantly diminished use of nouns (Bird et al., 2000; Blanken et al., 1987). It is argued that these results stem from pre-linguistic disorders in the formation of words that the participant intended to say (Bird et al., 2000). This could explain other findings, such as that in an interview situation, participants suffering from dementia were significantly more likely to omit words or substitute the word for another in a complex sentence (Meteyard and Patterson, 2009). Finally, as discussed in section 2.3.2, language production is found to be a factor which becomes increasingly impaired as AD progresses (NIA 2017).

3.4.4 Facial Expressions

Finally, we looked into research which assessed how facial expressions are affected in dementia, finding that there were two distinct ways in which dementia and facial expressions interact. Firstly, research into how individuals suffering from dementia produce facial expressions was explored. It has been found that, compared to controls, individuals suffering from dementia show an increased likelihood to produce a negative reaction, such as sadness, disgust, or anger, when exposed to sad stimuli in pre-recorded video footage (Asplund et al.,1995). These results have been echoed by other research which found that although individuals suffering from dementia showed fewer facial expressions which could be recognised as a clear emotion, significantly more negative facial expressions were produced than positive ones (Asplund et al., 1991). However, these results have been contradicted, as other research has found that in the case of fifty-eight participants with varying degrees of dementia, patients produced significantly fewer facial expressions displaying any emotion as compared with controls (Seidl et al., 2008; 2012).

Secondly, we reviewed research that has been conducted into the perceptions of facial expressions by individuals suffering from dementia; research in this area has shown that participants with dementia show no significant difference from controls in terms of recognising other individuals' facial expressions (Guaita et al., 2012). However, these results have been contradicted by the finding that while AD patients are completing a semantic task, they are significantly worse at recognising facial expressions than healthy controls (García-Rodríguez et al., 2012). Further contradictions have been found showing that participants suffering from dementia perform worse compared to healthy older adults at recognising all facial expressions aside from sadness and fear, which demonstrated no significant difference in recognition (Carvalho et al., 2014).

This phenomenon may hold diagnostic value for dementia as a decreased ability to produce and recognise facial expressions is less pronounced in natural aging, as research has found that individuals suffering from AD perform worse than healthy older adults when tasked with identifying the facial expressions of other individuals (García-Rodríguez et al., 2009). This provides a tangible element which can be assessed more easily with modern technology in a clinical environment, potentially improving the accuracy of future diagnoses of dementia.

3.4.5 Balance and Posture

Balance has long been known to share a relationship with dementia. Initial research conducted by Visser (1983) assessed the walking behaviour of individuals which were identified as suffering from “severe memory impairment and the associated behaviour disturbances” (Visser, 1983). It was noted that the individuals who were suffering from this impairment took significantly shorter steps, fewer steps, stepped more slowly, required supports to walk, and were more likely to sway while walking, compared to age-matched, cognitively-healthy controls (Visser, 1983). These findings were furthered by recent studies which have reported that individuals suffering from AD demonstrate greater sway velocity and reduced sway control when compared to cognitively-healthy controls (Sant’Anna et al., 2019). A meta-analysis of postural stability papers suggested that AD patients demonstrated reduced postural stability while standing and walking compared to cognitively-healthy controls (Mesbah, 2019). This review has also highlighted the relationship between posture as well as postural stability and cognitive functioning: Szturm et al. (2013) conducted a study where twenty cognitively-healthy a visuospatial cognitive task in standing conditions, and while walking on a treadmill. Findings reported a significant decrease in cognitive performance on the visuospatial task while walking compared to sitting (Szturm et al., 2013).

Following this, Smith et al. (2019) assessed the relationship between posture and selective visual attention. A study was conducted wherein fourteen participants completed a Stroop task, a task-switching trial, and a visual search task while sitting and standing. Findings reported that Stroop interference was significantly reduced in the standing compared to sitting. Furthermore, when participants were sitting, a greater reduction in accuracy occurred when switching tasks compared to the standing group. Finally, completion of the visual search task was slower for the standing group compared to the sitting group (Smith et al., 2019). There appears to be a relationship between balance, posture, and cognitive functioning worth exploring further. If this relationship can be replicated within cognitively-healthy populations, it may hold implications for assessing balance and posture in clinical contexts. See below for Table 2 which highlights the benefits and limitations of the non-invasive methods which could be used in a diagnosis of Dementia:

Table 2 The Benefits and Limitations of the Areas around Non-Invasive Dementia Research

Research Area	Benefits	Limitations
Neuropsychological Functioning	• Can test a wide variety of factors relating to dementia • Can demonstrate a causal effect • Some tests are sensitive • Can generate meaningful data without being invasive • Provides groundwork to build research • Results can be giving to the participant almost immediately	• A wide battery of tests are needed to generate a reasonable assessment of cognitive functioning • Tend to be ethnocentric • Many rely on language ability • Some are standardised; therefore, individuals can learn the tests
Hearing Loss	• Suggests clinical applications • Clinical applications can be implemented easily • An easy concept to understand for the layman	• Cannot be used to diagnose dementia alone • Only correlations have been found • Tests will require training to administer
Language Production	• Data is easy to analyse • Provides meaningful data without being invasive • Tests can be easily adapted for clinical use • Information from these studies can be used as a warning sign of dementia to the public	• Judging the words that participants used is interpretative • Substantially harder to test in earlier stages of dementia • Cannot be used alone to diagnose dementia • Tests require training to administer
Facial Expressions	• Has been witnessed in the earlier stages of dementia • Provides meaningful data non-invasively • Has potential to be used clinically • Depending on the measure used, can be an inexpensive test	• Contradictory findings have been abundant • Require specialist training to implement the testing • Requires software knowledge to interpret some of the data • Cannot be used alone to diagnose dementia
Balance and Posture	• Previous research has established a strong connection between postural stability and dementia • Has been witnessed in MCI • Is easily testable with the appropriate equipment • Non-invasive methodology	• There are ethical concerns with standing an individual with dementia on an elevated platform, do to risk of falling • More research is required to generate normative daa and assess whether this relationship can be witnessed within cognitively-healthy populations

3.5 Discussion

This article was designed to be a comprehensive review into the non-invasive ways in which dementia could potentially be diagnosed. What follows is a discussion of each of these areas, with a focus on how readily each feature of dementia could be implemented in a clinical capacity.

3.5.1 Neuropsychological Functioning

Testing neuropsychological function is fundamental to the development of clinical assessments of dementia. The clinical assessments for dementia that are already in wide use tend to be short assessments used to generate a score which indicates levels of cognitive functioning. This result is then used as a deciding factor in diagnosis of a cognitive impairment. The MMSE is widely used; however, the MMSE is overly reliant on language ability (Devenney and Hodges, 2017). In response to the over-dependence on language in the MMSE, the Rowland Universal Dementia Assessment Scale (RUDAS) was produced (Rowland et al., 2006). The RUDAS has been found to compare favourably against the MMSE without the dependence on education level or language ability (García-Rodríguez et al., 2009). The RUDAS requires patients to remember words, draw shapes, and perform actions. However, further research should be conducted before the RUDAS could be incorporated into standard clinical practice. This assessment could be computerised using recognition technology to assess whether the patient was performing the appropriate actions, or remembering words, thereby improving the efficiency of this assessment.

Whilst there has been interest in the MMSE and the Mini-Cog, the CANTAB battery has been universally found to be reasonably accurate, reliable and sensitive tool for the detection and diagnosis of dementia (Sahakian et al., 1988; Sahakian and Owen, 1992; Égerházi et al., 2007; Blackwell et al., 2004; Junkkila et al., 2012). Furthermore, it has been estimated that using the CANTAB battery in a clinical environment will cost 40% of the average price for diagnosing a patient (Housden et al., 2014). However, the cost of treatments for false positives that may be more prevalent for a lower-cost but less accurate test should be considered. Other research has concluded that using the CANTAB battery to assess visuospatial learning and memory holds potential diagnostic value for dementia (Blackwell et al., 2005).

Given the aim of this chapter is to identify potential areas of diagnostic interest relating to dementia, considerations must also be made into how readily the discussed criteria may be implemented into clinical practise. Neuropsychological assessments are already routinely used in the diagnostic process for dementia, therefore their implementation appears should be relatively painless. However, it is worth considering which neuropsychological assessments should be implemented.

One point which seems to have emerged from research into assessments of neuropsychological functioning is that the MMSE is largely derided in research papers; with authors citing the lack of reliability, accuracy, and over-reliance on language (Devenney and Hodges, 2017). This may go some way towards explaining why the MMSE is no longer recommended by NICE guidelines, instead recommending incorporating the Mini-Cog into a short screening process for dementia (NICE, 2018).

The Mini-Cog is not without limitations, however. Firstly, there is a limited number of studies which analyse the accuracy of utilising the Mini-Cog as a diagnostic tool for dementia in primary care settings (Seitz et al., 2018). Moreover, in a longitudinal study of cognitive impairment involving 581 participants over a six-month period, Carnero-Pardo et al. (2022) reported that the Mini-Cog was diagnostically useful in predicting cognitive decline. However, it was noted that the Mini-Cog was less reliable for individuals with lower levels of education and was deemed to be an inappropriate tool for assessing such individuals (Carnero-Pardo et al., 2022). The reliance on education which has been witnessed in the Mini-Cog further highlights the necessity for a diagnostic tool which avoids common pitfalls of paper-based neuropsychological assessments

Another point to consider is that none of the reviewed neuropsychological functions are exclusively affected by dementia. A stroke or brain tumours, for example, share some symptoms with dementia (Marshall, 2018). Therefore, tests of neuropsychological functioning should not be used to diagnose dementia alone. Furthermore, there are other external factors which should be considered when assessing neuropsychological functioning. Walters and Lesk (2015) conducted a study assessing the influence of the ToD and caffeine intake on older adult participants taking a battery of neuropsychological tests. It was found that test scores declined as ToD increased. Further findings indicated a significant interaction between caffeine intake, ToD and test scores. These results were furthered by Walters and Lesk (2016), who conducted a double-blind placebo vs. caffeine study on a group of healthy older adult participants. It was found that there was a significant interaction between age, caffeine, and scores on executive functioning and processing speed; the caffeine subgroup showed a decline in performance with increasing age (Walters and Lesk, 2016). This was an effect that was not seen in the placebo group. It was concluded that factors such as caffeine intake and ToD need to be considered when administering neuropsychological tests to older adults (Walters and Lesk, 2016).

3.5.2 Hearing Loss

The research from Uhlmann et al. (1989) into the relationship between hearing loss and dementia was explored here because of the potential applications for diagnosis of a cognitive impairment. Support for Uhlmann et al. (1989) comes from Lin et al. (2011), who conducted a longitudinal study on 639 individuals between the ages of thirty-six and ninety who were cognitively-healthy. They tested for hearing ability and cognitive functioning. Lin et al. (2011) returned 11.9 years later to re-test the participants, finding that the level of hearing loss positively correlated with a diagnosis of dementia. It could be argued that the samples used in these studies were from a concentrated area, and have issues of ethnocentricity when applied worldwide. However, a second piece of research from Lin (2011) shows that the same relationship between hearing loss and dementia can be seen even with a representative sample of the entirety of the United States. More research should be conducted utilising more diverse participant populations before the relationship between hearing loss and dementia can be witnessed from the perspective of a global population.

The final piece of supporting evidence for this relationship comes from Wong et al. (2014) who furthered the previous research by assessing how participants with appropriately fitted hearing aids perform on tests of cognitive function. In the case of thirty-four older hearing aid users, it was found that even with hearing-aid technology, participants suffering from hearing loss still performed significantly worse on the MMSE than healthy controls. These results seem to suggest that chronic hearing loss is related to cognitive impairment.

Given the limitations of the MMSE as discussed in section 3.5.1, most notably that NICE guidelines no longer recommend the use of the MMSE (NICE, 2018), further research may wish to consider exploring the relationship between hearing loss and cognition on separate neuropsychological assessments, such as the Mini-Cog.

One methodological issue to consider with all the reviewed literature in this area is that, as far as we are aware, none of the studies seem to consider the cause of hearing loss. Although the main cause of hearing loss in older adults is natural aging (NHS Choices, 2018), there are many other causes which can accelerate this process such as head injury, stroke, multiple sclerosis, or genetic factors (NHS Choices, 2018). Furthermore, the reviewed research does not currently consider whether the hearing loss reported by the participants was chronic or acute hearing loss. This should be the subject to future research.

Finally, considerations should be made regarding the feasibility of implementing hearing assessments into the process of achieving a dementia diagnosis. A first impression might suggest this should be a relatively simple inclusion, as hearing tests are already available through the NHS (Maidment et al., 2022). However, it is worth considering that audiologists are their own specialisation, therefore implementing hearing assessments into the process of achieving a dementia diagnosis may require the need of multiple specialists, which could complicate the procedure.

3.5.3 Language Production

Regarding the diagnostic value of language production as a test for dementia, the reviewed literature presents several discussion points. Firstly, it was witnessed that the language ability of individuals who have been diagnosed with dementia diminishes, regardless of age (Kemper et al., 2001). However, there is an issue that language production also worsens in natural aging (Kemper et al., 2001). This means that the older an individual, the more difficult it would be to identify deficits in language production for diagnostic purposes. Although individuals with dementia show impaired grammatical complexity and prepositional context, this is also seen in natural aging (Kemper et al., 2001).

Another area of consideration would be to consider speech impediments, such as a lisp or a stutter. These factors may potentially complicate the process of a language assessment. Currently, tens of millions of people around the world are living with a speech impediment, making them exceedingly common (Kourkounakis et al., 2020). Given this number, further research should be conducted in order to explore whether a speech impediment may confound the results generated in assessments of the relationship between cognitive functioning and language production.

Moreover, given that dementia is more likely to impact older adults, removable dentures may also have to be considered during assessments of language production. Previous research has reported that individuals who have previously has removable dentures installed in the previous two-week period demonstrated distinctly different pitch and sounds than after a two-week adaption period (Hussein and Hristov., 2020). This demonstrates that there are multiple factors to consider during an assessment of language production which must all be taken into account during the diagnostic process of dementia.

Another point to consider is that there are other causes of language production and speech impairments. These include Broca's and Wernicke's aphasia (Davis, 2007) or stroke (NHS Choices, 2015). Going forward, it would be worth considering advancements in speech recognition technology using deep learning computers for a potential role in the diagnosis of dementia. A recent meta-analysis has reported promising advancements in the abilities of deep learning computers to recognise speech (Latif et al., 2020). However, at time of writing, there is little to no research regarding the utilisation of deep learning technology for speech recognition in a diagnostic capacity.

Regarding the feasibility of implementing an assessment of language production into clinical practice, it appears that there are many factors which are currently unknown, such as aphasias or speech impediments which may influence the outcome of a language production assessment. More research is required into these areas before certain statements can be claimed on the efficacy of a language production assessment in a dementia diagnosis.

3.5.4 Facial Expressions

Research into how dementia affects an individual's ability to produce and recognise facial expressions was explored. It was found that participants suffering from dementia struggled with both demonstrating and recognising facial expressions, except for negative emotions, such as sadness and fear (Asplund et al., 1991; Blackwell et al., 2005). However, these results were contradicted by Blackwell et al. (2005) who concluded that participants suffering from dementia were less likely to recognise any facial expressions including sadness and fear. Further contradictions were noted by Guaita et al. (2009) who found that participants suffering from dementia were no worse at recognising facial expressions than healthy controls (Guaita et al., 2009). To consider why these inconsistencies are seen, it is worth considering the methodology employed by each researcher respectively.

Comparing the methodology of Asplund et al. (1991) against Seidl et al. (2008), there are clear differences. Asplund et al. (1991) focussed on participants who were in stage seven of AD (one of the final stages), whereas Seidl et al. (2008) focussed on fifty-eight participants with a range of cognitive impairments, from MCI to severe dementia. This may well explain the differences in the two studies. Furthermore, Asplund et al. (1991) used only four participants, all of whom were female. This presents difficulty in generalising the findings to the wider population. Whereas Asplund et al. (1995) utilised an even split of four male and female participants, showing no apparent gender effects.

Dementia has also been found to effect recognition of the facial expressions of others. Again, findings in this area showed contradiction. Some research has found that individuals suffering from dementia performed significantly worse than controls at recognising the facial expressions shown by others (García-Rodríguez et al., 2009; Carvalho et al., 2014), whereas other research showed that participants suffering from dementia were no poorer than controls at judging facial expressions (Guaita et al., 2012). Once again, the methodologies of these studies can be assessed to identify why these results are contradictory.

Firstly, in the study that found that participants suffering from dementia were not significantly different from controls at recognising facial expressions, Guatia et al. (2012), recruited seventy-nine individuals suffering from moderate to severe AD, as opposed to García-Rodríguez et al. (2012) and Carvalho et al. (2014) where the participants were considered as having 'probable dementia'. Furthermore, in each of these experiments, participants were shown a collection of faces demonstrating various emotional expressions, and participants were asked to identify the emotion based on the facial features. In the García-Rodríguez et al. (2012) study, participants were given a multiple-choice information sheet which listed which emotions were going to be shown. There was a similar scenario with Carvalho et al. (2014) as when participants were asked to identify the emotion they were looking at; they were presented with options as to what the correct answer might be. This was not the case for Guatia et al. (2012) where a multiple-choice option was not present, and participants were asked to guess which emotion they were being presented with. The study of Guatia et al. (2012) could be considered harder on their participants, resulting in poorer performance.

Another reason for the findings of García-Rodríguez et al. (2012) to be contradictory to those of Guatia et al. (2012) could be due to a distraction task used in the study by García-Rodríguez et al. (2012). This distraction task involved the participants watching a sequence of patterns on a screen while they were assessing the facial expressions. Also, they were given a time limit to look at the picture, which was not present in the other experiments. However, the result found by Carvalho et al. (2014) supported the results of García-Rodríguez et al. (2012) without the use of a distraction test. Carvalho et al. (2014) found the most sensitive test for identifying whether cognitive decline was due to natural aging or dementia was the Gandra-BARTA. This is an emotional recognition assessment which tasks individuals with looking at fifty-nine colour photographs of universally recognised emotions (fear, disgust, anger, happiness sadness and surprise). Participants were tasked with identifying the facial expression present in the photograph. However, there are limited research articles on Gandra-BARTA.

Future research into the relationship between facial expressions and dementia should consider utilising computerised deep learning. A recent study has found that deep learning technology utilising neural networks has good recognition accuracy in facial expression recognition and has certain advantages in small sample problems (Liu et al., 2020).

Finally, considerations must be made regarding the feasibility of implementing assessments of facial expressions into diagnostic contexts. The first area to consider is ethical questions regarding the recording of an individual's face, particularly individuals with dementia if video recordings are to be utilised. The way in which these recordings are made, stored, and shared is of paramount importance for the privacy of the individual. If it becomes the case that the consenting individual is diagnosed with dementia, this may complicate matters further.

More than ethical concerns, there are multiple external factors which may influence an individual's facial expressions during the diagnostic process. For example, if an individual is in a bad mood this may result in them demonstrating a greater proportion of negative facial expressions, which may in turn influence the results of a facial expression assessment. Also, we must consider individuals who have suffered a stroke and therefore may present altered facial expressions. Further research into the relationship between facial expressions and dementia is warranted in order to understand the potential benefits and limitations of analysing facial expressions in the diagnostic process for dementia.

3.5.5 Balance and Posture

Regarding the utilisation of balance and posture as diagnostic tools, the previous literature reported a series of findings which pointed to a correlation between poor postural stability, and poor cognitive functioning (Visser 1983; Sant'Anna et al., 2019; Mesbah, 2019). However, from the reviewed literature, it was unclear whether this relationship exists within healthy populations. Research is necessary to assess whether this relationship is witnessable within healthy populations, and if it is, there may be cause to pursue balance and posture assessments in dementia screenings in order to develop additional assessment criteria which is non-invasive and not language dependant. The closest research which has generated normative data was the research of Szturm et al. (2013) who reported findings that participants performed significantly worse on a visuospatial task while walking compared to sitting (Szturm et al., 2013). These findings demonstrate that external factors manipulating posture can influence performance on cognitive tasks. However, it is unclear whether an intrinsic relationship exists between a participant's innate postural stability and cognitive functioning. See Chapters Five and Six for a pair of studies investigating the relationship between postural stability, posture, and cognitive functioning in order to ascertain the applicability of assessing postural stability in dementia screenings.

This unclear relationship between balance and cognition makes it difficult to speculate on the feasibility of implementing balance assessments in the diagnostic process for dementia. If a relationship is established wherein poorer balance is related to poorer cognitive ability, this may be useful to implement into the diagnostic process, however this would not come without considerations.

The first consideration to make if a balance assessment is to be utilised in the diagnostic process for dementia is one of ethics. If a diagnosis of dementia is achieved it may have been unethical to have had that individual stand on an elevated platform in potentially compromising positions where they could be likely to fall. This issue could be offset by the use of hand supports, though the use of these could potentially void the balance data.

Given advancements in technology, it may be the case that this method of assessment is ethically appropriate only when balance platforms are developed which are flush against the floor, thus providing no additional elevation. Theoretically, it is already possible to build a Force Platform (FP) which measures balance into the floor, however this would likely incur a great monetary cost, and would make it difficult to update later to improved hardware later, as a new FP of the exact same diameter would be required.

Ultimately, the points raised above are speculative. More research is necessary into the relationship between balance and cognitive functioning before statements may be made on the feasibility of integrating a balance assessment into the diagnostic process for dementia.

3.6 Conclusion

This review has investigated the current state of the art in the non-invasive tools used for diagnosing dementia, with a focus on identifying potential applications of these tools for use in a clinical environment. It seems that, when used alone, none of the reviewed techniques can currently be used to diagnose dementia reliably and accurately. However, it is apparent that the CANTAB would be an improvement over the MMSE. However, with the CANTAB still being comparatively new, it will most likely need further research before it is considered valid and reliable enough to integrate into common clinical practice. Although, the idea of a technology based, computerised assessment for dementia has the potential to save both time and money in the future.

It would be difficult to recommend language production as a method of diagnosis for dementia at this stage. This review aims to explore the diagnostic value in these relationships; as such, the fact that an individual's language ability diminishes in natural aging as well as in dementia presents a complication with establishing a direct causal link between language production and dementia. These complications may be overcome with the integration of deep learning technologies into clinical analyses. However, further research is required before this could be stated for certain.

It is the opinion of the researchers that the role of facial expressions as a diagnostic tool for dementia is yet to be fully realised. As technology advances, the capability to track specific facial cues, such as blink rates or pupil dilation, is becoming ever more precise and readily available to the public. At present, the contradicting results highlighted by this article mean that more research should be conducted to settle the science on facial expressions and their relationship to dementia before they should be considered as a potential diagnostic tool for dementia. In the future, however, facial recognition technology which utilises deep learning could potentially open new avenues for exploration in this domain.

Based on the techniques reviewed here, there is potential for hearing loss to be integrated into a clinical diagnostic tool for dementia; however, this research is still in its infancy. Lin et al. (2011) and Lin (2011) concur that more research has to be conducted regarding how hearing loss interacts with dementia in the pre-diagnostic stages before we can consider using it in a clinical environment. More research should be conducted into the sensitivity, accuracy, and reliability of the Gandra-BARTA (Guaita et al., 2012), as initial results show potential for this method to be developed into a more robust assessment for dementia.

Non-invasive diagnoses remain an important area of research as limitations with invasive methods include the cost and discomfort to patients; whereas non-invasive diagnoses can be standardised assessments which make the diagnostic process faster and more affordable. However more research needs to focus on accuracy and reliability of any diagnostic paradigm.

3.7 Chapter Summary

This chapter has discussed the importance of an early diagnosis of dementia, while highlighting some of the difficulties involved in achieving such. This chapter has also introduced the currently utilised methodologies for generating a diagnosis for dementia. Following this, this chapter reported a meta-analysis of factors which have been found to be related to dementia, but as of yet have not found use in clinical contexts. This chapter highlights the feasibility and applicability of utilising these factors in order to generate or strengthen a diagnosis of dementia. The following chapter will contextualise the importance of an early and accurate diagnosis of dementia further by exploring the treatment options for dementia, both pharmacological and non-pharmacological, which may be offered to the individual who has received the dementia diagnosis.

3.8 Highlights

- A true diagnosis of AD cannot be achieved until post-mortem (Mosconi et al., 2008).
- It is difficult to discriminate between cognitive decline due to normal aging, or due to pathological abnormalities (Hedden and Gabrieli, 2004; Petersen, 2011).
- The MMSE is most used method of diagnosing dementia (Scheffels et al., 2020). Though, some researchers argue that the MMSE should be retired due to issues with reliability, validity, and ethnocentricity (Carnero-Pardo, 2014).
- The RUDAS has been found to compare favourably against the MMSE without the dependence on education level or language ability (García-Rodríguez et al., 2009).
- the CANTAB battery has been universally found to be reasonably accurate, reliable and sensitive tool for the detection and diagnosis of dementia (Sahakian et al., 1988; Sahakian and Owen, 1992; Égerházi et al., 2007; Blackwell et al., 2004; Junkkila et al., 2012).
- Hearing loss is positively correlated with a diagnosis of dementia (Lin et al., 2011), but more research is necessary before this can be proposed as assessment criteria for dementia.
- Language ability of individuals who have been diagnosed with dementia diminishes regardless of age (Kemper et al., 2001), meaning it is difficult to differentiate between normal aging and dementia. This makes language production difficult to propose as additional assessment criteria for dementia.
- Individuals with dementia struggled with both demonstrating and recognising facial expressions (Asplund et al., 1991; Blackwell et al., 2005). However other studies contradicted this (Blackwell et al., 2005).
- Before facial expressions can be considered as a diagnostic tool for dementia, future research should consider utilising learning technologies in order to see whether improvements in technologies reveal previously unseen relationships.
- Previous literature reported a relationship between poor postural stability, and poor cognitive functioning (Visser 1983; Sant'Anna et al., 2019; Mesbah, 2019). However, these results have not been assessed in cognitively-healthy populations. This should be a target of future studies before postural stability can be considered for use as a dementia screening tool.
- It is concluded that there is no single diagnostic tool that is universally effective at diagnosing all kinds of dementia equally.

Chapter Four

Pharmacological and Therapeutic Interventions for Dementia

4.1 Introduction

The previous chapter (Chapter Three) discussed currently used, and potential diagnostic tools for dementia, highlighting several promising areas of consideration. This present chapter will talk about treatments that dementia patients can expect, once a diagnosis is achieved, as dementia interventions and are fundamental building blocks of dementia strategies and policies at both national levels, as we as globally (Reilly et al., 2020). While it is the case that this thesis is concerned with non-invasive techniques for the detection and diagnosis of dementia rather than the treatment of dementia, treatments are explored in in this chapter in order to contextualise why achieving accurate diagnoses is paramount to the wellbeing of patients. This chapter intends to explore the relationship between diagnosis and treatment, commenting on the differing methods, their strengths, and their limitations.

Prior to any deliberation on the treatments for the dementias, it would be appropriate at this juncture to reiterate that dementia has no known cure (Singh-Manoux and Kivimalki 2010). As such, treatments for this illness are not curative, rather aiming to secure a higher quality of life for patients for as long as feasible. What follows is an exploration of the different methods of treating dementia which are used in common practise, starting with the pharmacological treatments, then moving onto non-pharmacological methods. The findings will then be drawn together in a conclusion.

4.2 Pharmacological Treatments

This chapter will begin by considering the pharmacological treatments for dementia. The pharmacological treatment of dementia is complicated due in part to the different types of dementia which, although displaying similar symptoms, may have differing root causes (Sink et al., 2005). This section explores both typical and atypical pharmacological interventions for dementia. their efficacy, benefits and limitations are explored by drawing from existing literature.

4.2.1 Acetyl-cholinesterase-inhibitors

The most common typical pharmacological intervention for dementia is a course of AChEIs, such as Aricept (Donepezil), or Galantamine (Knight et al., 2018). The function of these drugs is to increase the levels of the neurotransmitter acetylcholine in the body by inhibiting the enzyme which breaks it down (Mohammad et al., 2017). AChEI treatment is used due to findings that cholinergic dysfunction is associated with neuropsychiatric and functional deficits found in dementia (Trinh et al., 2003). However, research on the efficacy of AChEIs has yielded mixed results. Sink et al. (2005) conducted a meta-analysis on the pharmacological treatments for the neuropsychotic symptoms of dementia, reporting on eight studies (two of were meta-analyses themselves), they found that five of the eight studies reported statistically significant benefit from AChEIs (Sink et al., 2005). However, other findings report that a twenty-four or thirty-two milligram dose of galantamine held no benefit over a placebo (Rockwood et al., 2001), with Tariot et al. (2000) finding similar results except for the finding that a 16mg dose of galantamine did perform favourably against a placebo (Tariot et al., 2000).

More recent research into AChEIs comes in the form of a meta-analysis conducted by Knight et al. (2018). In this meta-analysis, eight studies were analysed to assess the clinical effectiveness of AChEIs under different conditions. They reported findings that after six-months of treatment, AChEI groups produced significantly better scores on the MMSE (Knight et al., 2018). Moreover, it was reported that AChEI treatment patients performed twice as well on the MMSE as controls in the case of patients suffering from Parkinson disease dementia and dementia with Lewy bodies (DLB), whereas for AD patients, only moderate effects were witnessed (Knight et al., 2018). With AChEIs being the most commonly prescribed pharmacological intervention for dementia (Knight et al., 2018), an early and accurate diagnosis of the correct dementia subtype would hold meaningful implications over the expected efficacy of the treatment course, after the reported findings that different dementia subtypes will influence the treatment efficacy (Knight et al., 2018). This contextualises the importance of an early and accurate diagnosis of not only dementia, but also the correct subtype of dementia.

4.2.2 Memantine Hydrochloride

The next pharmacological treatment for dementia to discuss is Memantine Hydrochloride (MH). MH belongs to a drug group known as N-methyl-D-aspartate (NMDA) receptor antagonists (Ivleva and Klimochkin, 2017). In AD, which is the most common form of dementia (Lee et al., 2017), a larger proportion of glutamate leaks from neurones, leading to more interaction with NMDA receptors. A concentration of glutamate this high in the nerve cells is toxic, causing the degeneration of the nerve cells (Busse et al., 2018). MH is used in this situation to reduce the amount of glutamate interacting with the NMDA receptors which reduces toxicity, while normalising the transition of glutamate between cells, and in turn slowing the decline of memory and cognition in AD (Ivleva and Klimochkin, 2017).

Research into the efficacy of MH has yielded promising results. In a meta-analysis on the efficacy of MH, Peng et al. (2013) reported that the drug was a ‘simple and safe’ pharmacological option when a diagnosis of a specific dementia subtype proves difficult (Peng et al., 2013). Furthermore, in their review, Peng et al. (2013) reported that MH shows to reduce the rate of cognitive decline in AD, Frontotemporal Dementia, DLB, Parkinson’s disease dementia, and Vascular dementia; although it should be noted that this was witnessed in various cognitive tests for differing dementia subtypes. Another strength of MH is that it can be safely used alongside other treatment drugs such as Donepezil as it does not inhibit the process of the AChEIs (Calhoun et al., 2018). Given the discussion in section 4.1.1 about the efficacy of AChEIs relative to dementia subtypes, this further demonstrates the need for an early and accurate diagnosis of dementia. If the dementia subtype is diagnosed as AD, for example, previous research has shown AChEIs to only have a moderate efficacy as a treatment (Knight et al., 2018). This in turn provides a stronger justification for prescribing the use of both AChEIs and MH in tandem, as an earlier prescription of the appropriate treatment will aid in ensuring the greatest quality of life for the patient for as long as possible.

4.2.3 Antipsychotics

The next pharmacological treatment for dementia to consider are typical and atypical antipsychotics. Antipsychotic medication is used to manage the behavioural and psychological symptoms of dementia (BPSD) (Sangani and Saadabadi 2017). Antipsychotics such as aripiprazole, olanzapine, quetiapine, or risperidone (Yunusa et al., 2021) function as dopamine blockers in the central nervous system, creating a sedating effect (Sangani and Saadabadi 2017). Previously, however, the safety of using antipsychotic medication on older adults has been called into question after research showed that the risk of death in older adults increases significantly in-line with this method of treatment (Sultana et al., 2019).

There are two forms of antipsychotic medication for dementia, known as typical and atypical (Ameer and Saadabadi, 2020). Regarding the efficacy of typical antipsychotic medication in dementia, finding literature which assesses specifically typical antipsychotics are both older and hard to find however two meta-analyses on typical antipsychotics were reviewed (Lonergran et al., 2002; Schneider et al., 1990). The specific drugs reviewed in these papers were Haloperidol, Thioridazine, Thiothixene, and Chloropromazine. Results were fairly poor, as it was shown that only eighteen out of 100 patients showed benefit beyond a placebo effect from neuroleptic drugs (Schneider et al., 1990). Furthermore, results of poor efficacy were seen regardless of the antipsychotic drug that was trialed. There is no clear evidence that typical antipsychotics hold any benefit toward the neuropsychological symptoms of dementia (Lonergran et al., 2002).

Atypical antipsychotics have produced more promising results. The difference between typical and atypical antipsychotics is that typical antipsychotics act on the dopaminergic systems, whereas atypical antipsychotics act on the serotoninergic systems (Dazzan et al., 2005). Atypical antipsychotics tend to be of a greater potency than their typical counterparts, and include Clozapine, Olanzapine, Risperidone, Quetiapine, Ziprasidone, and Aripiprazole (Yunusa et al., 2019).

Research into atypical antipsychotics has yielded more promising results than their typical counterparts, as in a meta-analysis, Sink et al. (2005) reported that in an analysis of six studies, Olanzapine and Risperidone showed benefits in the treatment of neuropsychiatric symptoms of dementia. They reported that of all the reviewed antipsychotics, a five-10mg dose of Olanzapine was at least modestly effective at treating the neuropsychiatric symptoms of dementia. Lee et al. (2004) argues that while atypical antipsychotics are being used more frequently to treat the neuropsychiatric symptoms of dementia, there is a separate domain that is equally important, and rarely assessed in pharmacological treatments of dementia. These symptoms are commonly referred to as BPSD. Recently there has been an impetus to treat BPSD in non-pharmacological frameworks (Livingston et al., 2017).

In recent years, meta-analyses have been conducted to assess the efficacy of the us of antipsychotics in dementia treatments. Tampi et al. (2016) identified sixteen meta-analyses that evaluated the use of antipsychotics in individuals suffering from dementia. Of these, 12 discussed the efficacy of treating dementia with antipsychotics. Of these 12, eight also studied the adverse effects of antipsychotic treatment. From this meta-analysis, it was ascertained that antipsychotics offer modest efficacy in treating symptoms such as psychosis, aggression and agitation in individuals suffering from dementia. However, their utility in treating dementia was offset by the potential of adverse side-effects, including death (Tampi et al., 2016). Therefore, it was concluded that antipsychotics should only be prescribed in the case of an individual failing to respond adequately to therapeutic interventions (Tampi et al., 2016).

A more recent meta-analysis from Yunusa et al. (2019) who specifically assessed the efficacy of atypical antipsychotics. In a meta-analysis of seventeen studies, it was found that there exists a trade-off between the more effective atypical antipsychotics and the increased likelihood of adverse side effects (Yunusa et al., 2019). This research concludes by asserting that there is insufficient evidence on which atypical antipsychotic is both the safest and most beneficial for the individual suffering from dementia, which warrants further investigation (Yunusa et al., 2019).

Finally, a recent study was conducted in Spain by Manzano-Palomo et al. (2020) who assessed the efficacy of antipsychotic medication in relieving the BPSD. In this study, 162 specialists (seventy-one psychiatrists, sixty neurologists, twenty-seven geriatricians, two psychogeriatricians, and two in internal medicine) were asked to fill in a 76-item questionnaire about the perceived effectiveness of antipsychotics in tacking BPSD. It was found that specialists strongly agreed that atypical antipsychotics were both safer and better tolerated than typical antipsychotics, and that the atypical antipsychotics should be more readily available to the patient (Manzano-Palomo et al., 2020). Given how recent research justifies the efficacy of antipsychotic medication in relieving the BPSD in dementia patients (Manzano-Palomo et al., 2020), this provides an impetus to achieve an early and accurate diagnosis of dementia, as there would be potential to begin a course of treatment sooner, resulting in earlier relief from the BPSD.

4.2.4 Antidepressants

The next form of pharmacological intervention for dementia is antidepressants. Antidepressants which can be used to treat dementia are typically serotonergic drugs (such as Sertaline, Fluoxetine, Citalopram and Trazodone), that is to say they are used to regulate the levels of the neurotransmitter serotonin (Quentin et al., 2018). The efficacy of these drugs, however, has shown to be lacking. Sink et al. (2005) conducted a meta-analysis on the efficacy of serotonergic antidepressants, finding that only the trial of Citalopram showed any benefit to the patient. They also reported findings that due to the lack of efficacy, there was a large drop-out rate for several of these studies. It was concluded that although there was a high tolerance rating for serotonergic antidepressants, they do not appear to hold any benefit for the treatment of the neuropsychological symptoms of dementia (Sink et al., 2005). Six studies were reviewed on the efficacy of serotonergic antidepressants as pharmacological interventions for dementia. Of the six studies reviewed, only the trial of Citalopram found to be of benefit (Sink et al., 2005). More recently, though, the use of treating dementia with anti-depressants has been questioned, as it has been reported that some anticholinergic anti-depressants can raise the risk of developing dementia (Alzheimer’s Association, 2018).

4.2.5 Aducanumab

Recently, the United States Food and Drug Association (FDA) has approved the use of aducanumab for the treatment of AD in the USA; this is the first time that a drug which modifies AD has been approved (Alzheimer's Society 2021). Aducanumab is an antibody which binds to, and dissolves amyloid β fibrils (Schneider, 2020). An early phase trial into the efficacy of aducanumab was conducted on 165 individuals with prodromal or mild AD (Schneider, 2020). In this trail participants received monthly intravenous doses of either 1mg, 3mg, 6mg, or 10mg of aducanumab. The results of this trial found that aducanumab significantly reduced amyloid β levels, and that half of participants who received the 10mg dose no longer had positive amyloid PET scans after a 12-month period (Schneider, 2020). While these findings appear to be promising, there is a controversy surrounding whether the reduction of AB plaques protects patients against cognitive and functional decline (Walsh et al., 2021). Two phase-three trials for the use of aducanumab were cancelled prior to the study closing due to a lower than 20% chance of the trials returning a positive finding, with the studies being regarded as "futile" (US Food and Drug Administration 2020). When the data were analysed, one of these trials reported no cognitive benefit of aducanumab, whereas the other trial reported that there were cognitive benefits (Walsh et al., 2021). However, further analysis found that there was a high likelihood that if the trials were completed, the results would have averaged out to show aducanumab was ineffective at protecting against cognitive and functional decline (Alexander et al., 2021).

An independent advisory committee for the FDA voted almost unanimously against approval of aducanumab for treating AD, due to a lack of efficacy (Mahase, 2021). The approval of aducanumab against the wishes of the advisory committee resulted in the resignation of three members who described the situation as “the worst drug approval decision in US history” (Mahase, 2021). While aducanumab may show promising results in the future, the efficacy of this pharmacological intervention is unclear at the current time. However, if in future aducanumab is found to be effective at protecting AD patients against cognitive decline, this further demonstrates the important of receiving an early diagnosis, as if AD is diagnosed sooner, the treatment can protect the patient for longer, thus improving quality of life.

As time has progressed, an increasing number of therapeutic interventions for dementia have become prevalent. The following section of this chapter discusses these therapeutic interventions, with regards to how they are administered and their efficacy at relieving BPSD.

4.3 Therapeutic Interventions

Due to the prevalence of treatment drugs in modern society, one would be forgiven for thinking ‘treatment’ and ‘drugs’ are synonymous. However, pharmacological interventions for dementia are increasingly being considered as a ‘second-line approach’ to treatment in lieu of therapeutic interventions (Nagata et al., 2020). Clinical guidelines bolster this statement by asserting that ‘good clinical practice’ would entail pharmacological interventions for dementia being used only after therapeutic interventions were deemed ineffective (Howard et al., 2001; Tampi, et al., 2016). These conclusions could likely have been drawn from findings that, in clinical trials, the efficacy of dementia treatment drugs was modest at best, with frequently high placebo response rates being witnessed (Yunusa et al., 2019). This paradigm-shift away from relying on medication as a first response could arguably be due in part to the International Psychogeriactric Association coining the expression BPSD (Finkel and Costa, 1996). The BPSD include delusions, hallucinations, agitation, aggression, depression, dysphoria, anxiety, elation, euphoria, apathy, indifference, disinhibition, irritability, lability, and aberrant motor behaviour (Mukherjee et al., 2017). This section intends to explore therapeutic interventions for dementia treatment which are concerned with BPSD, discussing their benefits and limitations, while reflecting on their place in the overall discourse of dementia treatments.

4.3.1 Reality Orientation Therapy

The first therapeutic intervention for dementia considered in this section is Reality Orientation Therapy (ROT). ROT was originally described as a technique to improve the quality of life for confused older adults (Taulbee and Folsom 1966) and has become a widely used management strategy for coping with dementia patients (Berg-Weger and Stuart, 2017). This therapy aims to aid dementia patients who are suffering from memory loss and disorientation by placing them in an environment which they can orient themselves to, while participating in games and activities to facilitate the presentation of personal and current information to the individual (Berg-Weger and Stuart, 2017). This procedure is conducted using props such as signposts and notices as memory aids (Kumar et al., 2019). Alternatively, 'Classroom' ROT sessions can be conducted in groups wherein 'orientation activities' typically display information such as the day, date, weather, their next meal, and their current location (Hanley, 2018).

A meta-analysis regarding the efficacy of ROT returned unclear results (Chiu et al., 2018). This study analysed eleven studies regarding the efficacy of ROT. It was reported from these analyses that all papers returned findings which suggested that ROT improved cognitive functioning in individuals with dementia. However, five studies reported that ROT did not ameliorate behavioural problems, and five also reported ROT held no influence over depressive symptoms (Chiu et al., 2018). However, other research has been less positive with the findings that ROT may remind patients of their disorientation, leading to further confusion (Webb, 2020). With Maki et al. (2018) reporting a lowering mood and increased anxiety in the individuals attending ROT sessions.

Furthermore, a recent meta-analysis of ten studies conducted by Carrion et al. (2018) analysed the efficacy of ROT at different stages of dementia: some studies included older adults at risk for dementia, MCI, mild to moderate dementia, AD specifically, or a combination of these. It was found that administration of ROT ranged from between one and three times per week, whereas the therapy duration ranged between six weeks to one year. Carrion et al. (2018) noted it was difficult to compare the studies to one another in terms of efficacy, as many studies utilised separate outcome measurements. Although, it was noted that most studies focused on cognition, memory, daily functioning, quality of life, and depression (Carrion et al., 2018). It was reported that ROT did not improve cognition in almost any study, although some studies did report that individuals suffering from dementia who received ROT intervention improved their memory (Baglio et al., 2015).

Carrion et al. (2018) went on to report that the quality of life did not improve significantly against controls for the dementia patient or caregiver upon receiving ROT intervention in the vast majority of cases. Similarly, only one study reviewed by Carrion et al. (2018) revealed that any impact of ROT on depression. Finally, it was reported that there were no significant differences in outcomes when findings were clustered together by severity of dementia (Carrion et al., 2018). It was concluded that ROT is not effective in slowing down the decline seen in dementia, nor does it help to improve cognitive functioning amongst individuals suffering from dementia (Carrion et al., 2018). This meta-analysis shows that ROT may not be considered as an effective intervention strategy for improving the lives of individuals suffering from dementia. Therefore, other forms of therapeutic dementia interventions must be considered. However, with the advent of fully-immersive VR, it may be possible to improve the efficacy of ROT by placing patients in a naturalistic virtual setting. Though, research is warranted in order to ascertain the truth of this. If fully-immersive VR can improve the efficacy of ROT, then there may be potential to use this over a greater period of time, in order to improve quality of life. A study assessing spatial memory in fully-immersive VR was conducted for this thesis. Refer to Chapter Nine for details on this study.

4.3.2 Validation Therapy

Validation therapy (VT) is characterised as a form of therapy designed to communicate with persons living with AD or other dementias (Wingbermuehle et al., 2014), which focusses on validating the personhood of individuals suffering from dementia (Berg-Weger and Stuart, 2017). VT is implemented through various techniques, including the use of non-threatening words to establish an understanding with the individual suffering from dementia, while maintaining eye contact and a gentle tone of voice (Scales et al., 2018). Touch may also be used if appropriate (Mitchell and Agnelli, 2015).

Research assessing the empirical value of VT is relatively thin on the ground; in a pilot study conducted by Morton and Bleathman (1991) the results of VT seem to suggest the effectiveness of the treatment varies greatly depending on the individual (Morton and Bleathman, 1991). Findings suggested that after VT, one of the participants doubled the amount of time spent in interactions whereas a different participant showed a marked decrease (Morton and Bleathman, 1991). Overall, general consensus on VT is that there is insufficient evidence from randomised trials to draw meaningful conclusions on the efficacy of the therapy (Cai et al., 2020). More research needs to be conducted on this therapy before the suggestion can be made to integrate it into standardised dementia treatment. Although, as pointed out by Douglas et al. (2004), it is difficult to generate meaningful results from double-blind experiments on therapeutic treatments, as the participants will always be aware that they are undergoing therapy.

Recently, Fuller (2021) conducted a study to directly compare the efficacy of VT and ROT. In this study intended to explore the experiences of familial caregivers who utilise these therapeutic techniques in the course of their caring duties over the course of five interviews. From these interviews it was reported that familial caregivers affirmed that ROT was more effective in the early stages. However, as the symptoms worsened and the illness progressed, it was reported that ROT had more of a distressing effect on the individual suffering from dementia. Once this happened, familial caregivers reported switching to VT. They found that this improved the relationship between caregiver and dementia patient, and that in the later stages, VT resulted in a lower incidence of the dementia patient acting out in fear and/or agitation (Fuller 2021). It was concluded that there are communication struggles between caregivers and dementia patients which change according to the progression of the disease (Fuller, 2021). This study suggests that there may not be one single best form of therapy for individuals suffering from dementia. Instead, as the illness progresses, a change in intervention methods may be necessary in order to ensure the dementia patient maintains the greatest quality of life for as long as possible. This shows the importance of generating an early diagnosis of dementia. If different treatments and therapies are more effective at different stages of the disease, then an earlier diagnosis could ensure that an individual is supported by the appropriate treatment at the right time.

4.3.3 Reminiscence Therapy

Much like with VT, Reminiscence Therapy (RT) concerns itself with the idea that dementia sufferers delve into the past as a comfort (Wu et al., 2018). Therefore, RT involves participants recalling their past, prior events, activities, and experience in order to give meaning to their lives (Park et al., 2019). The aim of this therapy is to promote cognitive well-being, while providing pleasure and cognitive stimulation (Park et al., 2019). One benefit of this particular therapy is that it is highly flexible, for example, music means different things to different people (Powell et al., 2019). In what is becoming a permeating theme of literature on therapeutic interventions for dementia, data sets which assess the efficacy and impact of RT are scarce. A recent meta-analysis, however, suggests that RT can lead to improvements in quality of life, communication, behaviour and mood (Woods et al., 2018). Moreover, RT has also shown positive effects in cognitively-healthy individuals. Research into the efficacy of RT comes from Wu et al. (2018) who assessed the efficacy of RT on cognitively-healthy older women living in care homes. In this study, twenty-seven women participated in a six-week intervention programme of individual RT in their homes, alongside completing a battery of emotional-state assessments. It was reported that RT helped to alleviate participants' feelings of anxiety and depression, it was also reported that participants were better able to regulate their own emotions following the therapy.

This research supports the use of RT as a therapeutic method of alleviating the psychological symptoms of dementia as well as improving the quality of life for cognitively-healthy individuals, thus further demonstrating the need of an earlier diagnosis. The earlier that dementia is diagnosed, the earlier RT can be administered, thus generating as much benefit as possible from this therapy.

4.3.4 Behavioural Therapy

Behavioural therapy (BT) has traditionally been grounded in Pavlovian principals of conditioning, while also integrating aspects of learning theory (Laing et al., 2021). The aim of BT is to eliminate the depression and anxiety of dementia sufferers while promoting positive programming methodologies which aid in the bolstering of functional behaviours (La Vigna and Donnellan, 1986; Tay et al., 2019). The therapist compiles information about behavioural symptoms into a data log where an analysis of the findings can be performed in order to generate interventions based on the findings (D'Onofrio et al., 2016). Again, it is the case that there are few studies exploring the efficacy of BT, as reported in a meta-analysis by D'Onofrio et al. (2016). However, there is evidence that BT has led to successful reductions in wandering, incontinence, as well as other 'stereotypical behaviours' by reducing the stress levels of the individual with dementia (Balk et al., 2019; Leo et al., 2017). Finally, it has been reported by Baenziger (2019) that the causes of behaviours seen in dementia are diverse, meaning that for BT to be most effective, the interventions must be tailored to each individual patient (van Kooten et al., 2017). Given that BT has shown to reduce stress in dementia sufferers (Balk et al., 2019) this further demonstrates the utility of an early diagnosis, by ensuring individuals are maintaining a greater quality of life for as long as possible.

4.3.5 Cognitive Stimulation Therapy

Although ROT (Taulbee and Folsom, 1966) has been in common usage for over half a century, there has always been the same criticism of this technique. The criticism being that studies which assess the efficacy of ROT were either too small or lacking in methodological quality (McDermott et al., 2019). Cognitive Stimulation Therapy (CST) was developed by adapting ROT to an evidence-based therapy concerned with cognitive stimulation (Spector et al., 2001). These sessions involve a multitude of activities including physical game playing, hearing sounds, recalling childhood memories, eating food, word association games, creativity activities, object categorisation, using money, number games, and team games (Alvares Pereira et al., 2020). Implicit ROT is integrated into each session by means of a welcome to each session, and each session follows the same structure (Lobbia et al., 2018). Previous research has found CST to improve general cognition, as well as patients' quality of life and communication; and is recommended by NICE for individuals suffering from mild to moderate dementia when tested on the MMSE, and the AD assessment scale for cognition and quality of life (Cheung and Peri, 2021; National Institute for Health and Clinical Excellence, 2018).

Research into CST has generated mixed results. In a single blind, controlled trial of 201 older dementia patients, Spector et al. (2003) found that CST interventions lead to significantly improved scores on an MMSE assessment. They concluded with the assertion that CST performs favourably to drug trials for dementia. However, these results are not found universally, as Yates et al. (2017) conducted a single-blind, randomised assessment on 356 individuals suffering from dementia and reported that CST intervention held no influence over cognition, or quality of life. These results were supported by a more recent study by Stewart et al. (2017) who conducted research on forty individuals with dementia and found that there was no reported improvement in the quality of life of dementia sufferers after CST interventions. They did, however, note that there was a significant reduction in depression in dementia scores. Before CST can be considered as a standardised therapeutic intervention for dementia sufferers, more research is necessary to build a greater understanding to how CST benefits individuals suffering from dementia, as results have proven inconclusive thus far.

Recently, research regarding the deliverance of CST and how the COVID-19 pandemic has impacted dementia care was conducted by Cheung and Peri (2021) who designed a virtual adaptation of CST (vCST) in order to explore how technology may be utilised to deliver group interventions for dementia during the Covid-19 pandemic. In this study, a group of CST leaders and facilitators in New Zealand moved their in-person CST groups into the virtual programme. Over fourteen sessions, twice a week, for seven weeks, ten groups of dementia patients who were receiving in-person CST were transferred to vCST using the Zoom videoconferencing platform to administer vCST. Their findings reported that vCST participants appreciated being able to connect to others virtually while they were unable to connect in-person due to the pandemic. It was reported that vCST could readily be adapted into an at-home approach to deliver CST. Cheung and Peri (2021) concluded that this research illustrates how the COVID-19 pandemic has increased the rate of innovation in dementia practice and that technology has the potential to enhance the holistic management of dementia (Cheung and Peri, 2021). As CST has shown to be a useful tool for improving quality of life (Cheung and Peri, 2021) this shows the importance of an early diagnosis. An earlier diagnosis can lead to earlier treatment, thus ensuring that the individual with dementia maintains an improved quality of life for longer.

4.3.6 Music Therapy

According to Gracia-García et al. (2017), BPSD are often the cause of referrals to a care-home or hospitalisation. It is argued that even modest benefits to quality of life could make the difference between living at home and institutionalisation (Herrmann and Black, 2000). Music therapy is a non-pharmacological intervention involving the systematic use of tunes, sounds and movements (Moreno-Morales et al., 2020). Early research into music therapy has reported to be effective in increasing the well-being of patients suffering from BPSD (Claire 1996). A recent meta-analysis of eight studies into the efficacy of music therapy on cognitive functioning, depressive states, and quality of life returned findings that music therapy improved the cognitive functioning of individuals living with dementia, as well as their general quality of life (Moreno-Morales et al., 2020). However, complications with assessing the efficacy of music therapy for people with dementia comes from contradictory findings of different research. In a meta-analysis, Pedersen et al. (2017) reported findings that music therapy held a mild to moderate influence over reducing agitation in dementia sufferers, whereas a separate meta-analysis by Van der Steen et al. (2017) found the opposite, that music therapy demonstrated no significant improvement on agitated behaviour, or any other behaviours.

More recently, music therapy has been split into two separate branches (i) Interactive Music Therapy (IMT), and (ii) Receptive Music Therapy (RMT). IMT involves interaction between the participants, such as singing or playing a musical instrument under the supervision of a trained professional (Tsoi et al., 2018). RMT, conversely, is a self-administered therapy where participants independently listen to music of their preference (Tsoi et al., 2018). In a meta-analysis of both these types of music therapy, involving over 1400 participants, Tsoi et al. (2018) reported that no significant difference was found between participants receiving IMT, RMT, and usual care on cognitive function. However, RMT was shown to reduce agitation reported by participants as compared to IMT or controls. These findings could explain the disparate results reported by Pedersen et al. (2017) and Van der Steen (2017) respectively. The reported findings from Moreno-Morales et al. (2020) that music therapy can improve both cognition and quality of life again contextualises the importance of an early diagnosis of dementia. As treatment can commence earlier thus providing greater benefit to the suffering individual.

4.3.7 Massage Therapy and Acupressure

Massage and touch are used as a non-pharmacological and psychosocial intervention in dementia (Wu et al., 2017). Massage Therapy (MT) is designed to alleviate the BPSD such as depression, anxiety, and aggression, and improve quality of life overall (Wu et al., 2017). The literature surrounding MT and its efficacy in treating dementia lacks a strict definition of what is considered a 'massage'. For example, early research from Smallwood et al. (2001) reported promising findings from a controlled study of twenty-one people with dementia. They showed that those who underwent aromatherapy and MT were significantly more sedate than controls. It remains unclear however what the word 'massage' in this context entails. As such, we can expect to find contradictory results from different studies. This is the case with Moyle et al. (2014) who conducted a study which involved twenty-six participants with moderate to severe dementia who received a 10-minute foot massage intervention in order to assess agitation levels. Findings reported that foot massages offered no significant alleviation in levels of agitation compared to controls (Moyle et al., 2014). Finally, a recent meta-analysis of eleven studies examined the efficacy of massage therapy on individuals suffering from dementia (Wu et al., 2017). It was reported that physical behaviours (both aggressive and non-aggressive) and verbal behaviours (both aggressive and non-aggressive) decreased significantly after receiving massage or touch therapy; however, scores of anger, sadness, or anxiety did not decrease significantly from the therapy (Wu et al., 2017). It was concluded that low sample sizes made it difficult to reasonably estimate the efficacy of massage or touch therapy in dementia (Wu et al., 2017).

Recently there has been an impetus to research the potential benefits of acupressure on BPSD over MT, as acupressure has shown to be more effective in improving depression and anxiety in people with dementia as compared to controls (Alm et al., 2018). Furthermore, acupressure performs favourably against MT at alleviating BPSD (Rodríguez-Mansilla et al., 2015). Rodríguez-Mansilla et al. (2015) conducted a controlled study on 120 individuals with dementia, where participants were either allocated to a control group, an acupressure group, or a MT group. It was reported that of the 111 that completed the study, the acupuncture group showed better improvements than the MT group in terms of pain and depression. This was found both during the treatment period, and one month later at a follow-up meeting.

Finally, acupressure has shown benefits to agitation when combined with aromatherapy. Yang et al., (2015) conducted a controlled study on 186 participants suffering from dementia and assigned them to one of three groups, an aromatherapy group, an aroma-acupuncture group, and a control group. Results showed that agitation was significantly lower in the aroma-acupressure and aromatherapy groups compared with the control group in both the immediate post-test period and after a post-assessment which took place 3 weeks later (Yang et al., 2015). It appears from the discussed literature that more research with greater sample sizes is warranted before massage and touch can be considered as a potential method for providing relief to dementia patients.

4.3.8 Animal Assisted Therapy

Animal-Assisted Therapy (AAT) is a therapeutic intervention which has been historically used to treat a range of neuropsychological disorders (Peluso et al., 2018). In dementia, AAT involves using trained or untrained animals to elicit a positive influence on aggression and anxiety to ameliorate quality of life (Peluso et al., 2018). With respect to the efficacy of AAT generally, research has revealed a meta-analysis of studies which reported that individuals who participate in AAT show improvements in memory, attention, communication, concentration, anxiety, loneliness, and sadness, among other benefits (Lasa et al., 2015). The BPSD in older adults with dementia often manifest as deficits in social interactions and communication and also, as depression, agitation, and aggressiveness (Peluso et al., 2018). However, none of the research mentioned previously is concerned with the efficacy of AAT on patients with dementia specifically. Research into the efficacy of AAT on BPSD yields mixed results. Mossello et al. (2011) reported that AD patients responded to AAT with decreased levels of irritability, aggression, loneliness and anxiety. This result has found to also be the case for patients suffering from vascular dementia (Banks et al., 2008).

However, contradictory findings have been witnessed from Majić et al. (2013) who conducted a controlled study on fifty-four nursing home residents suffering from unspecified dementias. After ten weekly sessions of AAT, it was reported that residents who participated in AAT showed no change in levels of aggression or agitation. Furthermore, the long-term effectiveness of AAT has been called into question. A controlled, longitudinal study involving twenty-seven participants suffering from senile dementia participated in AAT twice a week for six months. It was found that three months after these sessions had ended, the AAT group only demonstrated better performance on the Behavioural Pathology of AD Scale, and in nothing else (Kanamori et al., 2001). Given the mixed results witnessed in AAT, even if an earlier diagnosis of dementia is achieved, more research is still warranted before the exact efficacy of this therapy can be ascertained.

4.3.9 Aromatherapy

The final therapeutic intervention for dementia that this chapter will explore is aromatherapy. Several of the previously mentioned studies have jointly involved the use of aromatherapy, and, as in the case of Yang et al. (2015), it was the aroma-massage group which provided the greatest alleviation of agitation in dementia patients. However, it was also found that aromatherapy alone did significantly help to alleviate agitation in dementia patients (Yang et al., 2015). One difficulty with assessing the efficacy of aromatherapy is that often studies do not go into sufficient detail about the aromatherapy intervention to replicate the study exactly. A change in the quantity, or strength of the aroma solution could produce a disparate outcome. This was the case with O’Connor et al. (2013), who explored the efficacy of lavender oil as a means of alleviating agitation in sixty-four dementia sufferers. In a controlled, randomised, single-blind study, they found that lavender oil performed no better than placebo oil at reducing agitation in the participants. These results were furthered by Fu et al. (2013) who conducted a single blind study on sixty-seven dementia patients, wherein twenty-two would take part in bi-daily aromatherapy sessions over six weeks, and reported finding that agitation did not significantly reduce after treatment. These findings make it difficult to consider aromatherapy as an effective therapy to improve the quality of life for individuals with dementia.

4.4 Chapter Summary

This chapter has been an introduction to the various different intervention strategies for dementia, both pharmacological and therapeutic, while highlighting the efficacy of each, and using these treatments to contextualise why an early diagnosis of dementia is paramount. Finally, this chapter concluded by discussing some of the difficulties which arise from the differing intervention techniques with individual outcome goals. The following chapter (Chapter Five) is the first experimental chapter, concerned with exploring the relationship between postural stability and cognitive functioning within healthy populations.

4.5 Highlights

- Dementia interventions and are fundamental building blocks of dementia strategies and policies (Reilly et al., 2020).
- Dementia treatments are not curative, rather aiming to secure a higher quality of life for patients for as long as feasible.
- The most common typical pharmacological intervention for dementia is a course of AChEI, such as Aricept (Donepezil), or Galantamine (Trinh et al., 2003; Knight et al., 2018). However, the efficacy of AChEIs remains disputed.
- MH is a simple and safe pharmacological intervention for dementia (Peng et al., 2013).
- Atypical antipsychotics are both safer and better tolerated than typical antipsychotics for treating BPSD (Manzano-Palomo et al., 2020).
- Some anticholinergic anti-depressants can raise the risk of developing dementia (Alzheimer's Association, 2018).
- Therapeutic interventions for dementia differ in efficacy as the illness progresses (Fuller, 2021).
- A more flexible intervention strategy may be necessary in order to ensure the dementia patient maintains the greatest quality of life for as long as possible.
- Each dementia intervention strategy should be tailored to the individual patient.

Chapter Five

The Relationship Between Postural Stability and Cognitive Functioning

5.1 Introduction

Achieving accuracy in neuropsychological assessments is of absolute importance when considering their prevalence in diagnostic contexts. However, the most currently used method of diagnosing dementia in the UK has been criticised as lacking accuracy and reliability (Devenney and Hodges, 2017). There are a number of non-invasive factors identified in Chapter Three which could potentially be utilised in order to improve the accuracy of a dementia diagnosis, or to improve the accuracy of neuropsychological assessments in general.

This first experimental chapter explores the relationship between postural stability and cognitive functioning. Previous research has established that deficits in postural stability can be witnessed in both AD (Visser, 1983) and in MCI (Shin et al., 2011), which is thought in some cases to be a transitional stage into developing dementia (Sullivan et al., 2019). However, the relationship between postural stability and cognitive functioning within healthy populations is less clear. If such a relationship is witnessed to exist, postural stability may need to be a consideration in future diagnostic contexts.

5.1.1 Postural Stability and Cognitive Functioning

To win an ongoing fight against gravitational forces, the human spine must provide and maintain a balanced standing posture (Farcy, 2020). Balance (or posture control) in static situations, such as standing, requires the vertical projection of one's centre of mass so that it remains within the base of support (Tokur et al., 2020). To achieve this situation, a specific combination between shape and positioning of both the pelvis and spine is necessary (Roussouly, 2020). The pelvis is generally in a retroverted position and the spine presents successive curvatures (Roussouly, 2020). Balance is critical for posture control when standing upright and during cyclic tasks such as walking and running (Tokur et al., 2020).

Impaired postural stability is associated with many health conditions such as strokes, ear infections, hypotension, AD, and more (Winter et al., 1990). Initial research into the relationship between AD and balance comes from Visser (1983). Visser's research centred on eleven older adult individuals suffering from severe memory impairment and the associated behaviour disturbances, and eleven controls matched for gender and age (Visser, 1983). In this study, Visser conducted observations of balance and gait in the AD group and the control group. Both groups were tasked with completing a gait task and a static balance task (Visser, 1983). The gait task involved participants' walking along a six-metre platform in their shoes whereas the static postural stability task required participants to stand with their legs slightly apart and eyes open on a FP for ten seconds. Results showed that, compared with controls, the AD group took significantly shorter steps, walked more slowly, stepped less frequently, had a greater need for walking supports, and demonstrated a greater likelihood to sway while walking (Visser, 1983). These results have been reflected in recent studies which have reported that individuals suffering from AD demonstrate greater sway velocity with reduced sway control when compared to a healthy control group when measured using the Berg Balance Scale and a Nintendo Wii Balance Board (WBB) (Sant'Anna et al., 2019). Furthermore, a systematic review of articles suggested that older adults with mild to moderate AD demonstrated reduced postural stability while both standing still (static postural stability) and in motion (dynamic postural stability) compared to a control group without a diagnosed cognitive impairment (Mesbah, 2019).

MCI is widely believed to be a transitional stage between standard aging and AD (Sullivan et al., 2019). An estimated 40-60% of individuals over the age of fifty-eight suffering with MCI demonstrate underlying AD pathologies (Gillis et al., 2019). It has also been reported that in a study of 87 participants who self-reported memory impairment, participants who were allocated into an MCI group demonstrated an increased speed at which they would sway, and would sway a greater distance before correcting themselves, as compared to the non-MCI group (Shin et al., 2011).

Trapuzzano et al. (2020) conducted research which required thirty-four participants with MCI to complete the Mini-cog and a Four-Stage Balance Test (Trapuzzano et al., 2020). Here participants were tasked with standing in four progressively more challenging conditions and holding each position for at least 10 seconds. Stage one required participants to stand feet together, stage two required participants to stand semi-tandem, stage three required participants to stand in a tandem stance and stage four required participants to stand in a single leg stance. Participants were also tasked with completing a timed up-and-go test which assessed functional mobility, a 30-second chair stand test which measures lower extremity strength, and The Tinetti Performance-Oriented Mobility Assessment, which is used to measure balance and gait in older adults. It was reported that older adults with dementia demonstrated progressive deficits in areas of cognitive functioning and processing speed (Trapuzzano et al., 2020). A paired samples t-test was conducted on the findings, highlighting significant differences between the Four-Stage Balance Test ($p < 0.001$), the timed up-and-go test ($p < 0.002$), and the Tinetti Performance-Oriented Mobility Assessment ($p < 0.002$). It was concluded that cognitive impairment in domains of executive function and processing speed increased an individual's risk of falling, but this risk could be reduced with appropriately administered exercise programs (Trapuzzano et al., 2020). Results from other studies have demonstrated an increased fall risk, and a greater likelihood of suffering fall related injuries in patients with dementia as compared to cognitively-healthy older adults (Petersen et al., 2018).

Furthermore, other forms of dementia have also been thought to affect postural stability. Frontotemporal dementia (FTD) is characterised by progressive changes in behaviour and personality or language difficulties (Wauters and Van Broeckhoven, 2020). Research has reported that patients suffering from FTD demonstrate significant postural stability and gait impairments, with mediolateral (ML) (left and right) sway being more severely affected than AP (forward and backward) sway (Ganapathy et al., 2020).

In addition to individuals with cognitive impairments, research into the relationship between postural sway and cognition has returned the findings that postural sway increases with attentional demands in control populations (Pellecchia, 2003; Pellecchia, 2005). Pellecchia (2003) conducted a study on twenty control individuals between the ages of eighteen and thirty who were tasked with completing a series of cognitive trials. These trials comprised of a digit reversal task which required participants to listen to a pair of numbers and repeat these numbers backwards, a two-bit classification task which required participants to combine two single digits into a double-digit number and categorize that number as high (>50) or low (<50) and odd or even, and a task which required participants to start at a randomly chosen three-digit number and count backwards in threes. Participants completed these cognitive assessments while having their postural stability assessed by a FP. The results reported that while undertaking more cognitively taxing assessments, the total sway distance increased. It was noted that AP sway was more sensitive than ML sway in information reduction tasks such as digit reversal, digit classification, and counting backward in threes (Pellecchia, 2003). This indicates a relationship between cognitive load and postural sway, particularly on the AP axis.

Pellecchia (2005) conducted further research on postural sway and cognitive functioning; eighteen participants with no known neurological or balance disorders were randomly assigned to one of three groups. One group received dual-task training which involved the participants practicing counting backwards in threes while standing on a FP, the second group received single cognitive task training which involved them only practicing counting backwards in threes, and the third was a control group which received no training. The results showed that there was no significant difference in postural sway between the control group and the single cognitive task group. However, the dual task training group showed reduced postural sway while completing cognitive tasks. This reveals that practise effects are prevalent while exploring the relationship between sway and cognition, as the dual task group which had training in both the cognitive task and balancing on a FP showed reduced postural sway as compared to the groups without balance training (Pellecchia, 2005).

5.1.2 Aim of the Study

To extend the work in the field of balance and cognitive function, the aim of this research is to assess an intrinsic relationship between postural stability and cognitive functioning without utilising distraction tasks which were present in the research of Pellecchia (2003). As far as we are aware, there have been no studies investigating whether an intrinsic relationship exists between cognitive functioning and postural stability in healthy populations without distraction tasks. Removing distraction tasks is important as the cognitive assessments may interfere with postural sway. This study intends to explore a more robust measure of balance and cognitive functioning in healthy controls, rather than focussing on tasks that involve a distraction element. A full assessment of cognitive function and its link with postural stability may have implications for diagnosis of a cognitive impairment.

Currently, the most widely used screening tool for dementia is the MMSE (Scheffels et al., 2020). The MMSE is a five-ten-minute examination which focuses on the cognitive aspects of mental functioning (Folstein et al., 1975). However, the MMSE has been criticised for lacking validity and reliability (Carnero-Pedro, 2014). If the MMSE is to remain the most widely used screening tool for dementia, it is desirable to improve the diagnostic accuracy by assessing additional factors alongside those tested for by the MMSE. Therefore, this study aims to explore if a relationship between postural stability and cognitive functioning exists, as this could potentially add an extra dimension to assessment criteria which focuses on physiological factors, in order to be used alongside the MMSE in order to improve the accuracy and reliability of diagnoses.

In the current study, postural stability will be measured by a laboratory-based assessment of Centre of Pressure (COP). COP is defined as the point of application between the ground and the forces acting upon it (Li et al., 2020). Displacement of the COP can provide information into functional foot behaviour and balance performance by reporting sway speed, sway velocity, and leaning behaviours (Li et al., 2020).

COP can be reported by utilising FPs which contain transducers that measure force distribution between the feet to report pressure magnitude and the progression of COP (Clark et al., 2010; Mudge et al., 2020). COP trajectory can be plotted from pedobarography data to produce two-dimensional coordinates, which can be used to provide visual representations of COP trajectory in ML and AP axes (Mudge et al., 2020).

Recent studies report that utilising COP measurements to assess individual patient stability provides moderate to excellent test-retest reliability (de Jong et al., 2020). Furthermore, in stroke victims, COP measurements were reported to show high levels of within-test and between-test reliability when assessing trunk control in both quiet sitting tasks, and reaching tasks (Näf et al., 2020).

In the current study, COP will be measured by using the WBB FP (Nintendo, Kyoto, Japan). The WBB has been found to be a cheap and portable alternative to lab-grade FPs, while still giving accurate and reliable results, which goes some way to addressing the concerns with implementing in-lab equipment in clinical practice (Clark et al., 2010; Huurnink et al., 2013). Furthermore, the WBB has been found to accurately measure postural sway and postural instability (Meade et al., 2020; Jones, 2019).

In order to assess the accuracy and reliability of the WBB, Chang et al., tested the board against a more expensive rival in a series of three balance assessments, utilising both young and older adult participants. They reported finding no significant differences between the accuracy and reliability on any of the three tests between the WBB and the more expensive rival (Chang et al., 2013). This shows the WBB is a valid and reliable measuring instrument that is comparable to laboratory-grade FPs, which are the lauded as the “gold standard” for balance assessments (Alumona and Adegoke, 2020). Following this, Clark et al. (2018) conducted a systematic review on the accuracy and reliability of the WBB. In a review of twenty-five articles, they conclude that the WBB can be used as a reliable and valid tool for assessing postural stability. Furthermore, when combined with deep learning technology, the WBB has reportedly been able to interpret large amounts of data over extended periods of time in order to monitor an individual’s movements and provide data with the capacity to be implemented in rehabilitation tracking (Vincent et al., 2020).

COP will be measured using custom software developed by the University of Bradford which allows the WBB to communicate to a standard computer via a Bluetooth connection. The reason for using this software over the Wii Fit software which is bundled with the WBB is because it has been found that the WBB gives inaccurate and unreliable readings when used with its bundled software (Wikstrom et al., 2012; Hine, 2010; Beato et al., 2020).

The aim of the present study was to explore whether there is a relationship between postural stability and cognitive functioning within healthy populations. Based on literature from AD, MCI and dementia research, the hypothesis is that lower scores on assessments of cognitive functioning will be related to increased levels of postural sway.

5.2. Methods

5.2.1 Participants

The participant cohort consisted of twenty-four participants; eighteen males and six females aged as follows: 18-24 (n=5), 25-31 (n=7), 32-38 (n=2), 39-45 (n=6), 46-52 (n=3), 53-59 (n=1). Participants had no existing neurological disorder (Some examples would include epilepsy, stroke, AD, or Parkinson's Disease), no clinically diagnosed cognitive impairment or any implanted medical device, such as a pacemaker. Furthermore, none of the participants suffered disorders or illnesses affecting their postural stability. The study was approved by the University of Bradford Humanities, Social and Health Sciences Research Ethics Panel and all participants provided informed consent. Regarding sample size Li et al. (2019) studied the influence of back pack load on postural stability with a participant cohort of 20. Similarly, Arcioni et al. (2019) utilised twenty participants in a study in order to determine how postural stability influences cybersickness in fully-immersive VR. (A study regarding fully-immersive VR has also been included in this thesis, see Chapter Nine). Therefore, the aim was for approximately twenty participants to take part in keeping with the previous literature, but more could take part if they were interested.

5.2.2 Balance Assessment Apparatus

5.2.2.1 The Nintendo Wii Balance Board. The WBB is a FP with a useable surface of 45 cm × 26.5 cm which was originally sold alongside the video game Wii Fit for the Nintendo Wii gaming system. Similarly to laboratory grade FPs, the WBB contains four transducers which are used to measure force distribution and reports the resultant movements in terms of COP (Clark et al., 2010). The WBB has previously seen integration into clinical practice, with the hardware being utilised in programs of rehabilitation for neurological patients suffering from balance defects (Deutsch et al., 2008).

5.2.2.2 Balance Software. This balance software developed by the University of Bradford allows the WBB to communicate with a standard Personal Computer (PC) via a Bluetooth connection. This software receives the data from the four transducers in each quadrant of the WBB, and reports a COP reading for standing sway, which can be plotted on an X-axis for ML sway and a Y-axis for AP sway. The software takes twenty readings of COP per second, and outputs these readings for both the X-axis and Y-axis.

5.2.3 Procedure

Upon arrival, participants were greeted by the researcher and informed consent was given. The study began with participants standing on the balance board for 120 seconds, while the software assessed their COP. The board was faced towards a window for the participant's comfort, with a hand rail beside them. The hand rail was intended to only be used if the participant felt as though they were losing balance. Following the balance assessment, participants were offered a break before proceeding to participate in a series of cognitive assessments which consisted of a STM assessment, an LTM assessment, tests of WM, dual task assessment, and an associative learning task. Following the cognitive assessments, the participants were thanked, debriefed, and offered another opportunity to ask any questions they had before they left.

5.2.4 Cognitive Tests

All cognitive tests were designed by the researcher. The justification for the cognitive tests that encompass this battery is to assess various areas of cognition which are known to be affected in the earlier stages of dementia, such as STM, working memory, associative memory and executive functioning (Lim et al., 2019; Fraga et al., 2018; Rubiño and Andrés., 2018; Smith et al., 2019). However, a LTM assessment was also included in order to generate a more robust understanding of general cognition.

5.2.4.1 Word Recall. A word recall task was used in this study to assess short-term memory (Coltheart, 1981). This required participants to listen to a series of fifteen words which were controlled for imageability, familiarity, and length (Three syllable words between six and ten letters long) generated by the MRC Psycholinguistics database (Coltheart, 1981). Once the participants had heard this list, they were asked to recall the words and were given one point for each word correctly recalled. This was also used as a long-term memory assessment. After the participants had completed the other cognitive assessments, they were asked to recall as many words from the word list as they could. As for the short-term memory assessment, they were given one point for each word correctly recalled.

5.2.4.2 Digit Span Task. Digit span tasks, both forward and backward, are widely used to assess cognitive functioning (Wechsler, 1981). This task involves participants being read a series of numbers, starting with three digits which increased to nine. The participant was tasked with repeating the series of numbers back to the researcher, with one point being awarded for each correctly recalled series of numbers. This assessed STM. A backwards digit span task worked similarly, with the numbers increasing gradually from three to seven digits. However, in this task, participants were tasked with repeating the series of numbers they heard in reverse order, which assessed WM (Wechsler, 1981). For each series of numbers correctly recalled, the participant would be awarded a point.

5.2.4.3 Dual Task. The dual task test for this study consisted of two sections, one visual and one auditory. Participants saw a series of colours appear on the screen. As these colours appeared, participants would simultaneously hear a series of letters read out by the researcher. Following this, in the test phase, the participant was presented with a screen with a choice of 12 colours and asked to indicate which five of the colours were previously shown and to recall each letter they heard. Points were awarded separately for the colours and letters; with one point awarded for each correctly identified colour and one for each correctly identified letter.

5.2.4.4 Associative learning. An associative learning task is an assessment of visuospatial associative memory and requires the participant to learn an association between a visual stimulus and a spatial location (Égerházi et al., 2007). This test involved participants seeing boxes on a screen. These boxes had a shape inside. One by one, the boxes would open and close to reveal the shape inside for a brief period. After all the boxes had opened and closed, a shape would appear in the middle of the screen which had previously been seen inside of one of the boxes. Participants had to indicate which box they saw this shape in. After this, another shape would appear, and again, the participants would have to point to the box which corresponded to that shape. This would continue until all the shapes had a designated box. There were ten levels of increasing difficulty wherein each level would add more boxes and shapes. This test took approximately ten minutes to administer, and points were awarded only if the participant correctly identified the box belonging to every shape on that level.

5.2.5 Data Analysis

A general linear model multivariate analysis of covariance (MANCOVA) was run to compare each participant's balance results with their scores on the cognitive tests. Balance was measured using sway variability, which is defined as the standard deviations of COP in a specified direction (Pellecchia, 2003). Sway variability was used as it is common practise in many studies concerned with postural sway assessments (Pellecchia, 2003; Pellecchia, 2005; Riley et al., 2005; Kernozek et al., 2008; Quatman-Yates et al., 2015; Morelli et al., 2020). The standard deviation (SD) for each participant's AP and ML sway was ascertained by calculating the average amount of sway for each axis, then removing that average from each respective axis. Then the standard deviation could be calculated from these datasets. Age and gender effects were analysed to determine whether any significant results could be because of these factors.

5.3 Results

The aim of the study was to explore the relationship between postural stability and a wide assessment of cognitive functioning in cognitively-healthy participants. Each participant completed both a postural stability task, and a cognitive battery. It has been reported that age and gender can significantly affect scores obtained in both cognitive assessments (Jacova et al., 2007; Fields et al., 2011) and postural stability (Morelli et al., 2020), therefore any effects of these variables were analysed using a MANCOVA. The cognitive test scores and the balance results were the dependent variables, and age and gender were covariates. Wilk's Λ was not significant for both age ($p > .05$) and gender ($p > .05$), therefore will not be considered further. It has also been reported that ToD effects may influence results on assessments of cognition (Walters and Lesk 2015), therefore ToD that testing took place was analysed with a MANCOVA with cognitive test scores and balance results as the dependent variables, and ToD as a covariate. Wilks' Λ was not significant for ToD effects ($p > .05$). The data were normally distributed.

See Table 3 for scores on the cognitive assessments and Table 4 for the results of ML and AP sway.

Table 3 The mean and SDs for each cognitive assessment

Test	N	Min	Max	Mean	SD (+/-)
Word recall (STM)	24	3	10	5.92	1.53
Word recall (LTM)	24	2	8	3.96	1.88
Digit span (Forward)	24	5	13	8.42	2.15
Digit span (Backward)	24	3	8	5.75	1.75
Associative learning	24	3	9	5.13	1.39
Dual task	24	1	14	4.96	3.41

Table 3 shows the minimum, maximum, mean, and SD for participants' scores obtained on the cognitive assessments, including scores on the word recall tasks, the digit span tasks, the associative learning task, and the dual task.

Table 4 Descriptive statistics for SDs in ML and AP sway

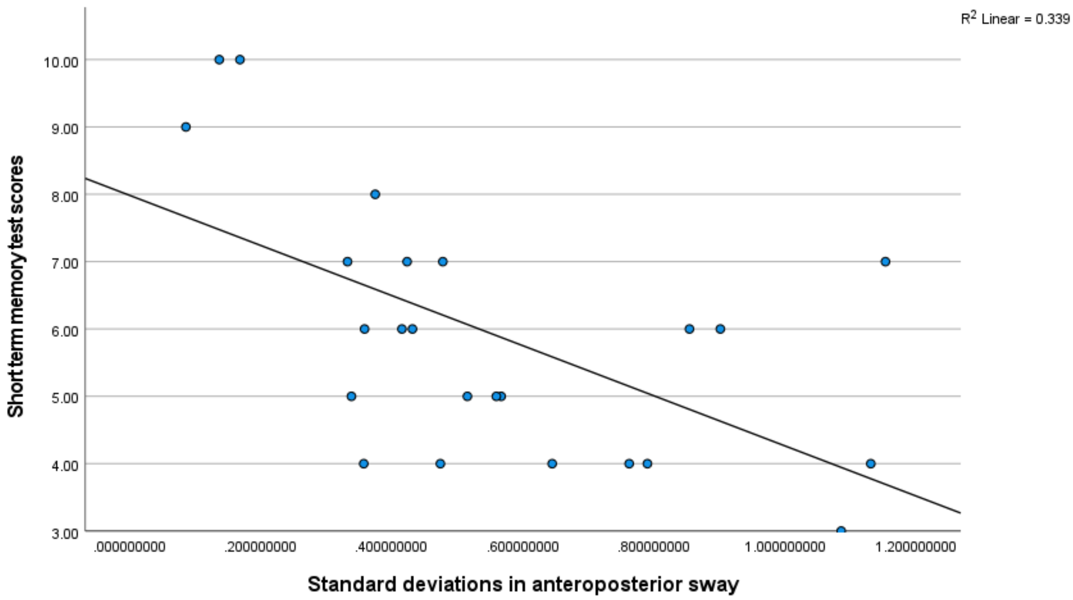
	N	Minimum	Maximum	Mean
ML sway SDs	24	0.12	1.28	0.49
AP sway SDs	24	0.09	1.15	0.56

Table 4 shows the minimum SD in AP sway is lower than the minimum SD in ML sway. Similarly, the maximum SD in AP sway is lower than the maximum SD in ML sway. However, the mean SD in sway is grater in AP than ML.

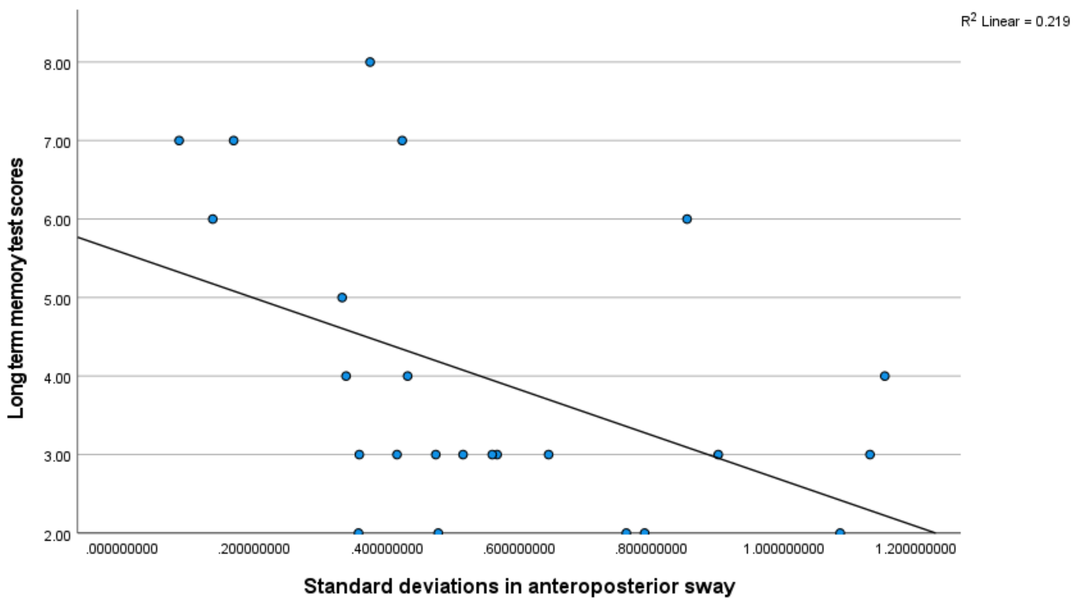
A composite memory score was generated by combining the scores of memory tests. This composite memory score was anaylsed against SDs in ML and AP sway using a multiple regression analysis. Results showed that AP sway could predict performance on cognitive test scores ($F(1,22) = 17.76$, $p < 0.01$) however, no significance was seen for ML sway ($p > 0.05$). To investigate this relationship further, the SD of ML and AP sway alongside all of the scores on the individual cognitive tests cognitive (STM, LTM, Backwards WM (BWM), dual tasks, and associative learning) were submitted to a general linear model MANCOVA where cognitive test scores were entered as the dependent variables, and standard deviations in ML and AP sway were entered as covariates. The MANCOVA returned significant results for AP sway with $F(5, 18) = 3.31$, $p < .05$; Wilks' $\Lambda = 0.52$, partial $\eta^2 = 0.48$. No significance was seen for ML sway $F(5, 18) = 2.11$, $p > .05$; Wilks' $\Lambda = 0.63$, partial $\eta^2 = 0.37$. The general linear model results showed that AP sway demonstrated a significant negative relationship with STM ($F(1, 22) = 11.30$, $p < 0.01$), LTM ($F(1, 22) = 6.18$, $p < 0.05$), BWM ($F(1, 22) = 11.05$, $p < 0.01$), and associative learning ($F(1, 22) = 12.72$, $p < 0.01$). However, results for the dual-task were found to be non-significant ($F(1,22) = 2.14$, $p > 0.05$).

Parameter estimates show a linear, negative relationship between standard deviations in AP sway and STM (B=-3.73, SE=1.11, t=-3.36, $p < .05$, 95%CI [-6.03, -1.43], LTM (B=-2.91, SE=1.170, t=-2.49, $p < .05$, 95%CI [-5.34, -0.48], BWM (B=-3.43, SE=1.08, t=-3.39 $p < .05$, 95%CI [-6.23, -1.83], and associative learning (B=-2.79, SE=0.78, t=-3.57, $p < .05$, 95%CI [-4.415, -1.17].

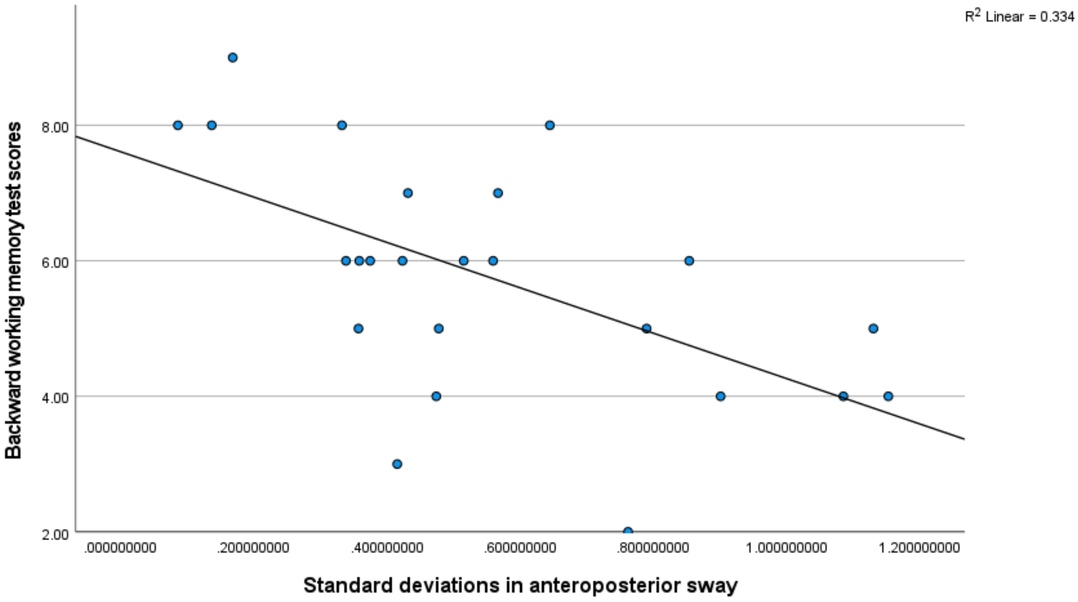
Figure 2 depicts graphs which plot the significant results shown in this study.



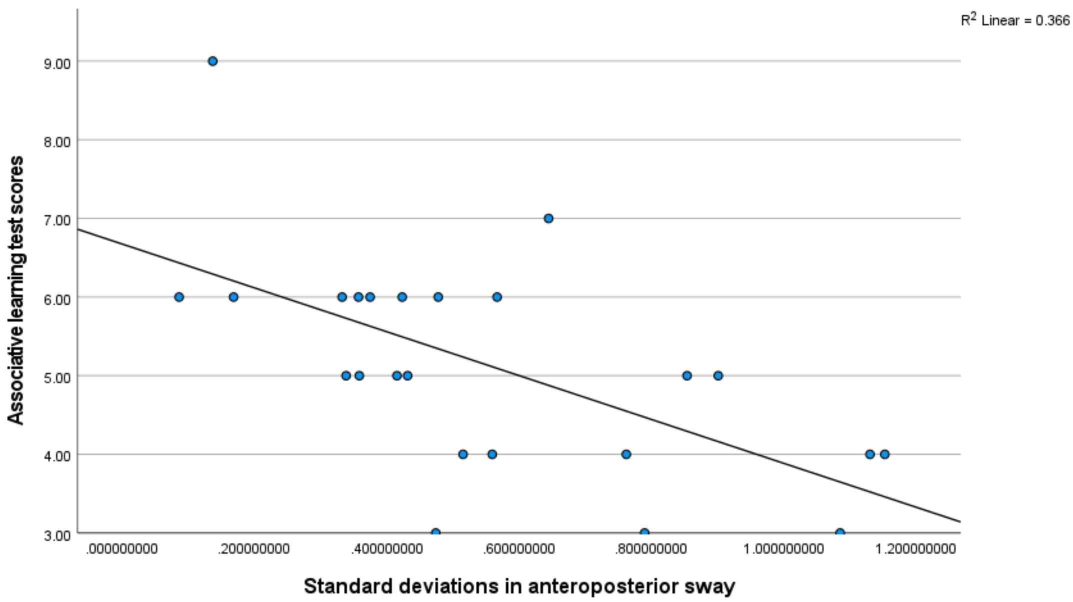
a



b



c



d

Figure 2 scatterplots demonstrating the interaction between standard deviations in AP sway and significant results on cognitive tests: STM (a), LTM (b), BWM (c), and associative learning (d). The scatter plots show a significant linear decrease in cognitive test scores as AP sway increases.

5.4 Discussion

The aim of the present study was to explore the relationship between postural stability and cognitive functioning in a cognitively-healthy population. We extended previous research that has focussed on cognitive distraction tasks and used a wider cognitive battery for assessment. In the present study, we investigated whether either ML or AP sway significantly affected cognitive functioning in a cognitively-healthy population by having participants stand on a WBB for two minutes and then perform a series of cognitive tests.

The results demonstrated that greater standard deviations in AP sway were significantly negatively related to scores on tests of STM, LTM, BWM, and associative learning. However, the results of the MANCOVA for ML sway were found to be non-significant.

The non-significant findings for ML sway are not surprising given that the WBB requires a side-by-side standing stance. Previous literature has reported that side-by-side standing uses the ankles to maintain balance results in fluctuations in AP sway instead of ML sway (Balasubramaniam et al., 2000). Furthermore, previous research into AD, MCI and postural sway comes from Leandri et al. (2009) who assessed sway in healthy controls against MCI and AD patients. They found that impairment in balance is a feature of both AD and MCI, and reported an apparent trend towards increasing AP sway between healthy controls and MCI and AD patients. Furthermore Gago et al. (2015) conducted a study on the influence of visual and auditory systems on postural stability in patients with AD and healthy controls. The study involved twenty-four AD patients and an equal number of age matched healthy controls were given a kinematic postural analysis wherein inertia measurement units were placed at the centre of mass of the body and readings were taken under four conditions: one stance with eyes open and eyes closed, and another with and without suppression of background noise. It was reported that in both groups, visual suppression negatively impacted postural stability, but also that the effect of auditory suppression on postural stability was more apparent on AP sway than ML sway (Gago et al., 2015).

Postural stability is already associated with many conditions in the domain of health care (Winter et al., 1990). Visser (1983) reported that AD patients presented significantly shorter step length, lower gait speed, lower stepping frequency, greater step-to-step variability, greater need of double supports, and greater levels of sway when compared against healthy controls. Sant'anna et al. (2019) also showed that individuals suffering from AD demonstrated greater sway velocity with reduced sway control when compared to controls in a study which utilised the WBB. The present study is consistent with these findings demonstrating that AP sway is significantly greater when scores on tests of cognition are lower. Importantly our findings are seen in cognitively-healthy participants which demonstrates an important way forward in the understanding of the link between balance and cognitive function at the pre-clinical level. Future research should investigate this further in a cognitively-healthy older adult cohort and monitor people over time, assessing any cognitive impairment and its progression. For example, assessing whether the measurement of balance sensitive enough to predict the decline from healthy populations, to MCI, to AD.

Furthermore, a systematic review by Mesbah (2019) suggested that older adults with mild-to-moderate AD demonstrated increased static and dynamic postural sway when compared to a control group without a diagnosed cognitive impairment. The results of the present study further the findings of Sant'anna et al. (2019) and shows that in addition to AD patients, there is a more sensitive relationship between AP sway and cognitive functioning which can also be witnessed in a healthy control group.

There is a potential relationship between the findings that cognitively taxing tasks increased the total sway distance in twenty healthy participants (Pellecchia, 2003), and the findings of the present study that greater SDs in AP sway were related to poorer performance on cognitive assessments which warrants further investigation. Pellecchia (2003) reported that the tasks which imposed a greater cognitive load resulted in increased postural sway, whereas the findings of the present study suggest a more intrinsic relationship between cognitive functioning and postural sway without the use of distraction tasks which were present in the research of Pellecchia (2003). This warrants further study as investigations into the relationship between postural sway and cognitive functioning may hold implications for future diagnoses of cognitive impairments.

Pellecchia (2005) also reported that, in a study of eighteen participants, a group which had training with both a cognitive task and a balance task performed better than groups that did not have such training. This indicates that practise effects may influence results in studies of postural sway and cognitive functioning (Pellecchia, 2005). Considering one of the aims of the current study was to assess the potential to utilise postural sway as a diagnostic tool for dementia, further research is needed in order to assess how long practise effects take to dissipate when assessing postural sway and cognitive functioning.

The WBB is lauded as a widely used and cost-effective tool which does not require the skill of a healthcare professional administer (Beato et al., 2020). Furthermore, the WBB has previously been shown to offer accurate measurements of postural sway (Meade et al., 2020). However, it has been argued that the WBB is not interchangeable with a lab grade FP, rather that it is comparable in certain circumstances which are to be considered cautiously (Bonnechere et al., 2016; Ruff et al., 2015). Moreover, there is debate regarding the WBB's inter-device reliability, and ability to assess COP in both static and dynamic conditions (Reed-Jones, 2014). The reason the WBB was utilised in the present study was due to its relatively low price and availability as compared to laboratory grade FPs. Given the overarching goal of the study is to explore the potential to incorporate postural stability into a dementia assessment, it is important to utilise equipment that could feasibly be implemented in a diagnostic capacity for cost and availability reasons.

Another example comes from Wikstrom (2012), who assessed forty-five recreationally active participants with lower extremity injuries to assess the reliability of the WBB. The study involved the participants completing a single-limb–stance task on a FP and the Star Excursion Balance Test during the first test session. Twelve Wii Fit balance activities were also completed during two test sessions separated by one week. Wikstrom reported finding that the Wii Fit balance activity scores had poor concurrent validity relative to COP outcomes. In addition, Wii Fit balance activity scores generally had poor intrasession and intersession reliability (Wikstrom et al., 2012).

It is well established that there is a negative relationship between aging and cognitive ability (Murman, 2015). However, in the present study, there was no effect of age on scores of cognitive functioning. One reason for this could be that the vast majority of participants reported being between the ages of eighteen and forty-five, and findings from previous research report that cognitive decline only begins around the age of forty-five (Singh-Manoux et al., 2012). No effect of age on any of the assessments, both cognitive and balance, add weight to the finding of a strong relationship between the two without these potential confounding factors influencing the results.

5.4.1 Methodological Considerations

In this study, participants were asked to wear sensible shoes and to keep their shoes on during the balance assessment. This was due to hygiene concerns. Previous research has shown that participants wearing athletic shoes exhibited less AP sway than barefoot participants, while ML sway remained unaffected (Smith et al., 2015). Given that the results of the current study indicate that AP sway is significantly related to a variety of cognitive domains, it may be useful in future to run a similar study with barefoot participants, in order to assess whether the relationship between postural stability and cognition is more pronounced under barefoot conditions. This is particularly important when considering balance assessment as a diagnostic tool for a cognitive impairment when accuracy of scoring is a priority.

Further methodological considerations include the ToD at which an individual at their optimal arousal alters with age (May, 2014). Previous research into ToD and cognition comes from Walters and Lesk (2015) who conducted a study on thirty-six older adult participants with a mean age of 72.53 (±6.09). Across two data sets that were analysed, significant ToD effects were seen in Pattern Comparison Speed, Letter Comparison Speed, a Trail Making Test, the MMSE, and the Graded Naming Test (GNT). They witnessed a decline in test scores as ToD increased. ToD effects have also been reported to hold influence over dynamic postural control in healthy populations (Gribble et al., 2007). However, Jorgensen et al. (2012) conducted research where thirty-four older adults were tasked with standing on a FP for thirty seconds which measured their sway behaviours. This was carried out at three points throughout the day: 9am, 12:30pm, and 4pm. It was found that there were significantly greater variations in sway behaviour between the readings taken at 12:30pm and the readings taken at 4pm. In the present study, no ToD effects were found. However, none of the participants in the present study were of the age specified in the research of Jorgensen et al. (men 72.9 ± 5.4, women 73.4 ±4.6) or Walters and Lesk (Jorgensen et al., 2012; Walters and Lesk, 2015). This could be considered as an area of additional research in future studies especially when considering assessing balance as a potential for diagnosing cognitive impairment in older adults.

Another methodological consideration should me made regarding other illnesses that may affect standing balance that were not specifically asked about in the exclusion criteria. For example, ear infections, vertigo, and travel sickness can all influence standing balance (Sabir et al., 2021; Balzanelli et al., 2021; Kumar et al., 2020.). While the present study only considered postural stability as a whole, future research may consider assessing whether factors such as these could influence the findings of the research.

Walters and Lesk (2015), also considered caffeine intake as a potential confounding variable. When controlling for caffeine, significant interactions were witnessed between caffeine, ToD and scores on the MMSE and the GNT (Walters and Lesk 2015). This would be useful to control for in future studies as Walters and Lesk (2015) have found caffeine to be a potential confounding variable for tests of cognition which is worthy of consideration. Previous research has found no significant relationship between caffeine and postural stability (Enriquez et al., 2009).

5.5 Conclusion

Poor postural stability has previously been associated with both AD (Visser, 1983) and MCI (Shin et al., 2011). In the present study, it was found that greater standard deviations in AP sway and poorer cognitive test scores showed a significant relationship in a group of cognitively-healthy participants. These findings present the potential to utilise postural sway assessments in order to improve the accuracy and reliability of diagnosis of cognitive impairment.

5.6 Highlights

- Abnormality in postural stability is associated with cognitive difficulties, including AD and MCI.
- The purpose of this study is to determine whether postural stability measurements are associated with cognitive functioning within a cognitively-healthy population.
- A sample of twenty-four cognitively-healthy individuals completed a balance task involving standing still for two minutes on a WBB, followed by a cognitive battery cognitive assessment.
- Results indicate that greater standard deviations in AP sway were significantly negatively associated with scores on tests of STM, LTM, BWM, and associative learning.
- These findings of a link between postural stability and cognitive function in cognitively-healthy participants have implications for clinical diagnostic processes in assessing a cognitive impairment such as AD. Future research is warranted in an older adult population and those with a cognitive impairment.

Chapter Six

The Effect of Posture Related Sports on Cognitive Functioning

Following the previous findings that AP sway shares a relationship with cognitive functioning (Chapter Five) this chapter builds on this by investigating whether sporting activities which have been reported to improve posture hold any influence over cognitive functioning. Previous research has shown a relationship between posture and cognitive functioning, (Szturm et al., 2013; Smith et al., 2019; Rosenbaum et al., 2017; Caron et al., 2020; Díez-Álamo et al., 2019; Peper et al., 2017), however, the relationship between posture-related sporting activities and their influence on cognitive functioning is less clear. The previous chapter looked at measuring posture in an experimental setting whereas this chapter looks at reporting of a person's general engagement in posture-related activity to see if the same effect is seen. If there is a positive effect of posture-related activities and cognitive function when measured this way it has the potential to have implications for public health.

6.1 Introduction

6.1.1 Posture and Cognition

In past decades, sportsmen were typically regarded in terms of their physical ability rather than their cognitive ability (Starkes, et al., 2001) and less research has been concerned with exploring cognitive factors which are involved in sports performance (Starkes et al., 2001). Postural control in static and dynamic situations is fundamental to participating in sporting activity. This requires the vertical projection of the centre of mass within the base of support by using specific shaping and positioning of the pelvis and spine (Tokur et al., 2020; Roussouly, 2020).

As such, it has been argued that humans are in a state of dual-tasking in every moment of daily life, as there is consistently some degree of cognition afforded to maintaining postural control (Rosenbaum et al., 2017). Previous research on postural control has revealed that maintaining a stable posture creates a variety of interactions with cognitive ability. For example, Szturm et al. (2013) conducted a study where twenty young, cognitively-healthy adults with no prior neurological impairment, musculoskeletal disorder, or medication which influenced their walking behaviour completed a visuospatial cognitive task in two conditions. These were (i) sitting, and (ii) walking on a treadmill. The visuospatial task utilised in this study was a computer-based game assessment called the Useful Field of View (UFOV). This assessment requires participants to select and ignore relevant and irrelevant information respectively (Ball et al., 2007). In this game, participants are tasked with moving an in-game paddle in order to 'catch' brightly coloured circles while ignoring triangles which move down the screen from top to bottom. The results reported that there was a significant decrease in cognitive performance on the UFOV while walking compared to sitting (Szturm et al., 2013). This concludes that divided attention while walking decreases performance in a visuospatial cognitive task, and that walking speed is an important consideration to make while assessing cognitive ability and its' relationship with locomotive rhythm.

Another example of the relationship between posture and cognition comes from Smith et al. (2019) who conducted a study to assess the extent to which posture can influence selective visual attention. In this study, fourteen participants completed a series of cognitive trials in both sitting and standing conditions. These cognitive trials included a Stroop task, a task-switching trial, and a visual search task. It was reported that the magnitude of Stroop interference was much lower in the standing condition than the sitting condition. It was also reported that the reduction in accuracy that occurs upon switching from one task to a different task instead of performing a subsequent task of the same design is reduced in the standing condition compared to the sitting condition. Finally, it was reported that participants searched a visual display more slowly when standing compared to sitting (Smith et al., 2019).

Furthermore, it has been reported that there are greater impairments in postural control when completing a spatial WM (SWM) task. Chen et al., (2018) conducted a study with the aim of exploring the neural mechanisms of spatial memory and non-spatial memory and their relationship with postural control. In this study, eighteen participants with normal or corrected-to-normal vision participated in a WM assessment where they would look at a fixation cross as a randomly selected English letter appeared on a screen in a randomly selected position. This served as a target stimulus. Subsequently, an interference stimulus in the form of separate letters were also shown. Finally, a probe stimulus letter was presented where the participants had to decide if it was a match or not. This took two forms. The first was a non-spatial WM (NWM) form, where participants had only to recall whether or not the probe stimulus was present. The second form was a SWM form wherein participants were also tasked with recalling the position of the target stimulus and whether or not the probe matched. While participants were completing this WM task, their COP trajectory was being tracked. It was reported that postural control reduced participants’ ability to discern the probe stimulus in the SWM trial, but did not affect performance on the NWM trial.

Posture has also been shown to influence memory recall and mood. Peper et al. (2017) conducted a study with a participant cohort of 216 college students who sat in either a slouched or erect position and asked to recall as many memories of hopelessness, helplessness, powerlessness, or defeat as possible, one after the other, for thirty seconds. Following this, they were asked to recall positive, optimistic, or empowering memories for thirty seconds. Participants would then switch to the other sitting position and were asked to repeat the process of first recalling negative memories, and then positive memories. Results showed that participants found it easier to recall negative memories in the slouched position and positive memories in the erect position (Peper et al., 2017). It was concluded that these findings hold implications for individuals receiving therapy to be cognisant of their posture (Peper et al., 2017), however, the question arises what other aspects of memory posture holds influence over.

To further investigate the effect of posture on recall, Díez-Álamo et al. (2019) conducted two experiments in order to explore contextual memory effects associated with body posture. In the first experiment, participants were tasked with adopting one of two postural stances, either sitting, or standing. They were then given a series of sentences to remember before being asked to recall the sentences in either the same postural stance that they received them in, or the opposite stance. Díez-Álamo et al. (2019) assumed that recall performance would be related to the body posture adopted during the encoding period, however, it was reported that there were no significant posture-dependant memory effects (Díez-Álamo et al., 2019).

Díez-Álamo et al. (2019) designed their second experiment to further explore whether posture could act as a “contextual modulator” for recollection. In this study, eighty-five participants were assigned to either sitting or standing conditions, while being given a series of actionable instructions, which were either congruent or incongruent to their condition. For example, to ‘ride a taxi’ was congruent with the sitting position whereas to ‘look in the post box’ was congruent with the standing condition. The theory was that participants would be more likely to recall the congruent actionable instructions to their posture condition during retrieval. However, similar to their first experiment, there were no significant posture-dependant memory effects (Díez-Álamo et al., 2019). These findings seem to contradict the findings of Peper et al., (2020), who reported that recall was influenced by posture, implying that there is a nuance in this relationship worth further investigation. Researchers have previously argued that the relationship between posture and attention has mainly been investigated in order to determine the effect of attention and cognition on the maintenance of posture, rather than the opposite (Rosenbaum et al., 2017).

To combat this, Rosenbaum et al. (2017) conducted a series of experiments on university undergraduate students with normal or corrected-to-normal vision, and no diagnosis of colour-blindness. Experiment one utilised a cohort of seventeen participants, where they were presented with a Stroop test consisting of seventy-two colour-word stimuli, with a 50/50 split of congruent to incongruent stimuli. Participants were asked to complete this test in two separate conditions - standing and sitting. Experiment two tasked sixteen participants with looking at a fixation cross on a screen. They would see an arrow either above or below the cross, and the arrows could either point upwards or downwards. Participants were tasked with declaring the direction of the arrow while ignoring spatial position. Similar to experiment one, there was a 50/50 split of congruent stimuli such as an upward arrow in the top position, to incongruent stimuli such as a downward arrow in the top position. Experiment three was run similarly to experiment one, but with extra care being taken to remove demand characteristics by keeping the experimenters blind to the hypothesis. Results showed that there was a significant relationship between reaction times of a Stroop test in congruent stimuli between the sitting and the standing conditions, where reaction times were lower in the standing condition. However, the sitting and standing conditions showed no significant interaction with incongruent Stroop stimuli. Rosenbaum et al. (2017) conclude by arguing that their findings demonstrate how body posture affects cognition and attention. This opens the door to additional avenues of research regarding the relationship witnessed between posture and cognitive functioning.

Following this, Caron et al. (2020) attempted to replicate the findings of Rosenbaum et al. (2017). This study consisted of a series of five experiments on university undergraduate students who reported normal or corrected-to-normal vision and normal colour vision. In experiment one participants completed a Stroop task in sitting and standing conditions. The experiment included congruent and incongruent stimuli, but also included 'neutral trials' which consisted of a series of three to five 'X's, matched to the number of letters and colour in the four colour words. These 'neutral' trials were absent from the research of Rosenbaum et al. (2017). However, this experiment failed to replicate the findings of Rosenbaum et al. (2017).

Experiment 2 was similar to experiment one, however, to more closely replicate the research of Rosenbaum et al. (2017), this time neutral trials were excluded. Again, this experiment did not demonstrate any influence of posture condition on the magnitude of the Stroop effect, asserting that this was due to the results that Rosenbaum et al. (2017) reported are less robust than the original report suggests (Caron et al., 2020).

Experiment three attempted to more closely replicate the conditions of the Rosenbaum et al. (2017) research by requiring the participants to use a keyboard to indicate their responses, instead of allowing vocal responses to the Stroop stimuli, which was permitted in the prior studies. Caron et al. (2020) reported no reliable influence of posture on performance, concurrent with the results of experiments one and two. Experiment four and Caron et al. (2020) manipulated posture conditions by having participants in the standing condition balance on one leg instead of two in order to exploit posture-related differences between the sitting and standing conditions. As previously, experiment four failed to produce evidence that posture influences the magnitude of the Stroop effect. Finally, experiment five aimed to more strictly replicate the methodology of Rosenbaum et al. (2017) by reducing the time between the trials from 2000ms to 1000ms. The reported results were consistent with the previous experiments; there was no effect of posture on the magnitude of a Stroop effect.

Overall, across each of the five experiments, Caron et al. (2020) reported a consistently strong Stroop effect in that performance was poorer on incongruent trials than on congruent trials. However, their data suggest there was no impact of posture on the magnitude of the Stroop effect. Moreover, they failed to replicate the findings of Rosenbaum et al. (2017). This opens additional avenues of research to explore in order in the discipline of posture and cognition; uncontrolled factors or variables such as individual differences in lifestyle choices may hold the explanation for these differing results.

The previous literature reviewed above implies that there exists a sensitive, albeit unclear relationship between posture and cognitive ability. However, as far as the researcher is aware, there are no studies which consider a participant's proclivity towards participation in posture-related sporting activities and whether this holds any influence on cognitive ability. This is an important area of study to consider, as if it is the case that propensity to take part in posture-related activity influences cognitive functioning, this may hold implications in a clinical and/or public capacity.

6.1.2 Aim of the Present Study

This study explores the relationship between posture and cognitive functioning further. The aim of the study was to evaluate whether participating in activities which require demanding levels of postural control can hold any influence over scores on tests of cognitive functioning. This may go some way towards explaining the contradictory findings that body posture affects cognition and attention (Rosenbaum et al. (2017) which was unable to be replicated in the five experiments of Caron et al. (2020). Further contradictions were seen between the findings of Peper (2017) who reported that posture influenced performance on a recall task, which were not replicated by Díez-Álamo et al. (2019). This was achieved by tasking participants with completing a self-report questionnaire on their posture-related sports activity, followed by a series of cognitive tests. Given that this thesis has the overarching aim of investigating non-invasive techniques to assess dementia, memory tests were chosen to look at in particular detail (Jacova et al., 2007). A reasoning test was also chosen as the previously mentioned literature was concerned with assessing attention (Rosenbaum et al., 2017; Caron et al., 2020). Previous research has established that the frontal lobe of the brain is responsible for both attention (Floden et al., 2011) and reasoning (Collins and Koechlin, 2012). Therefore, reasoning was used in this study.

As far as the researcher is aware, there have been no studies researching the effects of different posture-related activities on cognitive functioning.

6.2 Methods

6.2.1 Participants

The participant cohort consisted of forty-two participants of the following ages: 18-24 (n=7), 25-31 (n=3), 32-38 (n=8), 39-45 (n=4), 46-52 (n=4), 53-59 (n=4), 60+ (n=12). Participants had no existing neurological disorder or diagnosed postural condition, and all participants reported having a good understanding of the English language. The study was approved by the University of Bradford Humanities, Social and Health Sciences Research Ethics Panel and all participants provided informed consent. Regarding sample size, previous research into the relationship between sports and cognition has seen a variety of participant cohort sizes. In a study which explored the relationship between exercise and cognition in older adults Balsalobre-Fernández et al. (2019) utilised a participant cohort of 40. Whereas, in a study designed to explore the immediate effect of moderate-intensity exercise on cognitive performance Inoue et al. (2020) utilised twenty participants. Given this, the aim was for between twenty to forty participants to take part but more could take part if they were interested.

6.2.2 Posture Questionnaire

Posture was assessed using a self-report questionnaire which asked participants about their participation in posture-related activities (American Football, Ballet, Boxing, Clay Pigeon Shooting, Cycling, Diving, Football, Gymnastics, Handball, Horse Riding, Irish Dancing, Martial Arts, Pilates, Rock Climbing, Roller Boarding, Skateboarding Skiing, Snowboarding, Strength training, Stretching, Surfing, Swimming, Yoga), how often they participate in this activity (every day, five to six times a week, three to four times a week, one to two time(s) a week, several times a month, about once a month, several times a year, about once a year, never), and how much time they typically spend in a single session (over three hours, up to three hours, up to two hours, up to an hour, I do not participate in this activity). These sports were chosen due to the postural control required to participate in them.

6.2.3 Procedure

The present study was an online study. Individuals saw the advertisement and clicked on a link which took them to an onlinesurveys.ac.uk experiment. Participants were greeted by an introductory screen followed by a consent page. The study began with participants completing a self-report questionnaire on posture-related activities. Following this, participants were asked to participate in a series of cognitive assessments which consisted of word recall tasks, picture tasks, and tests of logical reasoning. Following the cognitive assessment, the participants were thanked, debriefed, and given the contact information of the researcher, for an opportunity to ask any questions they had, or if they wished to withdraw their results.

6.2.4 Cognitive Tests

The cognitive tests selected for this study were based on the findings of the previous study (Chapter Five). Given the aim of this thesis has an overall aim of providing new tools to improve the reliability and accuracy of paper assessments of dementia, testing different forms of memory was a priority. Reasoning was important as prior research has focussed more on attention, and the frontal lobe of the brain is responsible for both attention and reasoning (Floden et al., 2011; Collins and Koechlin, 2012). All cognitive tests were designed by the researcher.

6.2.4.1 Word Recall. STM was assessed by utilising a word recall task (Coltheart, 1981). This task required participants to listen to a series of fifteen words which were controlled for imageability and familiarity, generated by the MRC Psycholinguistics database (Coltheart, 1981). The participants saw a video where each of these words would briefly appear on a screen for two seconds each. After this, participants saw a fixation cross for three seconds, and then the entire list played over. Following this, participants were asked to type out as many words as they could remember, and were given one point for each word correctly recalled. This was also used as a LTM assessment. After the participants had completed the other cognitive assessments, they were asked to recall as many words from the word list as they could. As for the short-term memory assessment, they were given one point for each word correctly recalled.

6.2.4.2 Picture Tasks. The picture tasks required participants to watch three separate videos containing static images of animals, plants, and shapes. Following this, participants were asked a series of questions about the content of the images. For example, some questions asked about the number of animals in each picture, or the particular colour of each shape. Participants were awarded one point for each correct answer out of a possible 15.

6.2.4.3 Reasoning. The reasoning tasks required participants to read a statement and indicate with a yes or no answer whether the statement makes logical sense. This involved the utilisation of four separate logical fallacies: (i) Affirming the Consequent: this is the action of taking a true statement and fallaciously concluding the inverse (Gaul, 2018); (ii) Denying the Antecedent: this is the action of fallaciously inferring from the inverse that an original statement is valid (Gaul, 2018); (iii) Modus Ponens: This is the action of taking a general truth and inferring a subsequent proposition is valid (Gaul, 2018); (iv) Modus Tollens: this is the action of taking a general truth, and concluding that if the original statement is true, then so must be the contrapositive (Gaul, 2018). Participants were awarded one point per correct answer out of a possible 10

6.2.5 Data Analysis

A MANCOVA was run to compare each participant's questionnaire responses with their scores on the cognitive tests. Posture related sporting activity participation was measured using a self-report questionnaire. Age effects were analysed to determine the effect of age on both cognitive performance and posture related sporting activity participation.

6.3 Results

Given that previous research demonstrates contradictions into the effects of posture on cognition which could be because of external factors which may influence an individual's postural stability, such as posture-related exercise, the aim of the present study was to explore the relationship between participation in posture-related activities and their impact on cognitive functioning. The data were normally distributed.

See Table 5 for the descriptive statistics on the sports that participants took part in, Table 6 for the descriptive statistics for the amount of time spent participating in a single session of each sport and Table 7 for scores on the cognitive assessments.

Table 5 Descriptive statistics for the sports that participants take part in including the minimum, maximum, mean, and mode

Sport	N	Min	Max	Mean	Mode
Cycling	22	Never	3-4 Times a week	Several times a year	Never
Football (European)	10	Never	1-2 Time(s) a week	About once a year	Never
Pilates	9	Never	1-2 Time(s) a week	About once a year	Never
Strength Training	17	Never	1-2 Time(s) a week	Several times a year	Never
Stretching	33	Never	Every day	1-2 Times a week	Never
Swimming	37	Never	3-4 Times a week	About once a month	Never
Yoga	9	Never	Every day	About once a year	Never

Table 5 shows the descriptive statistics for the sparts that the participants reported participated in, including the minimum, maximum, and mean.

Table 6 Descriptive statistics for the amount of time spent participating in a single session of each sport.

Sport	N	Min	Max	Mean
Cycling	22	N/A	Up to 3 hours	Up to an hour
Football (European)	10	N/A	Over 3 hours	Up to an hour
Pilates	9	N/A	Up to 1 hour	Up to an hour
Strength Training	17	N/A	Up to 2 hours	Up to an hour
Stretching	33	N/A	Up to 2 hours	Up to an hour
Swimming	37	N/A	Up to 3 hours	Up to 2 hours
Yoga	9	N/A	Up to 3 hours	Up to an hour

Table 6 shows the descriptive statistics for the amount of time spent participating in a single session of each sport, including the minimum, maximum, and mean.

Table 7 The mean and standard deviations (SDs) for each cognitive assessment

Test	Min	Max	Mean	SD (+/-)
Word Recall (STM)	0.00	11.00	4.98	2.82
Word Recall (LTM)	0.00	10.00	3.67	2.65
Picture Tasks	1.00	15.00	7.81	2.95
Reasoning	4.00	10.00	8.17	1.50

Table 7 shows the descriptive statistics for the cognitive assessments including the minimum score, maximum score, mean score, and SD.

There can be significant effects of age and gender on scores of cognitive assessments (Jacova et al., 2007, Fields et al., 2011), and it has also been found that participation in physical activity decreases with age (Davison and Cowan, 2020). Furthermore, it has been shown that ToD may influence results on cognitive assessments (Walters and Lesk, 2015). Therefore, to investigate these potential confounding factors in the first instance, three separate MANCOVA analyses were carried out on the age group, ToD of participation, and the number of sports that a participant took part in against cognitive assessment scores. The MANCOVA analyses returned a non-significant Wilk's Λ analysis for ToD effects ($F(2, 39) = 0.77$, $p > .05$; Wilk's Λ = 0.96, partial η2 = 0.04). However, significant effects of both age group ($F(2, 39) = 3.52$, $p < .05$; Wilk's Λ = 0.85, partial η2 = 0.15) and the number of sports participated in ($F(2, 39) = 3.77$, $p < .05$; Wilk's Λ = 0.84, partial η2 = 0.16) were found. Therefore, interaction effects were investigated between age group x the number of sports participated on cognitive test scores. No significant interaction effects were found ($F(2, 39) = 0.46$, p = > 0.05, Wilk's Λ = 0.98, partial η2 = 0.02).

Individual sports were only considered for analysis if five or more respondents reported participating in that particular sport in any capacity. MANCOVAs were run on individual sports as the covariates and composite memory score and reasoning score as dependant variables, however, no significant relationship was found between any individual sport and cognitive functioning. A general linear model MANCOVA was run to compare the number of sporting activities each participant reported taking part in against scores on tests of cognitive functioning. As the current study is concerned with exploring the relationship between posture-related sporting behaviour and cognitive ability, summed memory test scores and the total reasoning score were entered as the dependant variables, with posture related sporting behaviour entered as covariates. The MANCOVA was significant with $F(2, 39) = 3.77$, $p < .05$, partial $\eta 2 = 0.16$. Parameter estimates confirm a linear, positive relationship between the number of sports participated in and summed memory scores (B=1.40, SE=0.56, t=2.51, $p < .05$, 95%CI [0.27, 2.52]). However, reasoning scores were non-significant ($F(2, 39) = 2.50$, $p > .05$, partial $\eta 2 = 0.06$). See Figure 3 for a graph demonstrating the linear relationship between the number of sports that participants took part in against composite memory scores.

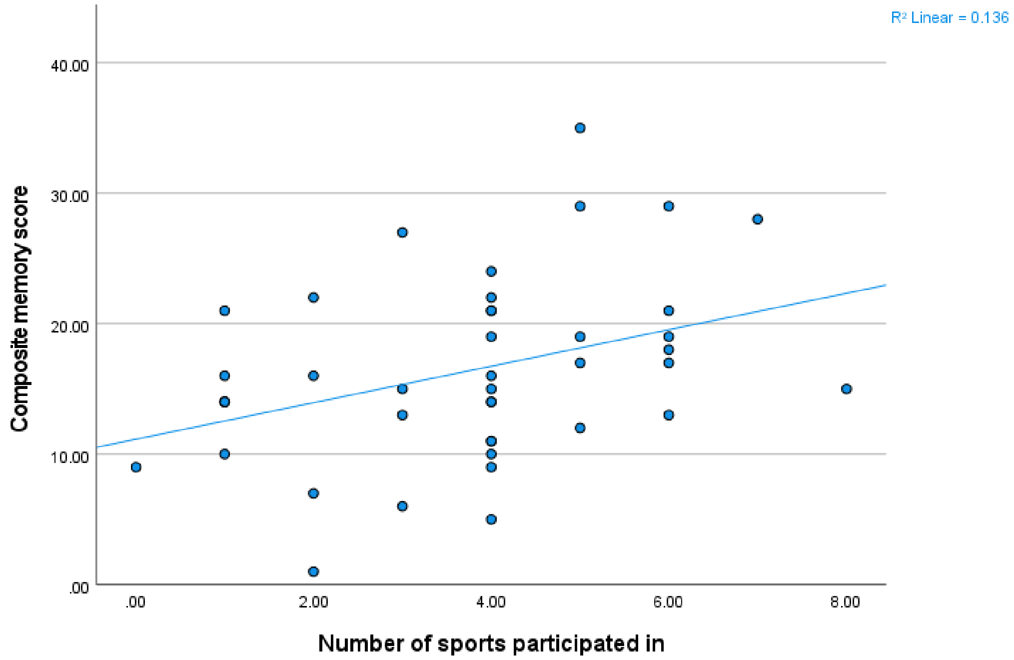


Figure 3 scatter plot demonstrating the relationship between the number of sports that participants took part in against composite memory scores. The scatter plots show a significant linear increase in composite memory scores as the number of sports participated in increases.

Overall, these results show a significant, linear, positive relationship between scores on memory assessments and participation in a greater variety of posture-related sporting activities. Following this, a MANCOVA was run in order to assess the relationship between cognitive functioning and the amount of time spent participating in a single session of each sport. However, no significant relationship was observed.

6.4 Discussion

Previous research has produced conflicting findings regarding the relationship between posture and attentional tasks (Rosenbaum et al., 2017; Caron et al., 2020). A similar contradiction has been seen in the relationship between posture and recall (Díez-Álamo et al., 2019; peper et al., 2017). However, no prior studies considered the effects that may occur in posture from participating in posture-related sporting activities, and whether high levels of participation in these sports may influence cognitive functioning. The aim of the present study was to explore this conflict and evaluate whether participating in posture-related sporting activities held any influence over scores on tests of cognitive functioning. The results demonstrated that individuals who participated in a greater number of posture-related sporting activities performed better in assessments of memory than those who participated in fewer. There was no effect on reasoning ability. However, no individual sporting activity demonstrated a significant relationship with scores on other cognitive assessments, nor did amount of time spent taking part.

The research of Rosenbaum et al. (2017) determined that there exists a relationship between posture and cognition as participants in a standing condition performed significantly better on a Stroop task than participants in a sitting condition. However, these findings have been contradicted by Caron et al. (2020) who conducted a series of four experiments attempting to replicate these findings unsuccessfully. The differences in these results suggests the possible existence of confounding variables which previous studies have not controlled for. The results seen in the present study could go some way to explaining the conflicting findings of Rosenbaum et al. (2017) and Caron et al. (2020), as each participant's sporting activity could have influenced their cognitive ability.

The present findings that sporting activities influence memory can be contrasted against previous research from Sánchez-Horcajo et al. (2015), who assessed the relationship between aerobic exercise and spatial orientation in adults and older men. In this study, participants were split into two categories: sportsmen and sedentary. When given a virtual reality spatial orientation task, it was found that sportsmen performed better than the sedentary participants. There is potential that the same mechanisms are at play between sportsman performing better in a spatial orientation trial and the present findings that the greater the number of sports that participants take part in relates to improved scores on memory assessments.

Our study furthers these findings by exclusively considering sports which have been found to particularly improve posture and showing that there is a relationship between participation in these sports and memory performance. For example, one mechanism which may be contributing to the relationship between sports and cognitive functioning may be noradrenaline release. Previous research has demonstrated that noradrenaline can facilitate and enhance memory consolidation, which is released when participating in aerobic exercise (Segal et al., 2012). Furthermore, it has been shown that in the case of twenty-four participants suffering from type-two diabetes, there is a significant reduction in plasma-noradrenaline when transferring from a period of prolonged sitting to light walking or simple resistance activities such as half-squats, calf raises, knee raises, and gluteal contractions (Dempsey et al., 2016). The relationship between noradrenaline and cognition may somewhat explain the findings of Szturm et al. (2013) that cognitive performance was worse when walking compared to sitting. However, this contradicts the findings of Segal, Cotman, and Cahill, (2012) who argued that noradrenaline can enhance memory consolidation. It could be the case that acute noradrenaline release has adverse effects on cognition, whereas prolonged release over time may be beneficial.

There is currently a dearth of research which considers posture related exercise and noradrenaline; however, the results of the current study suggest a positive relationship between posture-related activities and cognitive functioning, which warrants further investigation in order to ascertain whether noradrenaline plays a substantial role in this relationship. It is worth noting though that the findings of the present study failed to reveal a significant relationship between any single sport and cognitive functioning, regardless of the aerobic intensity of the sport. More heavily aerobic based sports should be considered for future research to explore whether such a relationship exists.

Furthermore, previous research has argued that participating in sports benefits cognition in other ways. In a meta-analysis, Furley and Wood (2016) explored the role of WM, attentional control, and expertise in sports. They concluded that that WM is a valuable tool to aid in the understanding human cognition and functioning in sporting environments, arguing that WM theory may be utilised in conducting research in a variety of settings and can inform evidence-based practice in sports. In a review of literature, Afonso et al. (2012) conducted a meta-analysis on attention, anticipation, and memory and their impact on decision-making in sports, concluding that memory provides a basis for attention and anticipation, while supporting intuitive and strategic thinking. This supports the findings of the present study and may explain why those who participated in a greater number of sports may have performed better on assessments of memory.

This study also highlighted that older individuals participated in fewer sports overall compared to younger individuals. To explore the influence that aging holds over postural stability Borel and Alescio-Lautier (2014) conducted a meta-analysis on the effects of aging on sensory systems and their impact on posture, balance, and gait, noting that cognitive training can improve performance on dual task management in older adults (Borel and Alescio-Lautier, 2014). This relationship between cognitive training and improving performance on dual tasks in older adults may go some way to explaining the witnessed findings that there is a relationship between cognitive ability, and participation in a variety of sport. However, further research is warranted to explore this relationship in the young-adult population to assess universality. Additional future studies may consider assessing memory capacity of sportsmen and non-sportsmen in order to assess the sensitivity of a potential interaction between participation in sports and cognitive functioning.

The findings of the present study may explain some of the findings of Chapter Five, which highlighted a sensitive, negative relationship between AP sway and cognitive functioning. It may be the case that participating in a variety of posture related sporting activity also assists postural stability, thus reducing AP and ML sway. This relationship warrants further investigation as there are potential applications of participating in sporting activities in order to maintain and improve cognitive health. Moreover, while the study of Chapter Five suggested the strength of this relationship in an experimental environment, the results of the present study build upon the prior findings by identifying a practical context wherein this relationship can still be witnessed. It was important to be able to expand the findings of the previous chapter into a practical, real-life environment. Moreover, these findings offer much greater ecological validity than can be afforded by a controlled lab-based experiment of postural stability measured by a WBB.

Whilst there was no age x sports activities interaction, an individual's age holds influence over the ToD at which they are at their optimal arousal (Hasher et al., 2005). Previous research into ToD and cognitive functioning from Walters and Lesk (2015) reported that in a study involving thirty-six older adults (mean age 72.53 ±6.09), ToD effects were found in tests of Pattern Comparison Speed, Letter Comparison Speed, a Trail Making Test, the MMSE, and the GNT. No ToD effects were witnessed in the present study; the exact reason for this is unclear, however a potential reason for this could be that this was an online study to be completed at each participant's leisure therefore the participant could have chosen to participate at their personal optimal arousal. Furthermore, Walters and Lesk (2015) have reported significant interactions between caffeine consumption and age on cognitive test scores. Caffeine consumption was not controlled in the present study and could be a potential confounding variable to address in future studies.

Methodological considerations should be made regarding overall participant fitness. In this present study, overall fitness was not controlled for. It may be reasonable to assume that individuals who reported participating in a greater number of sports, and spending more time participating in each sport would be generally more fit, however, this may not necessarily be the case. Previous research from Kennedy et al. (2018) investigated the relationship between fitness and cognition in an older adult population by providing 102 participants with a cognitive battery to assess cognition and a six-minute walk test to assess fitness. It was reported that greater fitness predicted greater performance on spatial working memory (Kennedy et al., 2018).

Further research into the relationship between fitness and cognition comes from Pentikäinen et al. (2019) who conducted a longitudinal study with the aim of assessing the relationship between cardiorespiratory fitness and cognitive performance in an older adult population. In a study of 421 individuals between the ages of sixty-seventy-seven, participants were tasked with a completing a cycling exercise task in order to assess cardiorespiratory fitness, followed by a cognitive battery assessment. After a twenty-four-month period, the participants were given the same tests again. It was reported that better cardiorespiratory fitness performance was associated with higher scores on tests of executive function, processing speed, and overall cognitive function.

The previously discussed research into the relationship between fitness and cognition were specifically concerned with an older adult population. However, the present study utilised a varied participant population with a greater proportion of younger adults. Previous research into the relationship between fitness and cognition in a which also considers younger adults comes from Stern et al. (2019) who conducted a community based clinical trial on 132 participants between the ages of twenty-sixty-seven. These participants were assigned to one of two groups. The first group would participate in aerobic exercise, whereas the second group would participate in stretching sessions. These sessions occurred four times a week over a period of six months. Participants would also complete a series of cognitive assessments. It was reported that the aerobic group presented significantly improved executive functioning scores than baseline, whereas this improvement was not witnessed within the stretching group. Moreover, the improved performance on the executive functioning task was more pronounced as age increased (Stern et al., 2019). This discussed literature around the relationship between fitness and cognition highlights how future research may consider asking participants about their general health, as well as which sports they participate in, and how long for.

Further methodological considerations must be made regarding the use of survey data and its' accuracy. Many people currently believe that online data collection is a boon to many domains of research, due to the ease and speed of data collection, as well as allowing for larger and more diverse participant populations (Latkovikj and Popovska, 2020). This, in turn, leads to greater statistical power, a reduced financial cost of conducting research, less wasted materials such as paper, and no need for face-to-face interactions (Latkovikj and Popovska, 2020).

However, there are also long-established limitations to consider while utilising self-report survey data as a methodology. One well known limitation is that of social desirability bias. For perceptibly moral behaviours, it is likely that people bias their responses in surveys to signal a more desirable social impression of themselves (Kaiser et al., 1999). As such, social desirability is regularly considered as a confounding variable in psychological research (Cerri et al., 2019). In order to explore the influence of social desirability bias in survey data regarding environmentalism, Vesely and Klöckner (2020) conducted a series of three meta-analyses based on twenty-nine previously published papers. From these papers, it was reported that correlations between social desirability and pro-environmental behaviours/intentions was relatively small, with correlations ranging between 0.06-0.11 (Vesely and Klöckner, 2020). However, it is concluded that this does not mean that social desirability should simply be ignored, as scales of social desirability are in their relative infancy, and too few studies exist to make such a claim (Vesely and Klöckner, 2020).

While previous research has reported that exercise can be overreported in survey-based studies on fitness (Brenner and DeLamater, 2014), it is difficult to know how this may have impacted the present study, as individuals who reported participating in more studies performed better on memory assessments.

Social desirability bias is not the only limitation of online survey data, however. As reported by (Latkovikj and Popovska, 2020), further limitations include questionable accuracy of some online sources, a requirement for internet access, issues with accessibility and/or financial costs of some online databases, account requirements for participants, knowledge of artificial intelligence, low motivation for continued participation, and unreliable answers (Latkovikj and Popovska., 2020).

Further research may consider assessing the relationship between sporting participation and cognition in a longitudinal study wherein participation in sporting activity may be witnessed, in order to assess whether the present findings were influenced by social desirability bias, or any of the other discussed limitations of utilising an online-survey methodology.

Our results suggest that there exists a relationship between posture and memory and that external factors, such as the variety of posture-related sports that an individual participates in, may affect the results of memory assessments. Further investigation and iteration in future studies is warranted in order to investigate this relationship. It is also important to generate a control group who do not participate in any sporting activities at all in order to compare results against and as stated earlier, looking at any influence of aerobic exercise should be considered. Furthermore, future research could consider a greater number and variety of sports in order to generate a more robust understanding of the relationship between sporting activity and cognitive functioning. Considering the impetus of this thesis is to explore non-invasive factors which may hold the potential to improve the accuracy of dementia diagnoses, further research might consider looking into the sporting behaviour and cognition of individuals suffering from dementia in order to gain a greater understanding of this phenomenon.

One methodological consideration worth making regards the specific sporting activities which were assessed in the online questionnaire. Given the study aims, this study was more focussed on specifically sporting activities with a posture related element. However, given that there is an established relationship between participation in sports and cognition (Pentikäinen et al., 2019; Stern et al., 2019; Kennedy et al., 2018), it may be relevant for future studies to consider asking about a wider variety of sporting activities in general, rather than posture related sporting activities specifically, in order to see if the same relationships may be witnessed.

6.5 Conclusion

Previous research into posture and cognitive functioning has yielded conflicting results. In this study, there was a significant relationship found between the number of posture-related sports that an individual participates in and scores achieved on memory assessments. Future study should investigate these findings against control groups in order to ascertain the sensitivity of this relationship. These results may hold applications for cognitive brain health and physical activity in particular those activities that have a strong posture element.

6.6 Highlights

- If differences are found to exist between participation in a variety of posture-related sports and cognitive functioning ability, this may prove to hold significant implications for cognitive health.

- The previous chapter highlighted a relationship between AP sway and cognitive functioning.

- The purpose of this study was to explore the relationship between a variety of posture-related sporting activities and their influence on cognitive functioning.

- This was an online study which utilised a self-report questionnaire in order to assess participants' sporting activity behaviour followed by memory and reasoning tests.

- It was found that participation in a greater variety of posture-related sporting activities was positively related to compound memory scores generated from the previously mentioned cognitive assessments.

- No affect was found for posture-related sporting activities and reasoning.

- These results expand upon the findings in Chapter five, and may hold applications in terms of making lifestyle changes to help maintain cognitive health.
- Future research should investigate whether this relationship can be witnessed in a greater number of participants, as well as a control group to assess the findings against. Furthermore, the role of sporting behaviour and cognitive functioning in individuals suffering from dementia should be considered.

Chapter Seven

Negative Facial Expressions Share a Positive Relationship with Cognitive Functioning

7.1 Introduction

While Chapters Five and Six discussed the effects of posture and cognitive function, this chapter considers a different non-invasive technique of assessing cognition, namely facial cues, which may have the potential to be utilised in a diagnostic capacity. Previous research has shown conflicting results in facial cues displayed by individuals suffering from AD. Some findings have demonstrated that dementia patients produce more facial expressions of negative emotions (Asplund et al., 1995; Smith, 1995) whereas others argue that AD patients present fewer recognisable expressions (Seidl et al., 2008; 2012). However, the relationships between facial cues and cognitive functioning in cognitively-healthy participants remain relatively unexplored. Given the overarching aim of the thesis is to look at techniques that can potentially be used for early diagnosis of a cognitive impairment i.e. when people are still performing at a normal level, as for all studies in this thesis, obtaining normative information on a cognitively-healthy population is the first step.

7.1.1 Background

Emotions are defined as patterns of automatic behavioural and hormonal responses which assist with survival, and result from external cues, bodily signals, and cognitive processes all working in tandem (Dolensek et al., 2020). Emotions, particularly facial expressions, are adaptive social and communicative tools which vary according to specific social contexts and differ across different cultures (Erickson and Schulkin, 2003; Cowen et al., 2021).

In a historical context, the study of facial expressions can be traced back to Charles Darwin, who, in 1872, wrote one half of one chapter entitled 'The Expression of Emotion in Man and Animals' (Darwin, 1872). In this manuscript, Darwin hypothesised the existence of innate survival-related functions of emotion expressions, rooted in a shared evolutionary heritage with other animals (Darwin, 1872). It has been argued that if Darwin is the progenitor of emotional expression research, that one could consider the second chapter of emotional expression research to be the cross-cultural exploration of emotion recognition led by Ekman and colleagues (Shariff and Tracy, 2011). In order to explore Darwin's (1872) hypothesis of innate emotions, Ekman et al. (1969) conducted a series of studies across New Guinea, Borneo, The United States, Brazil, and Japan. In this series of studies, thirty photographs were selected which presented one of six emotions: (i) happiness, (ii) surprise, (iii) fear, (iv) anger, (v) disgust-contempt, and (vi) sadness.

These would later come to be known as the six basic emotions (Kowalska and Wróbel, 2017). These photographs were transferred to projector slides and shown to participants for twenty seconds who were tasked with identifying which of the six emotions they were viewing. Similar recognition rates were reported for happiness, anger and fear in all participant groups, and for disgust, surprise, and sadness in two out of three participant groups. Furthermore, an emotional category was never misidentified by the majority of observers in more than one non-literate group of participants. The conclusion was drawn that the hypothesised pan-cultural elements in human emotion appeared to be largely supported (Ekman et al., 1969), but that more evidence was warranted (Ekman et al., 1969).

In order to further their finding, Ekman and Freisen (1971) conducted a study where 189 New Guinean adults and 130 New Guinean children, who did not speak English, and who had minimal opportunity to learn, imitate, or recognize Western facial expressions were read stories which corresponded to one emotion. For example, a ‘happy’ story was “His friends came over, and he is happy” whereas a ‘sad’ story was “His child has died, and now he feels very sad”. Following this, the New Guineans were presented with a series of pictures with each containing one of the six basic emotions identified previously. The participants were asked to identify the picture which displayed an emotion which was appropriate to the story. Results showed that both adults and children could accurately identify the correct facial expression which corresponded to the story they had heard. This supported the hypothesis that specific facial expressions are universally associated with specific emotions, regardless of language and culture (Ekman and Freisen 1971).

Some years later, Ekman et al. (1987) identified three limitations with their previous cross-cultural research. Firstly, the study had not been replicated, raising concerns with test-retest reliability. Secondly, not all six emotions that were portrayed were recognised accurately. American observers could not distinguish fear from surprise in New Guineans (Ekman et al., 1987). Finally, the faces used in the prior research were posed, not spontaneous. Researchers in the meantime had argued that, while posed facial expressions were seemingly universal, this was not necessarily the case for spontaneous facial expressions (Mead, 1975). In order to address these self-identified limitations, Ekman et al. (1987) conducted a follow-up study where college students across ten English-speaking and non-English-speaking, Western and Non-Western cultures (breakdown: Estonia (n=85), Germany (n=67), Greece (n=61), Hong Kong (n=29), Italy (n=40), Japan (n=98), Scotland (n=42), Sumatra (n=36), Turkey (n=64), and the United States (n=30)) participated in a more complex facial expression judgment task than was utilised in the work of Ekman et al. (1971).

In contrast to the previous study, participants were not limited to selecting only one emotion term per expression. Instead, they were permitted to identify multiple emotions, as well as the intensity of each emotion. Participants were gathered into groups and shown projection slides containing individual faces which were demonstrating a particular emotion for ten seconds. During this time, participants were instructed by observers to refer to their answer sheets and indicate their judgement of the emotion that was on display. Following this, participants were informed that the images may display multiple emotions and of differing strength before being shown the slides again. Upon second viewing, participants were tasked with indicating whether each emotion was present, or absent, and to indicate the strength of the emotion. Results showed a consistent and robust agreement across different cultures in identifying and interpreting expressions of emotion, while also identifying that there was strong agreement across cultures regarding the intensity of emotion in each given image, although there was some evidence that individuals would attribute a lower emotional intensity score to faces which they perceived as foreign (Ekman et al., 1987).

The historic research conducted by Ekman and colleagues solidified the understanding of the six basic emotions which are present and understandable irrespective of cultural influence, and are still the most widely accepted candidates for basic emotion today (Kowalska and Wróbel, 2017). With these basic emotions established, the doorway was opened to investigate the underlying mechanisms of these emotions, and how they interact with cognition.

7.1.2 Emotions and Cognition

Prior to the discovery of the basic emotions that are universal across cultures, research was already being conducted to understand the underlying mechanisms behind the cognition of emotion. Schacter and Singer (1962) developed a 'two-factor' theory of cognition which asserts that two mechanisms interact when a situation elicits an emotional response from an individual. Firstly, the sympathetic nervous system is aroused, and secondly, the cognition of the individual interoperates this arousal, depending on the context (Schacter and Singer, 1962). Appraisal theory (Schacter and Singer, 1962) argues that emotions are a response of this two-factor model wherein an individual performs an 'appraisal' of the situation (for example, "Is this situation a threat?") which results in the appropriate emotions being displayed. It has been argued that appraisal theories emphasise the importance of context in emotional processing, while eliminating any form of defined line between perception, emotion, or cognition (Seth and Tsakiris, 2018).

In the years that followed, research linked difficulties in generating and understanding facial expressions with a variety of mental health conditions, including schizophrenia (Mandal et al., 1998), dementia (Asplund et al., 1991; Seidl et al., 2008), AD (Arroyo-Anlló et al., 2021), and autistic spectrum disorder (Drimalla et al., 2021; Keating et al., 2021). From these relationships we can infer that there is a sensitive relationship between emotion and cognition. Similarly, yet conversely, alexithymia is a condition defined as the inability to identify and express emotions, consisting of four cognitive deficits; (i) in identifying feelings in themselves, (ii) describing feelings in others, (iii) externally oriented thinking, and (iv) limited capacity for imagination (Arroyo-Anlló et al., 2021). As with the previously mentioned mental illnesses, previous studies have observed that alexithymia is related to poorer performance of cognitive assessments (Arroyo-Anlló et al., 2021). In AD, facial expressions, and non-verbal communication in general becomes of increasing importance in caregiver-patient interactions, as the ability to communicate verbally degenerates in line with the illness (Seidl et al., 2012). However, little is known of the changes in facial expressions caused by AD (Seidl et al., 2012).

7.1.3 Facial Expressions and Dementia

Research regarding the relationship between dementia and facial expressions has yielded interesting and contradictory findings worthy of exploration (Asplund et al., 1991; 1995; Smith, 1995; Seidl et al., 2008; 2012). It has been found that individuals with severe dementia showed fewer facial expressions which could be recognised as a clear emotion, instead displaying only fragmentary expressions which were devoid of complex patterns, such as slight movements and changes in the face (Asplund et al., 1991). These results were furthered by research which found that individuals with dementia show an increased likelihood in producing a negative facial expression, such as sadness, disgust, or anger, when exposed to sad stimuli in pre-recorded pleasant or unpleasant video stimuli, compared to controls (Asplund et al., 1995). Similarly, Smith (1995) conducted research on thirteen individuals suffering from mild AD. Participants saw a series of 10-second clips showing a range of emotions and facial cues, some with sound and some without. Individuals with mild AD as compared to controls, demonstrated a disproportionate negative reaction towards the sad vignette, as well as demonstrating a much greater number of recognisable facial expressions during sad vignettes compared to controls, suggesting reduced control over negative emotions. The pattern of results thus far indicates that as degeneration proceeds, recognisable facial expressions become increasingly severely impaired.

The findings of Asplund et al. (1995) and Smith (1995) have been contradicted, however. Seidl et al. (2008) conducted a study where fifty-eight German nursing home residents with dementia participated in a population-based study on quality of life. In the study, each participant was shown a series of positive, negative, and neutral stimuli. Throughout the study, facial expressions were recorded on video. The video was then analysed. Results demonstrated that overall neuropsychological symptoms were not significantly associated with any particular facial expression, but instead with an apathetic expression which could not be clearly identified (Seidl et al., 2008).

Further research into the interaction between facial expressions and AD comes from Seidl et al. (2012) who conducted a study to investigate the apathetic facial expressions mentioned above by assessing forty-seven nursing home residents who were diagnosed with 'Probable AD' by the National Institute of Neurological and Communicative Diseases and Stroke/AD and Related Disorders Association. In this study, each participant was shown a series of ten images, either positive, negative, or neutral designed to either elicit an emotional reaction, or not. The participants saw each picture twice, firstly on their own, and secondly following on from a neutral face. Both times, participants had their faces videotaped. Seidl et al. (2012) reported three findings. Firstly, they found that apathy influences the observable impact that cognitive deficits have on facial expressions. Secondly, after controlling for apathetic facial expressions, cognitive deficits were associated with higher rates of displaying recognisable facial expressions. And finally, that apathy is significantly negatively correlated with displaying any facial expression. This research, particularly the findings on apathy, may go some way towards explaining the previous contradictory findings of Asplund et al. (1995) and Smith (1995) who reported that individuals with dementia had an increased likelihood of presenting a negative facial expression, whereas Seidl et al. (2008) reported participants with dementia were less likely to show any kind of recognisable facial expression.

In an attempt to understand the underlying mechanisms behind the presentation of emotions in AD, Burton and Kaszniak (2006) measured the emotional experiences and facial muscle activity of thirteen AD patients and twenty-one cognitively-healthy, age-matched controls. In this study, participants were tasked with looking at emotion-eliciting images, similar to previous studies. In this study, however, facial electromyographic (EMG) recordings were utilised in order to generate the data. It was reported that zygomatic activity (activation of a muscle group in the face which is associated with smiling (Larsen, Norris, and Cacioppo, 2003)) showed a significantly different, inverted pattern of activity between AD patients and controls. This may identify the exact underlying mechanism behind the changes in facial expressions between AD patients and healthy controls. Similar physiological responses to positive, negative, and neutral stimuli have also been found in FTD (Kumfor et al., 2019) demonstrating that this is a relationship which can be seen to exist across separate dementia subtypes. However, it is unclear whether this is a change which can be seen in the early stages of AD, FTD, or other dementias; and with respect to diagnosis, imaging technology is not used as often as paper-based assessments of dementia such as the MMSE (Marshall, 2018).

Given that paper-based assessments of dementia are standardised cognitive assessments, it begs the question whether the relationships seen between dementia and facial expressions can also be seen in cognitively-healthy controls. However, to the researcher's knowledge, the relationship between generating facial expressions of emotions and cognitive functioning has yet to be assessed within cognitively-healthy populations. Previous research has focussed on the ability of the cognitively-healthy to recognise facial expressions in others (Gollan et al., 2010; Horning et al., 2012; Alves, 2013). For example, Gollan et al. (2010) conducted a study where photographs of facial expressions of varying emotional intensities were utilised in order to determine discrimination accuracy in participants with major depression compared against controls. It was reported that individuals with depression showed very good recognition accuracy for sad faces but impaired recognition accuracy for other emotions compared to controls (Gollan et al., 2010).

Additional previous research into facial recognition and cognitive functioning comes from Horning et al. (2012), who conducted a study to assess the changes in expression recognition accuracy and sensitivity in ageing over the course of a lifetime. This was accomplished by participants completing a facial expression recognition task, which involved thirty-six trials. In these trials, participants were shown dynamic facial photographs of both men and women displaying a neutral face, which would then morph into one of the six basic emotions: fear, anger, sadness, disgust, surprise, and happiness. Participants were tasked with (i) identifying which emotion the neutral face had morphed into, and (ii) completing a series of cognitive trials assessing fluid intelligence, processing speed and memory. It was reported that the ability to accurately identify a facial expression was most accurate in middle-aged participants, with children and older adults being reported as the least accurate. It was also reported that cognitive functioning has a greater influence for adults aged forty-six and older on the accuracy trials, whereas cognitive functioning has a greater influence for adults aged twenty-five and older for the sensitivity trials. It is argued that this relationship suggests that emotion perception develops independently of cognition (Horning et al., 2012). While the findings of Horning et al. (2012) suggest that the recognition of emotion exists separately to cognitive functioning, less is known about the production of facial expressions and their relationship with cognitive functioning.

In a meta-analysis of studies regarding facial expression recognition and cognition, Alves (2013) analysed eleven papers on the subject published between 1993-2011. It was reported that recordings of facial expressions in motion improved the participants' ability to recognise the emotions which were on display. Furthermore, dynamic expressions tended to elicit a more intense response of the participant mimicking the face, resulting in greater neuronal activation. Alves (2013) concludes by arguing that studies which utilise dynamic facial expressions hold more ecological validity than studies which utilise static facial expressions, thus making dynamic facial expression studies a more appropriate method in research regarding emotion (Alves, 2013).

7.1.4 Aim of the Study

The aim of the present study was to explore the relationship between facial cues and cognitive functioning in a cognitively-healthy population. If an overarching aim in future work is to investigate this as a potential tool for diagnosis, and when people are at a stage when they do not show a cognitive impairment, it is important to investigate this in a group of cognitively-healthy participants in the first instance.

In the current study, expressions of emotions were measured by utilising facial analysis software which uses machine learning to determine the facial expression which is being generated by the participant. This software takes one reading every second and produces a number between zero and one for surprise, happiness, sadness, aner, fear, and disgust, as well as giving a reading for overall positive and negative emotions. These numbers correspond to how well each facial expression matches the characteristics of each emotion.

Based on previous findings that cognitive functioning in AD patients either demonstrate a greater frequency of negative expressions of emotions (Asplund et al., 1995; Smith, 1995) or fewer recognisable emotions at all (Seidl et al., 2008; 2012), it is unclear how facial expressions will interact with cognition in a cognitively-healthy adult population. Due to this, the hypothesis for the present study is that there will be that either neutral facial expressions, or negative facial expressions of emotions will be related to poorer performance on tests of cognitive functioning.

7.2 Methods

7.2.1 Participants

The participant cohort consisted of twenty-three participants; eighteen males and five females between the ages of eighteen and fifty-nine. Participants had no existing neurological disorder, no clinically diagnosed cognitive impairment, or any implanted medical device, such as a pacemaker. The study was approved by the University of Bradford Humanities, Social and Health Sciences Research Ethics Panel and all participants provided informed consent.

7.2.2 Facial Analysis Software

This unnamed facial analysis software (developed by Ugail and Al-Dahoud (2018) for the University of Bradford) uses machine learning to analyse a video recording of an individual. This software takes one reading per second of video and can report expressions of surprise, happiness, anger, sadness, fear, and disgust. It also reports overall positive and negative readings. Each reading produces a number for each facial expression between zero and one which signals how closely that expression matches each emotion.

7.2.3 Procedure

Upon arrival, participants were greeted by the researcher and informed consent taken. The study began with participants taking part in a series of cognitive assessments which consisted of a STM assessment, a LTM assessment, tests of BWM, a dual task, and an associative learning task. The dual task and associative learning assessment were computer-based assessments, wherein participants had their facial expressions recorded while they were completing these cognitive trials. Following the cognitive assessment, the participants were thanked, debriefed, and offered another opportunity to ask any questions they had before they left.

7.2.4 Cognitive Tests

All cognitive tests were designed by the researcher. See Chapter Five for a detailed explanation of the cognitive assessments used in this study.

7.2.5 Data Analysis

For a facial expression to be tracked as a specific emotion, it had to reach a 60% resemblance threshold; this was decided upon by the researchers due to the reported accuracy of the software being between 60-69% in previous trials (Ugail and Al-Dahoud, 2018). For the purposes of this study, if a facial expression did not meet the 60% resemblance threshold, it was not regarded as an expression of a clearly identifiable emotion and was designated as a ‘neutral’ expression. Once each reading was assigned an emotion, a percentage total of each emotion for the session was calculated and analysed.

7.3 Results

The aim of the present study was to explore the relationship between the generation of facial expressions and cognitive functioning. The data were normally distributed.

There can be significant effects of age and gender on scores of cognitive assessments (Jacova et al., 2007; Fields et al., 2011). Therefore, age and gender effects on the results were analysed using a general linear model univariate analysis of covariance (MANCOVA), where the scores on the cognitive tests were inputted as dependent variables, age was inputted as a covariate, and gender was a fixed factor. No significance of age ($p > .05$) or gender ($p > .05$) was found.

ToD has previously been shown to influence scores on tests of cognition (Walters and Lesk, 2015). To assess whether ToD held influence over the present results, a MANCOVA was carried out wherein composite memory scores, positive, negative, and neutral dominant facial expressions were entered as dependant variables, and ToD of participation was entered as a covariate. ToD effects were found to be non-significant (p > .05). See Table 8 for scores on the cognitive assessments, Table 9 for the descriptive statistics on the six basic emotions and Table 10 for the descriptive statistics on positive and negative emotions.

Table 8 The descriptive statistics for each cognitive assessment

Test	N	Min	Max	Mean	SD (+/-)
Word Recall (STM)	23	3	10	5.74	1.76
Word Recall (LTM)	23	2	8	3.83	1.80
Digit Span (BWM)	23	2	8	5.61	1.64
Associative Learning	23	3	9	5.09	1.41
Dual Task	23	1	14	5.09	3.42

Table 8 shows the minimum, maximum, mean, and SD for participants' cognitive assessment scores on the word recall tasks, the digit span tasks, the associative learning task, and the dual task.

Table 9 The descriptive statistics for dominant facial expression percentage displayed by participants

Emotion	N	Min	Max	Mean	SD (+/-)
Surprise	23	0%	3%	1.09%	1.00%
Happiness	23	0%	3%	1.57%	1.16%
Anger	23	0%	3%	0.57%	0.90%
Sadness	23	8%	27%	16.48%	5.66%
Fear	23	0%	1%	0.17%	0.39%
Disgust	23	0%	1%	0.04%	0.21%
Neutral	23	68%	89%	80.09%	6.24%

Table 9 shows the percentages for minimum, maximum, mean, and SDs for the six basic facial expressions of surprise, happiness, anger, sadness, fear, and disgust, as well as a neutral expression. As can be seen from the table, the highest percentage of facial expressions seen were neutral expressions. This is not surprising, given that if no expression met a 60% similarity threshold, the expression was regarded as a neutral expression.

Table 10 The descriptive statistics for dominant facial expression percentage between positive, negative, and neutral

Emotion	N	Minimum	Maximum	Mean	SD (+/-)
Positive	23	8%	23%	13.04%	4.37%
Negative	23	13%	61%	37.22%	13.64%
Neutral	23	31%	75%	49.74%	14.06%

Table 10 shows the descriptive statistics for the dominant facial expression percentage for positive, negative, and neutral expressions, including the minimum, maximum, mean, and SD. Similarly to Table 9, the highest percentage seen were for neutral expressions.

A general linear model MANCOVA was run to compare positive, neutral and negative facial expressions against cognitive test scores. As the aim of the current study was to explore the relationship between facial cues and cognitive functioning, summed memory test scores and dual task performance were entered as the dependant variables, with positive, negative, and neutral facial expressions being entered as covariates. Only negative facial expressions returned significant findings with $F(2, 18) = 4.49$, $p < .05$; Wilk's $\Lambda = 0.67$, partial $\eta2 = 0.33$. Both positive facial expressions and neutral facial expressions returned a non-significant Wilk's Λ. The between-subject effects returned a significant positive relationship between negative facial expressions and composite memory score ($F(1, 19) = 9.23$, $p < 0.01$). Parameter estimates confirm a linear, positive relationship between negative facial expression frequency and composite memory score (B=0.29, SE=0.09, t=3.14, $p < .01$, 95%CI [0.10, 0.33]). See Figure 4.

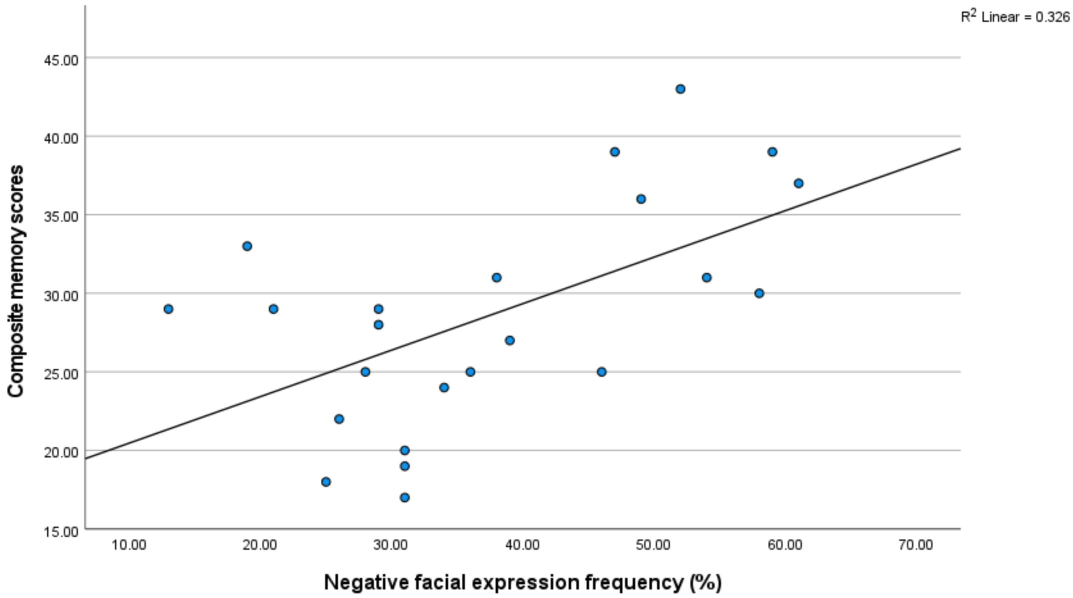


Figure 4 scatter plot demonstrating the relationship between negative facial expression frequency against composite memory score. The scatter plot shows a significant linear increase in composite memory test scores as negative facial expression frequency increases.

A follow-up MANCOVA was run to compare each of the six basic emotions against cognitive test scores. In this analysis, cognitive test scores (composite memory and the dual task) were entered as dependent variables with the six basic emotions and a neutral emotion were entered as covariates. However, none of the six basic emotions individually returned a significant Wilk's Λ when assessed against cognitive test scores. A MANCOVA was then run, in order to compare the individual cognitive assessments which made up the composite memory score with positive, negative, and neutral emotions. In this analysis, each individual cognitive assessment (STM, LTM, BWM, associative learning, and dual task) were entered as dependent variables, with positive, negative, and neutral expressions being entered as the covariates. However, there was no significance for any of these individual cognitive assessments.

Overall, these results show a significant, linear, positive relationship between scores on memory assessments and a greater frequency of demonstrating negative facial expressions. However, no significant relationship was witnessed between any individual facial expression of emotion and cognitive functioning.

7.4 Discussion

The aim of the present study was to explore the relationship between facial cues and cognitive functioning within a cognitively-healthy population. This study furthers previous research that has focussed on cognitive load and reported contradictory findings regarding facial expressions and cognition. In the present study, we investigated whether the frequency of displaying particular facial expressions significantly affected cognitive functioning in a cognitively-healthy adult population by recording their facial cues during a series of cognitive tests. Based on previous findings that cognitive functioning in AD patients either demonstrate a greater frequency of negative expressions of emotions (Asplund et al., 1995; Smith, 1995) or fewer recognisable emotions at all (Seidl et al., 2008; 2012), it was hypothesised that either neutral facial expressions, or negative facial expressions of emotions will be related to poorer performance on tests of cognitive functioning. However, the null hypothesis failed to be rejected in both studies.

The results demonstrated that a greater frequency of negative facial expressions shared a significant, positive relationship with composite memory test scores. This is surprising, as previous literature has reported that AD patients either demonstrate a greater frequency of negative expressions of emotions (Asplund et al., 1995; Smith, 1995) or fewer recognisable emotions at all (Seidl et al., 2008; 2012). It was hypothesised that a negative relationship between negative facial expressions or neutral facial expressions and cognitive functioning would be seen in the cognitively-healthy population, however, the opposite was the case. If future studies can replicate these findings, there may be implications not just for bolstering the accuracy of dementia diagnoses, but as a factor that can be assessed in every study which utilises cognitive assessments as a methodology.

Generating or understanding facial expressions has previously been associated with a wide variety of conditions in the domain of mental health, including schizophrenia (Mandal et al., 1998), dementia (Asplund et al., 1991; Seidl et al., 2008) and AD (Arroyo-Anlló et al., 2021), and autistic spectrum disorder (Drimalla et al., 2021; Keating et al., 2021). Furthermore, alexithymia results in difficulties in generating or understanding facial expressions, and has shown to be related to poorer performance on cognitive assessments (Arroyo-Anlló et al., 2021). The findings of the present study compare interestingly against previous research.

Asplund et al. (1991) conducted a study where four participants with severe AD were presented with pleasant and unpleasant stimuli and their expressions were then quantified using a facial action coding system (FACS). It was found that individuals with AD showed an increased likelihood in producing a negative reaction, such as sadness, disgust, or anger, when exposed to sad stimuli in pre-recorded video footage. However, it was noted that complex facial expressions which could be interpreted as expressions of emotions were not seen (Asplund et al., 1991). Similarly, Asplund et al. (1995) conducted a study where four participants suffering from severe AD had their faces videotaped by two cameras during five caregiving activities (i) morning care, (ii) playing music, (iii) rocking in a rocking chair, (iv) eating, and (v) being read to. Facial expressions were judged by a single observer using an unstructured naturalistic method, and also by the FACS. The observer watched these recordings, and then provided verbal descriptions of the facial expressions observed. It was reported that there was only 48% agreement between the two systems (Asplund et al., 1995). This shows that different methods which are used to analyse facial expressions can generate strikingly different results from the same set of data.

In two ways, the findings from the present study diverge from the findings of Asplund et al. (1995). Firstly, in the present study, it was found that a greater frequency of negative facial expressions demonstrated a positive relationship with scores on tests of memory, whereas in the previous, it was found that individuals suffering from dementia produced more negative expressions (Asplund et al., 1995). Given that some neuropsychological assessments for dementia, such as the MMSE are assessments of general cognition (Bora et al., 2015), it would stand to reason that the production of negative facial expressions would share a negative relationship with cognitive functioning in healthy populations, however, this was not the case. While this was not expected, based on the previous literature (Asplund et al., 1995; Smith, 1995; Seidl et al., 2008; 2012), these previous studies were not analysing the facial expressions displayed by individuals while they were participating in cognitive assessments; thus, these findings are difficult to compare to the previous. It may be the case that concentration is influencing the facial expressions being recorded, although, after a thorough literature review, nothing could be found which assessed the influence of concentration on the production of facial expressions. The finding of the present study which suggests a positive relationship between negative facial expressions and memory is worthy of further exploration. Investigation of facial expressions, specifically whilst performing the cognitive assessment, which patients will be completing anyway in a clinic, may hold implications for cognitive assessments in the future.

The second way that the present findings deviate from previous findings is the lack of a relationship found between neutral facial expressions and cognitive functioning. Previous research from Asplund et al. (1991) reported that individuals with severe AD showed fewer facial expressions that could be specifically recognised as a clear emotion. There are several reasons why the results of the present study may deviate from the findings of Asplund et al. (1991). Firstly, there are methodological considerations to make. As seen in the research of Asplund et al. (1995), using different tools to measure facial expressions can result in drastically different findings. Given the technological advancements that have been made since 1991, it is not surprising then, that the present findings which utilised state-of-the-art machine learning technology found results which might seem to contradict what has come before. Furthermore, the participant cohort of the present study was comprised of cognitively-healthy controls whereas those of Asplund et al. (1991) consisted of four patients which were categorised as having severe AD (Asplund et al., 1991).

Previously, Seidl et al. (2008) conducted a study with a sample of fifty-eight nursing home residents with varying degrees of dementia, including MCI and cognitively-healthy controls. Participants were presented with a series of positive, negative and neutral visual stimuli while their facial expressions were videotaped. It was reported that dementia patients produced significantly fewer facial expressions displaying any emotion as compared with controls. This could go some way toward explaining why, in the present study, there was no significant relationship found between neutral facial expressions and cognitive functioning within cognitively-healthy populations. This could demonstrate that dementia may induce a flattening effect on facial expressions which worsens in line with the cognitive degeneration seen in the illness, resulting in the lack of recognisable facial expressions which are seen within the individuals suffering from severe dementia, but not in cognitively-healthy populations.

Importantly, our findings are seen in cognitively-healthy participants which demonstrates and provides an insight into the understanding of the link between facial cues and cognitive function at a pre-clinical level. Between the pre-clinical level, and the time at which an individual develops dementia, there may be an apparent inverse from negative facial expressions relating positively to cognitive functioning, to relating negatively with cognitive functioning. This may be due, however, to the different cognitive tests used between the present study, and previous research (Asplund et al., 1995; Seidl et al., 2008;2012). Future research should investigate whether this inversion occurs when AD patients and cognitively-healthy controls are assessed with the same cognitive tests. A separate factor worth consideration would be to explore the facial expressions of emotion in people with MCI, as this is widely believed to be a transitionary stage between normal aging and AD (Sullivan et al., 2019).

Previous research has revealed a negative relationship between aging and cognitive ability (Murman, 2015). However, no effect of age on scores of cognitive functioning was found in the present study. This may be due to the participant cohort consisting of individuals between the ages of eighteen and forty-five, tending towards the lower end, whereas findings from previous research reports that cognitive decline only begins around the age of forty-five (Singh-Manoux et al., 2012). The absence of age effects strengthens the findings that negative facial expression frequency whilst carrying out a cognitive assessment is positively related to scores on tests of memory.

It has been almost 150 years since Charles Darwin wrote ‘The Expression of Emotion in Man and Animals’ thus fathering the origin of facial expression research. Since then, research has expanded to show that some emotions can be witnessed across a diverse series of cultures and peoples (Ekman et al., 1969; 1987; Ekman and Friesen, 1971), and that emotions are related to cognition in a series of conditions, such as schizophrenia, dementia, AD, and autistic spectrum disorder (Mandal et al., 1998; Drimalla et al., 2021; Asplund et al., 1991; Seidl et al., 2008; Arroyo-Anlló et al., 2021; Keating et al., 2021). Which brings us to the novel and unexpected findings of the present study, that negative expressions of emotion are related to improved cognitive performance. Even though the methodologies of the current study and that of Asplund et al. (1995) and Smith et al. (1995) were significantly different so cannot directly be compared, the fact that the findings are opposite from relevant research (Asplund et al. (1995) Smith, (1995) and Seidl et al. (2008; 2012)) only serves to show how complex the relationship between facial expressions of emotion and cognitive functioning is, and how much more there is to understand.

The strength and novelty of the current study is that this was found whilst participants were simultaneously carrying out a cognitive assessment so this has the potential to be added as an additional factor/variable in scoring the cognitive assessment. Implementing facial analysis software in a clinical context does come with its own set of considerations, however. Firstly, the tools required to conduct facial analyses include a computer and camera which is set to record the patient's facial expressions. This will incur a monetary cost in equipment, as well as in time required to set up the software, analyse the video footage, and interpret the findings. For facial analysis software to give accurate readings, participants must have their full face in clear view of the camera at all times. Therefore, patients will not be able to move around as much as they may like, which may cause discomfort. Furthermore, there are ethical issues to consider for individuals who may not be comfortable with having their faces recorded. Finally, if an individual does consent to having their face recorded, there are strict General Data Protection Regulation (GDPR) guidelines that must be followed regarding who is permitted to see this footage, and how long the footage may be kept.

In the present study there were no significant results found for the dual task. The dual task involved participants hearing a series of letters, while seeing a series of colours appear on a screen one at a time. Participants were tasked with recalling each letter and colour. It happened that in this data set, almost every participant correctly recalled all the letters in the sequence; it was on the colours that they performed better or worse. How the dual task was analysed in this study was that the total number of letters correctly identified was subtracted from the number of colours correctly identified to produce a difference in scores. For the purposes of this study, the greater the difference, the worse the participant performed. It may be the case that the dual task was too easy in terms of the letters. In future, potentially a longer string of letters should be utilised in order to prevent the participants from performing at ceiling level for that portion of the dual task.

7.4.1 Methodological considerations

Regarding methodological considerations, previous research has shown that the ToD at which an individual is at their optimal arousal is dependent on age (Hasher et al., 2005; Walters and Lesk, 2015). See Chapter Five for a detailed discussion of ToD and age. However, in the present study the ToD will have influenced light levels. Light levels were not controlled for while utilising the facial analysis software (Ugail and Al-Dahoud, 2018). Future studies should consider taking measurements at differing ToD as different light levels may influence the readings given by the software. Furthermore, English and Carstensen (2014) conducted a study in order to assess emotional states in the morning compared to the evening. This study involved individuals filling in a journal in the morning and the evening wherein they reported their feelings. In the case of 135 participants between the ages of twenty-two and ninety-five, it was reported that individuals feel less positive and more negative in the evenings, compared to the mornings (English and Carstensen, 2014). Also, older participants reported experiencing positive emotions more frequently than younger adults (English and Carstensen, 2014). ToD effects were not witnessed in the present study for emotions. This could potentially be because all participation took place in the late morning or early afternoon, whereas the English and Carstensen (2014) study took place in the morning and evening. Nonetheless, given that the present data suggest that facial expressions of emotion are related to cognitive functioning, future research should make considerations for the ToD at which individuals participate in assessments of cognitive functioning.

Another methodological consideration to make regards the lifestyle and hobbies of the individuals taking part in the study. It could be argued that if an individual were to enjoy puzzles or problem solving, that this may influence their facial expressions while taking part in the cognitive assessment. However, it doesn't necessarily follow that just because some individuals enjoy completing puzzles in their spare time that they are expressing positive emotions in this instance. For example, someone who enjoys cycling does not necessarily demonstrate positive facial expressions while on a bike ride. Furthermore, given that negative facial expressions were associated with improved memory performance, that would mean that individuals who complete puzzles in their spare time would perform worse than those who do not. While the degree to which an individual enjoys puzzles was not controlled in this study, this may be an interesting are of exploration in future studies.

7.5 Conclusion

Facial cues have shown to be related to many cognitive impairments (Mandal et al., 1998; Asplund, Norberg, and Adolfsson, 1991; Seidl et al., 2008; Arroyo-Anlló et al., 2021; Drimalla et al., 2021; Keating et al., 2021). In the present study, it was found that a greater frequency of negative facial expressions was positively related to compound memory scores generated for tests of cognitive functioning. These present findings present a previously unseen relationship between facial expressions and cognitive functioning. If further research reflects the findings of the present study, and is reflected across age groups and cultures, there is potential for facial analysis software, and negative facial expressions in particular, to be utilised as a tool for assessing cognition, without dependencies on words, language, or vocalisations.

7.6 Highlights

- Emotions are automatic behavioural and hormonal responses which assist survival. They arise through a series of external cues, bodily signals, and cognitive processes.
- Prior studies have linked difficulties in generating and understanding facial expressions with a variety of mental illnesses, including schizophrenia, dementia, AD and autistic spectrum disorder.
- The purpose of this study was to explore the relationship between facial cues and cognitive functioning within healthy populations whilst carrying out a cognitive testing session.
- Preliminary results indicate that a greater frequency of negative facial expressions shared a significant, positive relationship with composite memory test scores.
- These present findings present potential for utilising facial analysis software, and negative facial expressions in particular, as a tool for assessing cognition.
- Facial expression analysis could be used as another variable when analysing a cognitive assessment.

Chapter Eight

Blink Rates and Cognitive Functioning

8.1 Introduction

The previous chapter established a relationship between negative facial expressions of emotion and performance on a series of cognitive tests. However, there is more information that these video recordings can provide, namely blink rates. Vision is intrinsically linked with cognition. Everyday environments are so complex that we adapt to selectively engage only with the most relevant stimuli (Ranti et al., 2020). Humans can look at stimuli which, if not regarded as relevant, can be disregarded and may not even be processed (Simons and Chabris, 1999). More so than vision, blinking has previously demonstrated a relationship with various cognitive functions, including attentional load and cognitive fatigue (Maffei and Angrilli, 2018), attentional control (Unsworth et al., 2019), and WM (Rac-Lubashevsky et al., 2017; Ortega et al., 2021).

Previous research into blink rates and cognition has yielded conflicting results with older studies reporting that blink rates share a negative relationship with cognitive load (Holland and Tarlow, 1972) and that while participants are performing mental exercises such as counting, their blink rates were reduced (Holland and Tarlow, 1975). It was inferred from these findings that blinking interrupts cognitive processing (Holland and Tarlow, 1972). However, more contemporary studies have identified that higher blink rates are correlated with improved neural activation required to complete cognitive tasks (Kuwamizu et al., 2020), and that blink rates are positively correlated with WM performance (Ortega et al., 2021). Given the overarching aim of the thesis is to look at techniques that can potentially be used for an early diagnosis of cognitive impairment, this relationship warrants investigation.

8.1.1 Background to Blinking

One of the most frequent human actions is the act of blinking (Hoppe et al., 2018). Previous research has shown that people blink, on average, between twelve-fifteen times each minute with an interval of between two-ten seconds between each blink (Doughty, 2001; Abusharha, 2017). The primary function of blinking is to clean the surface of the eye, while providing a normal distribution of a moist film across the eye (known as the ‘tear film’) which protects the ocular surface, thereby aiding in the maintenance of visual quality. (Bentivoglio et al., 1997; Tutt et al., 2000; Portello et al., 2013; Abusharha, 2017; Hoppe et al., 2018).

Blinking can be either voluntary or involuntary; indeed, humans often remain unaware of their eye-blinking behaviour in everyday situations (Ranti et al., 2020). However, human eye-blinking behaviour is regulated by the body to be inhibited at specific moments in order to minimise the loss of visual information which occurs as a result of having closed eyes during a blink (Ranti et al., 2020).

Historically, research regarding human blinking was conducted by Ponder and Kennedy (1927) who investigated blinking in a variety of situations. One study involved assessing blink rates in a light room compared to a dark room, or while a participant was reading, whereas another consisted of the researchers blowing cigarette smoke in the participants' faces. Their study assessed blink rates by the use of physical pads attached to the eyelids of participants, which, when participants blinked, would move material into position to complete a circuit creating an electrical current which could be recorded and identified as a blink. It was reported that blink rates remained “relatively steady” while experimental conditions remained constant. However, once the conditions were changed (going from reading to speaking in conversation, for example) the blink rates altered substantially (Ponder and Kennedy, 1927).

8.1.2 Blink Rates and Cognition

In the years that followed the research of Ponder and Kennedy (1927), researchers began to note that there may exist a relationship between blinking and cognition, which started with the finding that individuals who were daydreaming were blinking less than those who were not (Antrobus et al., 1964). The theoretical framework behind this relationship began to crystalise in the 1970s. Holland and Tarlow (1972) conducted two studies in order to build on the findings of Antrobus et al. (1964) to determine the influence of cognitive load on blink rates. In the first study, participants were tasked with remembering a sequence of four, six, or eight digits while their blink rates were recorded. Whereas in the second, participants were tasked with completing mental arithmetic while their blink rates were recorded. It was found that in both studies, blink rates were low when cognitive load was high, and also that blink rates were high when cognitive load was low. It was speculated that blinking may interrupt cognitive processes involved in memory (Holland and Tarlow, 1972).

In order to explore this relationship further, another study was conducted by Holland and Tarlow (1975) who conducted assessments to explore how counting might influence blink rates. Participants would have their blink rates recorded while the researchers asked the participants to count. It was noted that while participants were counting to themselves, their blink rate was significantly reduced. It was inferred from this finding that while individuals manipulate information in their own minds, blink rate is reduced, and that this happens because blinking disrupts cognitive processing and is therefore inhibited in order to aid in cognitive processing (Holland and Tarlow, 1975).

As time has progressed, the use of electronic devices has become a large part of everyday life (Rosenfield et al., 2015). Previous studies have shown that symptoms of optical/visual discomfort occur at a higher magnitude when viewing electronic displays as compared to printed materials (Chu et al., 2011; Abusharha, 2017), and that viewing computer screens has a suppressing effect on blink rates (Patel et al., 1991). In order to explore the influence of cognitive demands on blink rates with the use of visual screens, Rosenfield et al. (2015) conducted a study where sixteen participants were tasked with reading passages of text both on a digital screen and a hard printed copy. These passages varied in their levels of cognitive demands, in terms of sentence structure and syntactic complexity. While participants were reading these passages, their faces were being recorded. It was reported that the method of information presentation (screen vs print) held no influence over blink rates. However, while participants were reading the more cognitively demanding passages, their blink rates were significantly lower (Rosenfield et al., 2015). This contradicts the idea that digital screens suppress blink rates, which was reported by Patel et al. (1991), and it was concluded that modern digital screens may be closer in format to printed materials than old digital displays. This finding was reflected by Abusharha (2017) who reported that performing long reading tasks both on digital screen and on print both suppressed blink rates.

More recent research into the relationship between blink rates and cognition comes from Kuwamizu et al. (2020) who argue that eye blink rate can be measured as a non-invasive biomarker for dopaminergic activity in the brain (Kuwamizu et al., 2020). In order to assess whether this was the case, a study was conducted where thirty-five cognitively-healthy males aged eighteen to twenty-four were tasked with staring at a fixation cross, while their blink rates were analysed. Following this, participants completed an aerobic fitness test until they reported feeling exhausted, at which point they completed a Stroop task. Analysis revealed a correlation between greater aerobic fitness performance, performance on the Stroop task, and an increased eye blink rate. Moreover, higher blink rates were correlated with improved neural efficiency where executive function was high while left dorsolateral prefrontal cortex activation was relatively low. It was concluded from this study that blink rates mediate associations between aerobic fitness and executive function through neural efficiency. This finding seemingly contradicts previous findings from Holland and Tarlow (1972; 1975) which report a negative relationship between blink rates and cognitive functioning. Again, further research is warranted.

Recent research has identified that blink rates can measure attentional load and cognitive fatigue (Maffei and Angrilli, 2018), as well as attentional control (Unsworth et al., 2019). Further studies have also shown that blink rates can track real-time changes in WM demands (Rac-Lubashevsky et al., 2017). To better understand the relationship between blink rates and WM, Ortega et al. (2021) conducted a study with the goal of exploring the fluctuations in blink rates during different phases of a WM task that was seen in the study of Rac-Lubashevsky et al. (2017). Ortega et al. (2021) ran two experiments in this study. Both experiments were similar in nature, only differing in the method by which blink rates were analysed. Experiment one had nineteen participants, and measured blink rates using an MRI scanner. Experiment two used electroencephalogram (EEG) technology to measure blink rate. In both experiments, participants completed a modified version of the Sternberg WM Task (Sternberg, 1966). This task had three sets of fifty-four WM trials. These trials consisted of an encoding period where participants saw three successive novel scenes for 1400ms each, a delay period where participants would see a fixation cross for either two, five, or nine seconds, a probe period which consisted of participants either seeing a new stimulus that had not been seen before or an image which they had seen previously within the encoding period, and a post-probe scrambled stimulus period where participants would see a scrambled image, similar to television static, signifying the end of the trial. Results revealed that, in both experiments, blink rates were positively correlated with WM performance during the delay period (Ortega et al., 2021).

The previously discussed literature in this section paints an inconclusive picture regarding the relationship between blink rates and cognitive functioning. Older research has established that there is a negative relationship between blink rates and cognitive functioning (Holland and Tarlow, 1972; 1975) and more contemporary research has identified a positive relationship between blink rates and cognition (Kuwamizu et al., 2020; Ortega et al., 2021). It is unclear why more contemporary studies seemingly find the inverse of older studies; however, it is clear that further investigation is warranted. Considering this thesis is concerned with non-invasive techniques which could be utilised to improve the accuracy of a dementia diagnosis, it would be pertinent to consider the relationship between blink rates and dementia.

8.1.3 Blink Rates, Dementia, and MCI

Research regarding the relationship between dementia and blink rates is sparse. However, previous research has identified that blink rates could be utilised to discriminate between AD and vascular dementia. Vascular dementia is the second most common form of dementia after AD (Mohammadian et al., 2015) therefore, the ability to reliably discriminate between these two conditions is important in a diagnostic context. Mohammadian et al. (2015) conducted a study where eighteen patients with AD, seventeen patients with vascular dementia, nineteen patients with mixed dementia, and twenty controls had their blink reflex examined. It was determined that blink latency could differentiate between patients with vascular and mixed dementia as compared with patients with AD and controls. However, there was no significant difference reported between the AD group and controls (Mohammadian et al., 2015).

Further research into the relationship between dementia and blink rates was conducted by Bonanni et al. (2007) where the supraorbital nerves were stimulated with an electric current in order to induce blink behaviour in twenty-six patients with DLB, twenty-six patients with multiple system atrophy, twenty-six patients with Parkinson's disease, twenty patients with AD, twenty with progressive supranuclear palsy, and thirty healthy controls. Participants were seated in a quiet room, where the electrical equipment was attached, and an electrical impulse was administered for 0.1ms in order to induce a blink reflex. It was reported that blink reflexes were only significantly delayed in participants with DLB as compared to other patients or healthy controls. It was concluded that the findings in the DLB patients may indicate that blink rates are affected by dysfunction of the reticular brainstem (Bonanni et al., 2007). Following this research, Anzellotti et al. (2008) conducted a follow-up investigation where twenty-six patients with DLB and twenty AD patients were given clinical, neuropsychological, and blink reflex evaluations (i) prior to donepezil administration (ii) one week after being administered donepezil, and (iii) two weeks after being administered donepezil. It was reported that donepezil administration could correct the alterations of blink rates in patients with DLB (Anzellotti et al., 2008). It was concluded from this research that a delayed blink reflex is sensitive to cholinergic modulations (Anzellotti et al., 2008).

Furthermore, an interesting interaction has been found between blink rates and MCI. This is a salient area of research, as previously discussed, as MCI in some cases is thought to be a transitionary period between normal aging and AD (Sullivan et al., 2019). Ladas et al. (2014) conducted a study with thirty-six patients with MCI and thirty-three controls who had their blink rates recorded under resting conditions with the use of two electrodes above and below the left eye. Following this, the participants had their cognitive functioning assessed by a battery of cognitive assessments, including the MMSE and the MoCA. It was reported that participants with MCI exhibited a significantly higher blink rate than cognitively-healthy controls, and that a high blink rate was negatively related to scores on the MoCA. It was concluded that an abnormally high blink rate may be a potential biomarker for the transition between normal aging and AD. This is directly relevant and important to this thesis because blink rates could be a utilised as a biomarker for the transition from normal aging and MCI as suggested by Ladas et al. (2014), there is potential for blink rates to be utilised in a diagnostic capacity.

One common pathology of AD is a reduction in brain dopamine levels compared to healthy, age-matched controls (Pan et al., 2019). It has also been reported that individuals with reduced dopamine levels blink less often than those with higher dopamine levels (Paprocki and Lenskiy, 2017). It was theorised that concentration of dopamine in the pre-frontal cortex and accumulation of gamma-Aminobutyric acid in the visual cortex cause this relationship, as both neurotransmitters are associated with both blinking and cognition (Paprocki and Lenskiy, 2017). Further investigation into this relationship is important as, while there is little research on blinking and AD, if a relationship can be formed between low blink rates and poor cognition in healthy populations, it may hold implications for future cognitive assessments.

8.1.4 Aim of the Study

The aim of the present study was to explore the relationship between facial cues and cognitive functioning further. It is not yet clear if there is any relationship between blink rates and cognitive function in cognitively-healthy populations If a relationship is seen there may be implications for neuropsychological assessment in either clinical or experimental contexts in the future. In the current study, facial analysis software was used to measure blink rate (blinks per minute) and cognitive function was assessed using a cognitive battery assessment (see Chapter Five for more detailed information on the cognitive battery utilised in this study).

Based on the conflicting studies which report that blink rates may either be positively or negatively related to cognition (Holland and Tarlow 1972; 1975; Kuwamizu et al., 2020; Ortega et al., 2021), the hypothesis for this exploratory study is that there will be a relationship between blink rates and cognitive functioning, however the direction this relationship may take remains unclear.

8.2 Methods

8.2.1 Participants

The same participant cohort took part in this study as the study detailed in Chapter Seven. As an exploratory study, it is difficult to know how many participants would be an appropriate number to recruit. Related research exploring the relationship between dopamine synthesis capacity and blink rates utilised a participant cohort of twenty (Sescousse et al., 2018), therefore twenty participants was the aim although more could take part if they were interested.

8.2.2 Blink Rate Analysis Software

Blink rates were measured by utilising facial analysis software which analyses pre-recorded video footage of faces and is algorithmically designed to recognise when the participant in said pre-recorded footage blinks. The software records every time a participant blinks during a recording, and then reports blink rates as a ‘blinks-per-minute’ average reading. It is this score that was entered for data analysis. Accuracy of this software was confirmed by the researcher taking a random sample of videos and counting the blink rates by hand to ensure the software was reporting blinks accurately.

8.2.3 Cognitive Tests

All cognitive tests were designed by the researcher. See Chapter Five for a detailed explanation of the cognitive assessments used in this study.

8.2.4 Procedure

This study utilised the same procedure as described in Chapter Seven. See Chapter Seven for a detailed explanation of the procedure used in this study.

8.2.5 Data Analysis

Firstly, a linear regression analysis was conducted in order to assess participants' scores on tests of cognitive functioning against their average blink rate while performing cognitive tasks. Because of the previously discussed relationship between blink rates, dementia, and dopamine suggesting that lower blink rates are related to lower levels of dopamine, and also that dementia patients present lower levels of dopamine (Paprocki and Lenskiy, 2017; Pan et al., 2019) and bearing in mind that participants were cognitive-healthy individuals, this study also went on to determine how well the individuals with the lowest blink rates performed as compared to the participants with moderate to high blink rates. To this end, the blink rates were quartiled, with the lowest 25% of blink rates being compared against the remaining 75%. Age, gender, and ToD effects were previously analysed for this participant cohort regarding the cognitive tests, this analysis can be seen in Chapter Seven. Age, gender, and ToD were also analysed against blink rates. The findings are reported below.

8.3 Results

The aim of the present study was to explore the relationship between blink rates and cognitive functioning in a group of cognitively-healthy participants. The data were normally distributed. As reported in the previous chapter (Chapter Seven) there can be significant effects of age, gender, and ToD on neuropsychological assessment scores (Jacova et al., 2007; Fields et al., 2011; Walters and Lesk, 2015). Please see Chapter Seven for a detailed report on the age, gender, and ToD effects regarding this particular cohort, as well as Table 11 which reports the descriptive statistics for cognitive performance. There was no effect of age, gender and ToD on the cognitive assessments ($p > .05$). Age and gender effects on blink rates were analysed using a general linear model ANCOVA, where blink rate was the dependent variable, age was a covariate, and gender was a fixed factor. In both cases, for age and gender there were no significant effects seen, with $p > 0.05$ for both. See Table 11 below for the descriptive statistics of participants' blink rates per minute.

Table 11 Descriptive statistics for blink rates per minute

N	Minimum	Maximum	Mean	SD (+/-)
23	14.10	33.50	23.07	6.20

Table 11 shows the descriptive statistics for blink rates per minute, including the minimum, maximum, mean, and standard deviation.

At first, blink rates were compared against composite memory scores in a MANCOVA analysis, wherein each cognitive assessment (LTM, STM, BWM, associative learning and a dual task) were entered as dependent variables, and blink rates were entered as a covariate. No significant effects found ($p > 0.05$). Following this, a composite memory score was generated by adding together the scores on tests of LTM, STM, BWM, and associative learning. A MANCOVA analysis was then run with composite memory score and dual task scores as dependent variables and blink rates as a covariate. Again, no significance was seen. However, often in dementia research, differences in results can only be seen at the extreme ends of the data (Hata et al., 2019; Reckrey et al., 2020). Therefore, following this, the bottom 25% of blink rates were analysed against the remaining 75%. A t-test was run to compare participants scores on tests of cognition against low and high blink rate groups. The t-test analysis reported a significant relationship between blink rates and cognitive performance ($t(11.02) = 2.62$ $p < .05$). See figure 5 below for a bar chart demonstrating the relationship between low or high blink rates and scores on tests of cognition.

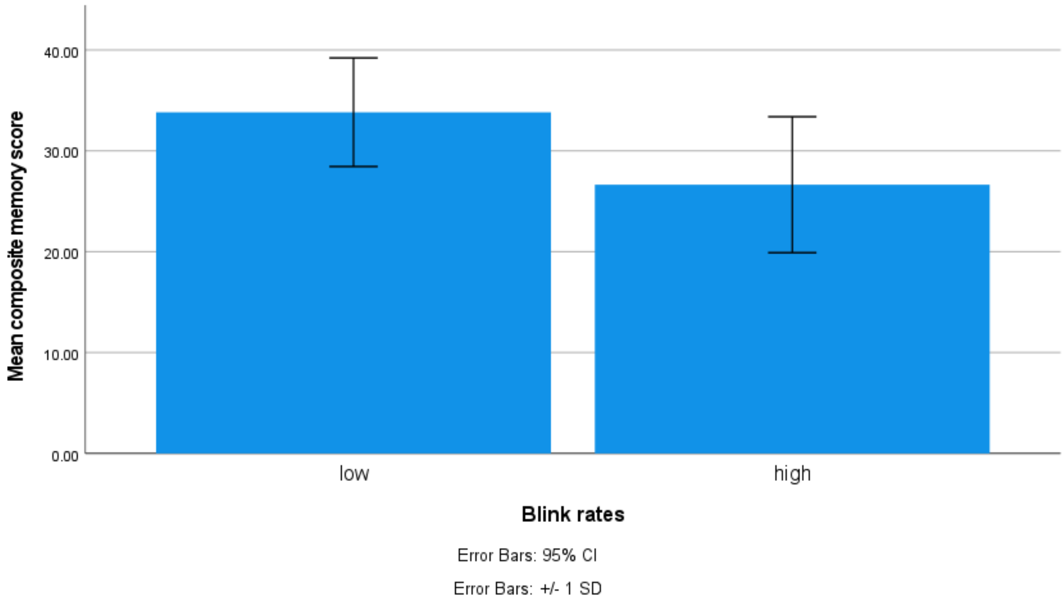


Figure 5 bar chart demonstrating the relationship between the bottom 25% of blink rates and the remaining 75% of blink rates against composite memory score. The bar chart shows a significantly higher composite memory test scores for the bottom 25% as compared against the remaining 75%.

Following this, further investigation was conducted on the individual memory assessments which comprise the composite memory score. A general linear model multivariate analysis of variance (MANOVA) was conducted with each memory assessment entered as dependent variables and the two blink groups entered as a fixed factor. The MANOVA returned a significant Wilks' Λ ($p < 0.05$), and significant findings for blink group and STM ($F(1, 21) = 6.70$, $p < 0.05$) and LTM ($F(1, 21) = 9.84$, $p < 0.01$).

Parameter estimates show a linear, negative relationship between standard deviations in blink rates and STM (B=1.93, SE=0.75, t=2.59, $p < .05$, 95%CI [0.38, 3.48], LTM (B=2.27, SE=0.37, t=3.14, $p < .05$, 95%CI [0.76, 3.77]. See Figure 6 below for a bar chart demonstrating the relationship between low or high blink rates and scores of STM and LTM.

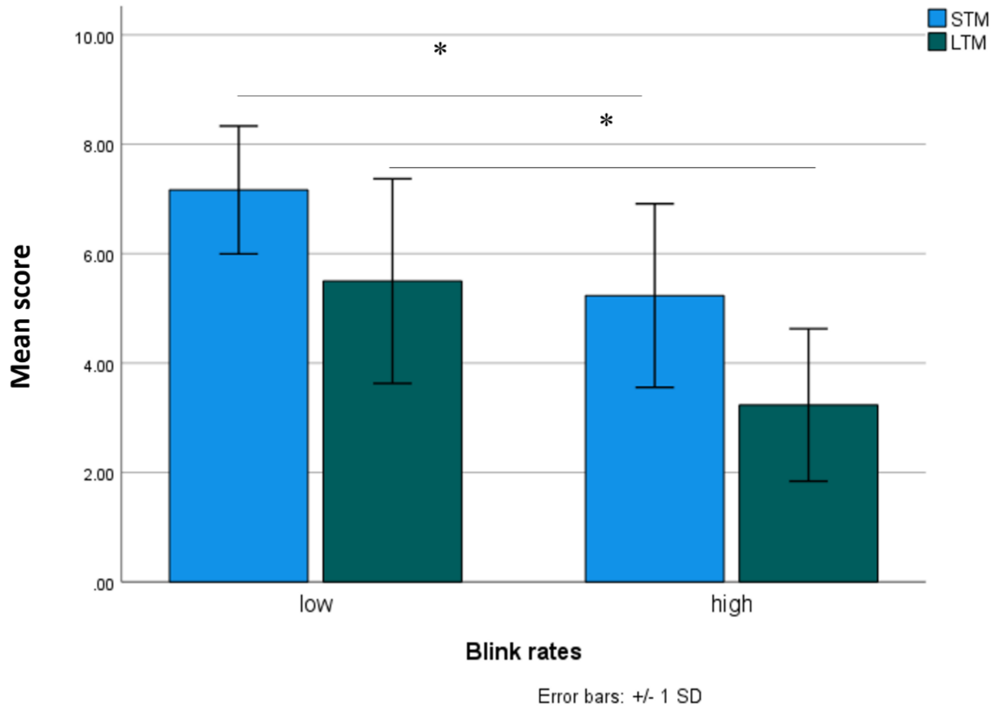


Figure 6 bar chart demonstrating the relationship between the bottom 25% of blink rates and the remaining 75% of blink rates against STM, and LTM. The bar chart shows significantly higher STM and LTM test scores for the bottom 25% compared against the remaining 75%. * = $p < 0.05$

Overall, no significance was seen between the blink rates of individual participants and their scores on tests of cognitive functioning. However, when the blink rates were quartiled, a significant relationship was seen between the bottom 25% of blink rates and composite memory scores. Further analysis revealed a significant relationship particularly between the bottom 25% of blink rates and scores on tests of LTM and STM. No significant relationship was reported between low or high blink rates and the dual-task ($p > 0.05$).

8.4 Discussion

The aim of the present study was to explore the relationship between blink rates and cognitive functioning in a cognitively-healthy population. This research builds on the previous findings from Chapter Seven which report that there exists a relationship between facial expressions of emotion and cognitive functioning. This research also builds on previous research by assessing a wider cognitive battery, while providing data in cognitively- healthy controls to discuss against findings from the dementia, AD, and MCI literature. The results of this present study demonstrated that individuals who produced the bottom 25% of blink rates performed significantly better in assessments of memory than participants who produced the remaining 75% of blink rates. There was no such finding for blink rates when not quartiled.

The findings of the current research that participants who produced the lowest 25% of blink rates performed better on assessments of memory than the remaining 75% are surprising when compared to contemporary research conducted by Kuwamizu et al. (2020) who reported that, in the case of thirty-five cognitively-healthy males aged eighteen to twenty-four, a correlation was found between greater aerobic fitness performance, Stroop performance, and increased blink rates. The results of the present study also offer conflicting data from that of Ortega et al. (2021), who reported that in a series of experiments blink rates were positively correlated with WM performance. There are clearly significant methodological differences between the current study and the research of Kuwamizu et al. (2020) and of Ortega et al. (2021) which may go some way towards explaining the contradictions. Firstly, Kuwamizu et al. (2020) took blink rate readings at rest whereas the current study assessed blink rates during a cognitive assessment. Previous research has demonstrated that concentration has a suppressive effect on blink rates (Rosenfield et al., 2015). It is not unreasonable to assume therefore that the findings of the current study (low blink rates showing improved performance on tests of cognition) may simply be due to greater levels of concentration from the participants.

It makes good sense that the more someone is concentrating the better their performance would be. While this is intuitive, it stands to reason that the same should apply to other studies, however, as discussed, both Kuwamizu et al. (2020) and Ortega et al. (2021) reported positive relationships between blink rates and cognitive functioning. This creates a need for further research in this area to fully understand the interaction between blink rates and cognitive functioning. Furthermore, a greater variety of cognitive assessments were utilised in the present study than were used in the research of Kuwamizu et al. (2020) who only assessed visual attention; therefore, the findings may be incomparable. The research of Ortega et al. (2021) utilised neuroimaging technologies to measure blink rates, and also only assessed WM. The present study, however, measured blink rates using facial analysis software and assessed a more diverse cognitive battery. These factors may explain the differences found between the present research, and prior research. Having said this WM was assessed using the Digit Span Backwards task and we still found no significant relationship with either individual blink rates, or low vs high blink rates.

While the findings of the present study seemed to contradict contemporary findings in similar areas, older studies have reported similar findings, such as in the case of Holland and Tarlow (1972; 1975) who asserted that blinking disrupts cognitive processing. Thus, blinking is inhibited during cognitive processing, resulting in a lower blink rate being related to an increase in cognitive performance. One similarity between Holland and Tarlow (1972; 1975) and the present study was that blink rates were measured during the cognitive assessment, rather than at rest. This may go some way toward explaining why the present findings support Holland and Tarlow (1972; 1975), yet contradict Kuwamizu et al. (2020), and Ortega et al. (2021). However, there are methodological inconsistencies between the present research, and the research of Holland and Tarlow (1972; 1975) that make direct comparisons difficult to achieve too. For example, Holland and Tarlow (1972) only assessed participants' mental arithmetic ability, whereas the present study utilised a broader cognitive battery. Similarly, Holland and Tarlow (1975) only asked participants to think about counting. Furthermore, Holland and Tarlow (1972; 1975) measured blink rates while being observed, whereas the present study utilised facial analysis software which required participants to look at a screen. The reason that this is worth consideration is that there is current disagreement within the scientific community about the influence of digital screens on blink rates (Mehra and Galor, 2020; Rosenfield et al., 2015).

Previous research has reported that there is no significant difference in blink rates between AD patients and healthy controls (Mohammadian et al., 2015). However, the same relationship has not been seen in MCI, which is thought to be a transitional stage towards the development of AD (Sullivan et al., 2019), as previous research has reported that individuals with MCI produce a significantly higher blink rate than cognitively-healthy controls (Ladas et al., 2014). This creates an unclear interaction between blink rates and cognitive functioning, as the findings of the present study highlighted that individuals with the lowest bink rates performed better on a series of memory assessments than the rest of the participant cohort, but this is not found to also be the case for MCI, and in AD the interaction disappears entirely. The findings of the present study, alongside the conflicting findings with AD and MCI highlight the necessity for further investigation in this field, as the science on blink rates and cognition needs to be settled in order for blink rates to be considered in a diagnostic capacity, thus potentially aiding in a neurological diagnosis. Such further research may take the form of a longitudinal study which observes the differences in blink rates as individuals develop through the stages both MCI and AD, thereby offering a concrete roadmap of the changes to blink rates alongside cognitive decline.

8.4.1 Methodological Considerations

Regarding methodological considerations for the cognitive battery, please refer to Chapter Seven, as this study utilised the same cognitive battery and participant cohort as outlined in Chapter Seven. This includes discussions of ToD regarding emotional states, however, ToD was not controlled for in regarding blink rates, as previous research has found that there is no significant effect of ToD on blink rates (Ugwu et al., 2021). The present study analysed the influence of ToD on blink rates, however, no significance was found.

Other methodological considerations to make regards the point at which a blink in measured. Previous research has detailed differences between blinking, and half-blinks. Kaaman and Bornemark (2017) identify half-blinks as behaviour which is an intentional slight close of the eyelid, which may be distinguishable from a standard blink. However, there is little to no agreement regarding at what point a half-blink becomes a blink. This may also contribute to the conflicting findings which have been found throughout past research in the domain of eye blink studies. There must be a clear distinction between where a half-blink becomes a full blink, in order to increase the accuracy and replicability of studies going forward. A consensus must also be reached on whether half-blinks are of value to measure as part of more general blinking behaviour. The software utilised in the present study discriminated between blinks and half-blinks by measuring when the two eyelids meet. However, other software may be less precise by only tracking the top eyelid, thus recording a half blink as a blink.

Further methodological considerations should be made regarding potential confounding variables that were not controlled for in this instance. For example, some medications or tiredness may influence a participant's blink rates (Van Slooten et al., 2019; Shamini et al., 2022). Given the exploratory nature of this study, it was unclear what findings would be witnessed. Potential confounding variables such as medication or tiredness will be useful consider for future iterations of this study. However, regarding tiredness, while this was not explicitly asked, time-of-day effects were analysed and found to be non-significant.

8.5 Conclusion

Previous research into the relationship between blink rates and cognition have yielded conflicting results. Older research, such as the work of Holland and Tarlow (1972; 1975) reported a negative relationship between blink rates and cognitive ability, whereas more contemporary research from Kuwamizu et al. (2020), and Ortega et al. (2021) reported precisely the opposite- that there was a positive relationship witnessed between blink rates and cognition. However, the present study reported findings more in line with the research of Holland and Tarlow (1972; 1975), that individuals who produced the bottom 25% of blink rates performed better on tests of cognition than the remaining 75%. Whilst this is interesting, before blink rates may be considered as a diagnostic tool in a clinical context, broad agreement is necessary on a standardised assessment mechanism for blink rates, in order to improve study replicability. The role of concentration in blink rates should also be established as control data and a larger sample should be used, especially if quartile analysis is to be employed.

More research is required into the relationship between blink rates and dementia before the suitability of analysing blink rates in clinical contexts can be discerned. It stands to reason that individuals with AD in particular should blink less often than healthy controls, as the neurotransmitter dopamine is responsible for both blinking and cognitive functions (Paprocki and Lenskiy, 2017), and levels of dopamine in AD patients is significantly lower than in the healthy population (Pan et al., 2019). This has found to be the case in MCI, which is thought to be a transitionary stage between normal aging and AD (Sullivan et al., 2019). However, the same interaction not been found in individuals with AD (Mohammadian et al., 2015). This interaction is only complicated further by the present findings that individuals who blink less often performed better on a series of memory tests. These contradictions further highlight the need for standardisation in blink rate studies, and further demonstrate the necessity of further research in this area.

8.6 Highlights

- Vision and cognition are intrinsically linked. Complex everyday environments require us to adapt, and selectively engage with relevant stimuli (Ranti et al., 2020).
- Blinking is the process of momentarily closing the eye in order to clean the surface of the eye, while providing a ‘tear film’ for eye protection (Abusharha, 2017; Hoppe et al., 2018). Blink rates are a measure of how often blinking occurs.
- Previous studies have reported both a positive relationship (Holland and Tarlow 1972; 1975) and negative relationship (Kuwamizu et al., 2020; Ortega et al., 2021) between blink rates and cognitive functioning.
- Given the aim of the thesis is to look at potential techniques for the detection and diagnosis of dementia, this relationship warrants further investigation.
- There is little research into the relationship between dementia and blink rates, but inconsistent findings exist.
- The results of this study show that individuals who produced the bottom 25% of blink rates performed better on tests of cognition than the remaining 75%.
- It is concluded that standardisation is necessary for future blink rate studies in order to improve replicability and allow for meaningful comparisons to be drawn between studies.
- Further research is required before blink rates may be considered as a potential non-invasive diagnostic tool in neuropsychological assessments.

Chapter Nine

Assessing Spatial Memory in a Fully-Immersive Virtual Reality World

9.1 Introduction

The previous experimental chapters of this thesis have explored non-invasive factors which may hold the potential to improve the accuracy of a dementia diagnosis while avoiding external factors. This is important to achieving
an early and accurate diagnosis of dementia, as well as correct identification of the dementia subtype.

In the case of AD, achieving accurate scores in tests of cognition is time-sensitive as different parts of the brain degenerate at different rates (Duarte et al., 2020). It is thought that the EC is the first area of the brain to show degeneration in AD (Howett et al., 2017) which is implicated in spatial memory (Sekeres et al., 2018). Spatial memory refers to one’s ability to find their way in familiar and unfamiliar surroundings (Costa et al., 2020). Moreover, the EC is sensitive to an increased tau load, which may go some wat towards explain why spatial memory is affected in the earlier stages of dementia (Ridler, 2018).

In previous years, spatial memory has been assessed by using navigation through a virtual environment, on a screen, instead of using more naturalistic methods. However, it is unclear whether new technologies which afford a greater capacity for naturalism may offer distinct and separate findings than previous studies which used less naturalistic methods.

9.1.1 Spatial Memory

Goal-directed navigation through spatial environments is fundamental for daily life (Hilliard et al., 2019) for example when finding our way to the supermarket, or navigating in our own homes. Spatial memory is often one of the earliest functions of memory to degenerate in AD (Quimas Molina da Costa et al., 2018) which may result in an individual becoming lost or disoriented in familiar or unfamiliar surroundings (Quimas Molina da Costa et al., 2018). As it is one of the first cognitive functions to deteriorate in AD (Quimas Molina da Costa et al., 2018), it is a useful area to assess for early diagnostic purposes. However, some neuropsychological tests of spatial navigation have been criticised for their lack of ecological validity which makes generalising the findings to real-world navigational difficulties problematic (Werner et al., 2009).

9.1.2 Virtual Reality

Moore’s law states that every 12-18 months the number of transistors on a circuit board doubles (Moore, 1965). This allows for the development of more computationally demanding software over time. Computer technology has progressed so far that fully three-dimensional (3D) virtual environments can be generated and utilised to mimic everyday tasks which is referred to as VR. VR has been used for the treatment of physical disorders since 1994 (Diaz-Perez, and Florez-Lozano, 2018) and in recent years, it has been argued that VR technology holds the potential for psychological evaluation (Diaz-Perez and Florez-Lozano, 2018).

Previous research into on-screen VR cognitive functioning comes from Lesk et al. (2014) who developed a VR simulation designed to assess visuospatial memory. The researchers created a virtual environment which aimed to investigate cognitive functioning in a group of healthy older adult participants, and those with MCI. This virtual environment required participants to follow a virtual path to reach a destination (Lesk et al., 2014). There were five levels of increasing difficulty on the virtual reality task with each level involving more complex routes and junctions. Following this, participants were given a cognitive battery assessment which involved the GNT. the CANTAB, the MMSE, and a word recall task. The results reported significant correlations of scores on one level of the virtual environment task with existing neuropsychological tests. Furthermore, the test discriminated between the healthy older adult group and the MCI group. Furthermore, Pengas et al. (2010) conducted a study which utilised a virtual environment in order to discriminate between AD patients, semantic dementia patients, and healthy controls (Pengas et al., 2010). Topographical memory was assessed by tasks including a Virtual Route Learning Test (VRLT). The results demonstrated the VRLT achieved 95% sensitivity and 94% specificity in differentiating between AD patients and healthy controls (Pengas et al., 2010).

Werner et al. (2009) developed a virtual supermarket environment in order to assess the feasibility and validity of diagnosing patients with MCI by using a 'Virtual Action Planning Supermarket' (VAP-S) (Werner et al., 2009). This experiment tasked participants with finding seven items from a shopping list within a supermarket setting, and then purchasing them at a counter in the virtual environment. The results showed that the score on the VAP-S was not able to discriminate between MCI participants and controls when used alone. However, when MMSE scores were combined with the total distance in meters traversed by the participant and analysed together via a discriminant analysis, this became sensitive enough to differentiate between the groups (Werner et al., 2009).

All of the discussed studies in this section up to this point have utilised VR as an assessment method. However, the advent of new technologies has rendered "VR" as a problematic term as it has become less clear to what "VR" refers. For clarity, this article will refer to virtual environments which take place on a computer screen as on-screen VR, whereas the fully-immersive 3D experience which utilises a VR helmet will be referred to as fully-immersive VR.

It has been argued that on-screen virtual environments can provide the user with a high level of immersion, and that participants often report that they feel as though they were within the ‘game’ or ‘scene’ (Duffy, 2009). It has also been argued that on-screen assessments can cover a much larger spatial area than standard tests (Duffy, 2009). However, recently there have been criticisms of on-screen assessments, as it is argued that fully-immersive VR can provide a more immersive experience and a more natural interaction between the participant and the surrounding environment (Corriveau Lecavalier et al., 2018). There are fewer studies that have investigated fully-immersive VR, however, previous research into fully-immersive VR and spatial memory comes from Quimas Molina da Costa et al. (2018) who assessed spatial orientation and spatial memory in thirty-one healthy adults by tasking them with completing a SOIVET-Maze task. This task assessed the participants’ ability to navigate a 3D environment by utilising a map in front of them and the SOIVET-Route, which assesses visuospatial memory and topographical landmark recognition. Their results showed that fully-immersive VR technology is an effective tool for assessing spatial orientation and spatial memory. Further research into fully-immersive VR comes from Ouellet et al. (2018) who created a virtual shop task for participants to complete, similar to the VAP-S study from Werner et al. (2009). This task involved assessing navigation, interaction and conversation in a group of thirty-five MCI participants. It was found that performance correlated with scores on traditional memory assessments. These results support the ecological validity of using fully-immersive VR as a tool for assessing memory.

9.1.3 Aim of the Study

This study explored the relationship between spatial memory and cognitive functioning. The aim of the study was to evaluate the use of a newly developed fully-immersive VR test. This was achieved by tasking participants with completing a series of timed mazes. The data were analysed by comparing scores on the fully-immersive VR assessment against cognitive tests.

9.2 Methods

9.2.1 Participants

The participant cohort consisted of twenty-nine participants (fifteen males and fourteen females). Participants belonged to the following age groups; (i)18-25 n=7), (ii) 25-31 (n=8), (iii) 32-38 (n=7), (iv) 39-45 (n=4), (v) 46-52 (n=0), (vi) 53-59 (n=2), (vii) 60+ (n=1)

Participants had no existing neurological disorder, no clinically diagnosed cognitive impairment, no uncorrectable vision impairment that would prevent the VR headset from functioning correctly, and consented to following the health and safety guidelines of the Oculus Rift VR headset. All participants were recruited from the University of Bradford, both current students and members of staff. The study was approved by the University of Bradford Humanities, Social and Health Sciences Research Ethics Panel and all participants provided informed consent. Regarding sample size, previous research into the relationship between fully-immersive VR and cognition comes from Ijaz et al. (2019) who conducted a fully-immersive VR assessment on spatial navigation in a pre-dementia screening assessment which utilised twenty participants. Similarly, Simpson et al. (2017) utilised twenty participants in a fully-immersive VR study which also contained several cognitive tests. As such, the aim for this study was to recruit twenty participants but more could take part if they wished to.

9.2.2 Spatial Memory Assessment Apparatus

9.2.2.1 The Oculus Rift VR Headset. The VR headset used in the present study was the Oculus Rift VR headset production model (Facebook Technologies LLC, 2020). The production model incorporates a dual organic light-emitting diode (OLED) display with a resolution of 1080 ×1200 pixels per eye, with a supported refresh rate of 90Hz (Facebook Technologies LLC, 2020).

9.2.2.2 Unity. The software used to develop the VR mazes was a program called Unity. Unity is a cross-platform game engine developed by Unity Technologies (Axon, 2016). The engine can be used to create three-dimensional, two-dimensional, virtual reality, and augmented reality games (Takahashi, 2018). In the present study, the VR mazes were created on a grid structure, wherein each subsequent maze would increase in difficulty by increasing the size of the grid, allowing for a greater number of junctions and branching paths.

9.2.3 Procedure

The study began with participants being greeted and providing informed consent. Following this, they were asked to wear the Oculus Rift VR headset and hold onto the accompanying touch controllers. With the headset on, the participants found themselves in an open empty space in order to get accustomed to the experience of fully-immersive VR and its controls.

Following this, participants removed the headset and were presented with an overhead map of the maze they were about to enter. Participants had up to three minutes to learn and remember the route out of the maze. They then entered the maze and were timed on how long it took them to escape. This was repeated for all levels of the maze. The mazes increased in complexity with each successive level. Difficulty was defined based on the size of the maze, the number of junctions, and the number of branching paths. In the present study participants were given a series of six fully-immersive VR mazes of increasing difficulty. Following the maze task, participants were offered a break before proceeding to participate in a cognitive assessment. Following the cognitive assessment, the participants were thanked, debriefed, and offered another opportunity to ask any questions they had before they left.

9.2.4 Cognitive Assessments

All cognitive tests were designed by the researcher. Each participant completed a series of six fully-immersive VR mazes, and a neuropsychological cognitive battery assessment. The following cognitive tests were given to the participants: A word recall task, a digit span task, a dual task, and an associative learning task. These cognitive assessments were the same as utilised in Chapter Five. See Chapter Five for a detailed breakdown of these assessments.

9.2.5 Data Analysis

The data was analysed using a general linear model MANCOVA to compare each participant's maze completion times with their scores on the neuropsychological tests.

9.3 Results

The aim of the study was to explore the relationship between spatial memory and cognitive function in a fully-immersive VR world. We also wished to assess whether the increased capacity for naturalism offered by a fully-immersive VR experience (Corriveau Lecavalier et al., 2018) could be used in cognitive assessment.

There can be significant effects of age and gender on both spatial memory (Chen et al., 2020) and on scores of neuropsychological assessments (Jacova et al., 2007; Fields et al., 2011). Therefore, age and gender effects on the results were analysed.

A MANCOVA was carried out with neuropsychological assessment scores and VR maze times as the dependent variables, and with age and gender as covariates. No significance of age or gender was found for either neuropsychological assessment results or VR maze times. Furthermore, ToD may also influence results on cognitive assessments (Walters and Lesk, 2015). A MANCOVA was carried out with ToD of participation as the independent variable and neuropsychological assessment scores and VR maze times as the dependent variables. ToD effects were found to be non-significant. The data were normally distributed.

The descriptive statistics for each neuropsychological assessment and each level of the VR maze task can be seen in tables 12 and 13 respectively.

Table 12 The mean and standard deviations (SDs) for each neuropsychological assessment

Test	Min	Max	Mean	SD (+/-)
Word Recall (STM)	3	11	6.17	2.51
Word Recall (LTM)	0	9	5.21	2.41
Digit Span (Forward)	3	12	7.52	2.53
Digit Span (Backward)	3	10	5.69	1.90
Dual Task (Letters)	21	30	27.52	3.11
Dual Task (Colours)	15	30	22.31	4.42
Associative learning	6	10	6.38	2.19
Dual Task (Combined)	0	13	5.21	3.53

Table 12 shows the descriptive statistics for the cognitive assessments including the minimum score, maximum score, mean score, and SD.

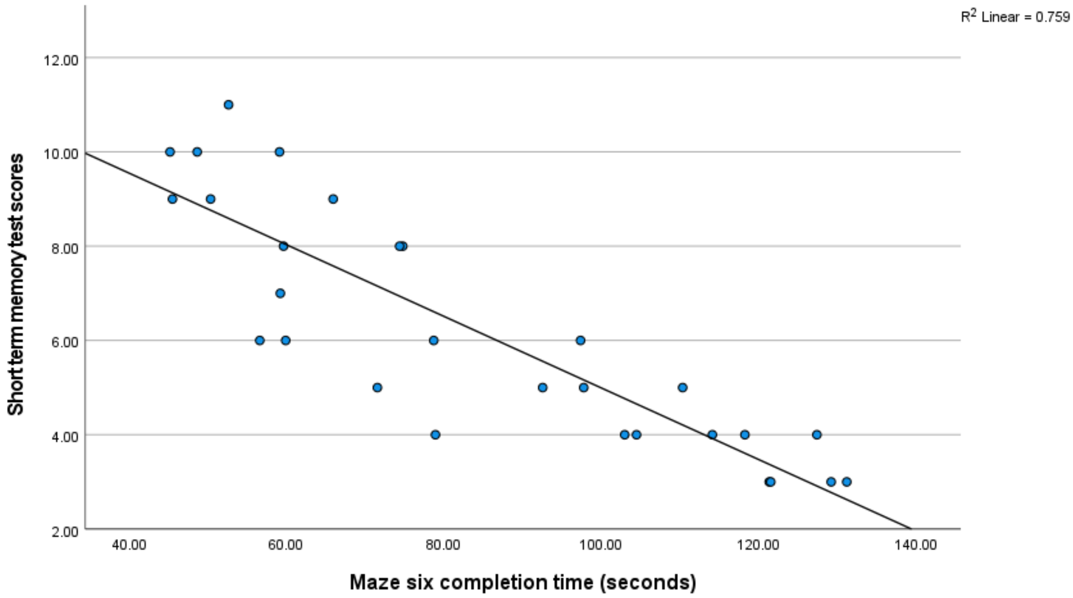
Table 13 The mean and SDs for each level of the VR maze assessment

Level	N	Min (seconds)	Max (seconds)	Mean	SD (+/-)
One	29	12.59	57.71	30.40	12.11
Two	29	12.21	38.98	23.45	8.47
Three	29	17.93	50.19	30.69	10.86
Four	29	28.26	73.41	47.18	13.92
Five	29	30.49	98.54	66.26	34.96
Six	29	45.20	131.10	84.43	28.74

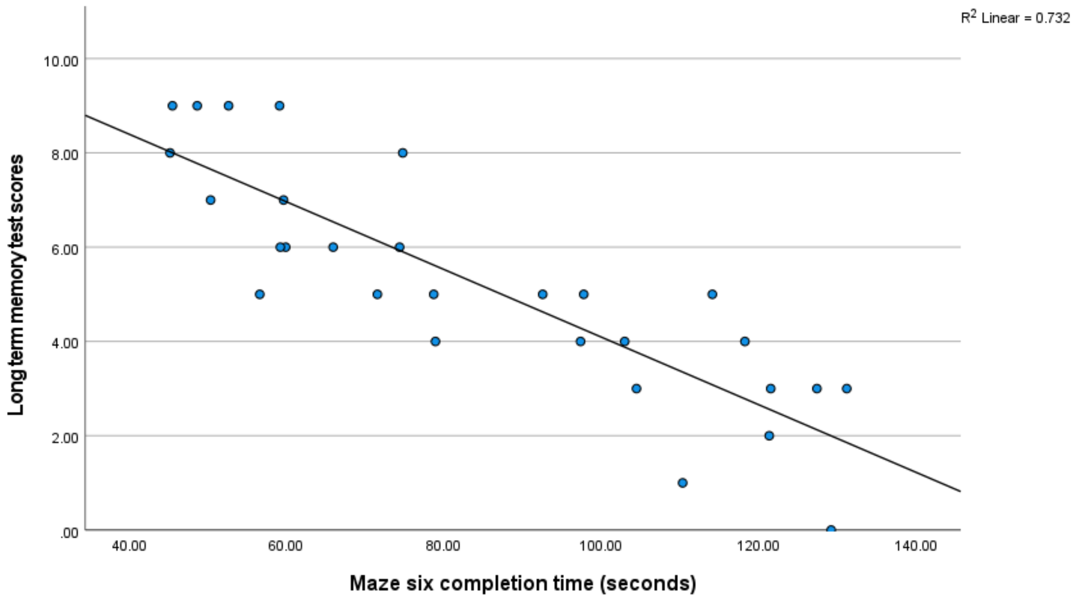
Table 13 shows the descriptive statistics for the VR maze times, including the minimum time, maximum time, mean time, and SD.

The results of all six levels of the maze assessment and neuropsychological tests (Word recall, STM/LTM, Digit Span, Dual task, associative learning) were submitted to a MANCOVA analysis using SPSS where neuropsychological assessment scores were entered as the dependent variables with the VR maze level scores entered as the covariates.

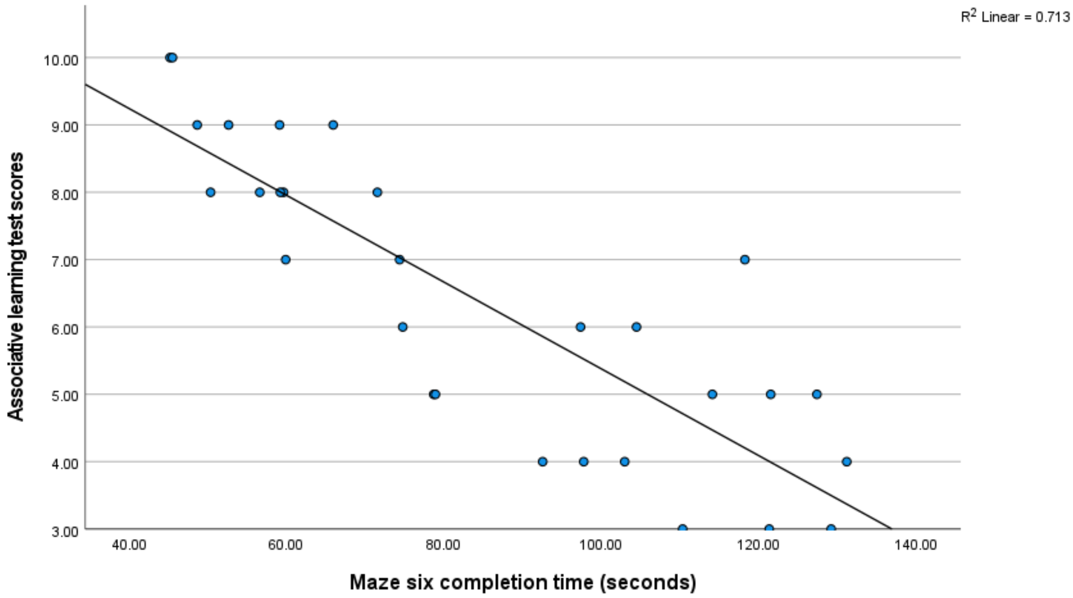
The MANCOVA analysis revealed a relationship between VR maze level 6, which was found to have a relationship with STM ($F(1,22) = 20.20$ $p < 0.01$), LTM ($F(1,22) = 09.10$ $p < .01$), associative learning ($F(1,22) = 08.75$ $p < .01$), and the dual–task test ($F(1,22) = 04.64$ $p < .05$). No significant findings were found between any of the cognitive assessments and levels one to five of the VR maze task. Only VR maze level 6 reported significant findings $F(6, 17) = 3.20$, $p < .05$; Wilk's $\Lambda = 0.47$, partial $\eta^2 = 0.53$. Figure 7 depicts graphs which plot the significant results recorded in this study.


R2 Linear = 0.759
12.00
10.00
8.00
6.00
4.00
2.00
Short term memory test scores
40.00
60.00
80.00
100.00
120.00
140.00
Maze six completion time (seconds)

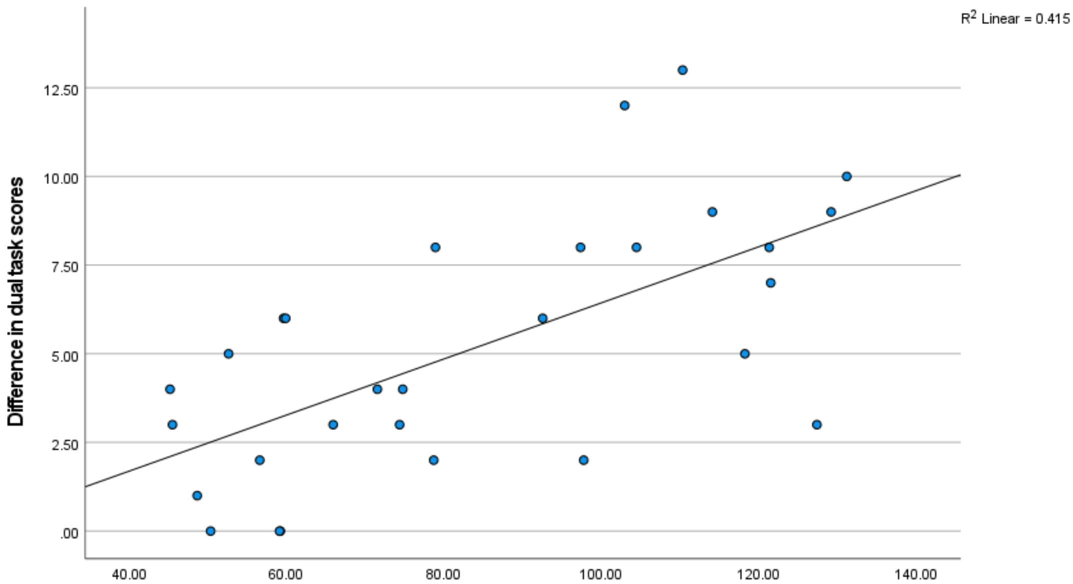
a


R2 Linear = 0.732
10.00
8.00
6.00
4.00
2.00
.00
Long term memory test scores
40.00
60.00
80.00
100.00
120.00
140.00
Maze six completion time (seconds)

b



c



d

Maze six completion time (seconds)

Figure 7 scatter plots demonstrating the interaction between maze completion times and significant results on cognitive tests: STM (a), LTM (b), associative learning (c), and the dual task (d), The scatter plots show a significant linear decrease in cognitive test scores as maze completion time increases, except in the case of the Dual Task, wherein the difference between the results of the letters task and the colour task are significantly positively related with maze completion times.

Parameter estimates confirm a linear, negative relationship between VR maze level 6 completion time, and STM (B=-0.65, SE=0.02, t=-4.49, $p < .05$, 95%CI [-0.10, -0.04]), LTM (B=-0.04, SE=0.01, t=-3.02, $p < .05$, 95%CI [-0.07, -0.01]), and associative learning (B=-0.04, SE=0.01, t=-2.96, $p < .05$, 95%CI [-0.06, -0.01]). Parameter estimates also show a linear, positive relationship between differences between VR maze level 6 completion time, and the Dual Task scores (B=0.06, SE=0.03, t=2.15, $p < .05$, 95%CI [-0.01, -0.12]).

9.3.1 Previous VR experience

All participants reported familiarity with using computers in their everyday lives, whereas five participants reported having previous fully-immersive VR experience. A univariate analysis of variance was carried out between participants who reported previous fully-immersive VR experience and those that had not. Results were non-significant ($F(1,27) = 1.09$, $p > 0.05$.).

9.4 Discussion

VR is a useful tool to assess cognitive tasks in healthcare, particularly regarding navigational difficulties (Rizzo and Kim 2005). The aim of the present study was to explore the relationship between spatial memory and cognitive functioning in a fully-immersive 3D VR world. The results demonstrated that greater maze escape time on the most difficult maze level was significantly negatively related to scores on tests of STM, LTM, associative memory, and positively related to score differences on the dual task. In the VR study of Lesk et al. (2014), of the five levels given, level four significantly correlated with scores on the CANTAB, an associative memory task and the GNT. Given the different methodologies between this study and the present study the results are difficult to compare. However, based on the results of the present study a further logical area of research would be to see if more levels of increasing difficulty of the VR maze task would demonstrate an even stronger relationship. This findings from this study concur with the work of Quimas Molina da Costa et al. (2018), who asserted that fully-immersive VR technology is an effective tool for assessing spatial orientation and spatial memory. However, the present study deviates from and expands upon the findings of Quimas Molina da Costa et al. (2018) as they were not relating the spatial memory assessment to scores of cognitive functioning. Furthermore, Quimas Molina da Costa et al. (2018) did not assess spatial memory without the aid of anchor points, such as landmarks. The current study, however, shows that even without a requirement for landmarks, fully-immersive VR is a sensitive tool for the assessment of spatial memory.

Regarding landmarks, this study demonstrates interesting findings when compared to the work of Uddin et al. (2017) who conducted a study where participants completed a series of spatial memory trials using Command Maps. Uddin et al. (2017) reported that for small grid menus, the artificial landmarks held no significant influence over performance, whereas for medium and large grids, the anchor marks improved performance significantly. It could be the case that the results of the present study are in line with the findings of Uddin et al. (2017), as the mazes may have been small enough that landmarks were not necessary, which supports the findings that small grid menus, the artificial landmarks hold no significant influence over performance. Future research should investigate cognitive performance compared with much larger fully-immersive VR mazes, both with and without landmarks, in order to assess whether the findings of Uddin et al. (2017) regarding landmarks can be directly translated from on-screen VR to fully-immersive VR.

Finally, the present study furthers the findings of Ouellet et al. (2018), who created a VR shop task, which supported the ecological validity of using fully-immersive VR as a tool for assessing WM and has extended this to spatial memory.

9.4.1 Methodological Considerations

There exists an established negative relationship between aging and cognitive functioning (Murman, 2015); previous research has reported that poor performance may be a result of increasing age of the participant cohort (Tombaugh and McIntyre 1992). However, in the present study, there was no effect of age on scores of cognitive functioning. This could be due to the age of the participant cohort, as many participants reported their ages between eighteen and forty-five. This may explain the lack of age effects in the present study, as it has been reported that cognitive decline begins around the age of 45, meaning this would not hold an influence over younger participants (Singh-Manoux et al., 2012).

The ToD at which an individual is at their optimal arousal alters with age (Hasher, et al., 2005). Previous research into ToD and cognitive functioning comes from Walters and Lesk (2015) wherein a study was conducted on thirty-six older adult participants (mean age 72.53 ±6.09). Two data sets were analysed which reported significant ToD affects in tests of Pattern Comparison Speed, Letter Comparison Speed, a Trail Making Test, the MMSE, and the GNT. This could be considered a valuable area of additional research when considering VR as a potential tool for diagnosing cognitive impairment in older adults. The present study found no ToD effects on either the cognitive assessment or the maze task, highlighting its potential for diagnostic with limited confounding factors. Walters and Lesk (2015) have also reported significant interactions between prior caffeine intake and age on some cognitive tests. Caffeine intake was not controlled in the present study and should be investigated in future iterations of this study.

Our results suggests that the increased capacity for naturalism offered by fully-immersive VR may interact with the results on cognitive assessments in ways that on-screen VR may not. This warrants further investigation and iteration in future studies. Previous research has raised concerns about possible side effects of using a virtual world, including concerns of the participant disorientation or nausea during the task (Farmani and Teather, 2018) referred to as cybersickness. Given one aim is to assess this technique as a potential diagnostic tool, how well it is tolerated by users is important. Cybersickness is defined as a form of motion sickness (Quimas Molina da Costa et al., 2018). It is believed that cybersickness results from a conflict between visual stimuli and other sensory information, such as auditory, vestibular and proprioceptive stimuli (Quimas Molina da Costa et al., 2018). In the present study, we had only one report of cybersickness.

Some participants reported that they found the test too easy, whereas others reported that both maze levels five and six were quite complex. This is also demonstrated in the results with participants performing at ceiling level in the easier levels. None of the participants reported struggling to use the apparatus after they acclimated themselves to the virtual world in the practice area. As discussed earlier, prior familiarity with fully-immersive VR held no influence on performance in either the maze task or cognitive assessments. It is unclear why VR maze one took, on average, more time to complete than VR maze two. This may be due to VR maze one being the first. While participants had an opportunity to familiarise themselves with the controls and the experience of fully-immersive VR, it may be the case that this practise did not translate into familiarity with turning corners and recalling a path. Future research should present participants with a test trial first. Another future direction that would be useful to explore would be to assess many different forms of VR against each other, including on-screen VR, fully-immersive VR, augmented reality, and others, in order to assess how each different form of VR compares when tested directly against each other.

9.5 Conclusion

Navigational difficulties can be one of the earliest symptoms of AD (Quimas Molina da Costa et al., 2018). In this study, there was a significant relationship found between VR maze six, and scores of STM, LTM, associative learning, and a dual task, with no effect of age or gender. Future study will investigate larger fully-immersive VR mazes, both with and without landmarks, in order to ascertain exactly where the ceiling-level is for VR maze difficulty and whether this has the potential to be used as a clinical tool for neurological assessment.

9.6 Highlights

- Computer technology has previously been used to assess cognition in a variety of ways and has provided opportunities to mimic common everyday life situations within the computational environment.
- The advent of fully-immersive VR provides much greater potential for naturalistic assessments than can ever be offered by traditional, computer-based, on-screen assessments.
- If differences are found to exist between traditional computer-based assessments and fully-immersive VR assessments, this may prove to hold significant implications for utilising technology for computer-based assessments of AD.
- The purpose of this study is to explore whether the greater capacity for naturalism afforded by fully-immersive VR generates results which conform to previous results witnessed in traditional, computer based, on screen assessments.
- A sample of twenty-nine (age = eighteen to sixty) cognitively-healthy individuals (gender = fifteen male, fourteen female) from the University of Bradford were tasked with completing a series of six timed VR maze tasks of increasing difficulty followed by a cognitive battery assessment.
- Preliminary results indicate that the length of time it takes to escape VR mazes significantly negatively related to scores on tests of short term memory (STM) ($F(1,22) = 20.20$ $p < 0.01$), Long Term Memory (LTM) ($F(1,22) = 09.10$ $p < 0.01$), an associative learning task ($F(1,22) = 08.75$ $p < 0.01$), and the dual task ($F(1,22) = 04.64$ $p < 0.05$).
- These findings hold potential to be used as a possible method of assessing cognitive functioning in healthy populations and hold implications concerning AD and dementia assessments.
- The findings are similar yet distinct from traditional, computer-based, onscreen assessments, making it difficult to recommend implementation of complex and expensive VR systems in place of traditional computer-based assessments in a clinical environment without further investigation.

Chapter Ten

General Discussion and Summary

10.1 Introduction

The overarching goal of this thesis was to provide an understanding of non-invasive methods which may have the potential to be used to strengthen the accuracy of a dementia diagnosis. All the experimental chapters in this thesis utilised a quantitative experimental methodology. This involved the administration of a cognitive battery of assessments which assessed various domains of neuropsychological functioning which are often used, or related to, the domains assessed in clinical contexts. The methods assessed were postural stability, facial cues (both emotional expressions and blink rates) and fully-immersive virtual reality.

This thesis has demonstrated a sensitive link between postural control and cognitive functioning. Firstly, in Chapter Five greater standard deviations in AP sway were significantly negatively associated with scores memory tests. The shows that a link between postural stability and cognitive function in cognitively-healthy participants may have implications for clinical diagnostic processes in assessing a cognitive impairment such as AD. These findings were reaffirmed and built upon in Chapter Six, which indicated that participation in a greater variety of posture-related sporting activities was positively related to compound memory scores generated from a series of memory assessments. Moreover, as an online study recruiting a number of individuals, these findings offered greater ecological validity than can be afforded by a controlled experiment cementing the findings of Chapter Five.

Following these findings, this thesis pivoted attention to a different non-invasive technique which could be implemented in a diagnostic capacity, namely, facial cues. In the first study looking at facial cues, the findings suggested that a greater frequency of negative facial expressions shared a significant, positive relationship with composite memory test scores, thus providing potential for utilising facial analysis software, and assessment of negative facial expressions in particular, as a tool for assessing cognition. Following this, these findings were furthered by Chapter Eight, which considered a separate facial cue, blink rates. It was found that individuals who presented the lowest 25% of blink rates performed significantly better on a series of memory assessments than the remaining 75% of participants.

Finally, Chapter Nine assessed spatial memory using fully-immersive VR. It was demonstrated that improved performance on a series of fully-immersive VR mazes was significantly positively related to scores on cognitive tests. Moreover, it was found that these relationships were only present on the most difficult of mazes, which was not seen in previous findings of on-screen assessments of spatial memory.

This final chapter will talk on the motivations for conducting the previously described research while collating the results and discussing potential future directions of study. as well as a discussion on the implications and applications of the findings. This Chapter concludes with an overall summary of the thesis.

10.2 Motivation for Research

The global population is aging (Khow and Visvanathan, 2017). As individuals live longer, there is an increased prevalence of age-related illnesses such as dementia (Ragin, 2017). Dementia has been identified as one of the most severe health challenges facing the world at this time (Prince et al., 2015), with an estimated 850,000 Britons currently suffering with dementia, costing individuals and the government a combined £34.7 billion annually (Alzheimer’s Society, 2020). It is thought that over one million individuals in the UK will be suffering from dementia by the year 2025 (Prince, et al., 2015). The annual cost of dementia is set to rise sharply over the next two decades, to £94.1 billion by 2040 (Alzheimer’s Society, 2020); whereas worldwide, there are currently around fifty million people suffering from dementia (WHO, 2020), costing individuals and the government a combined total of $818 billion annually (Prince, et al., 2015; Livingston, et al., 2020).

An early diagnosis of dementia is vital (Kumar and Day, 2020). It will assist in alleviating some of the economic burdens of the condition, while also ensuring that the individual suffering from dementia is living the highest quality of life possible for as long as possible, as treatments could be initiated sooner. Furthermore, an early and accurate diagnosis of dementia is particularly important for clinical trial research as clinical trials rely on specific classifications of individual dementia subtypes (Lesk et al., 2009).

However, an early diagnosis of dementia is difficult to achieve. As a neurodegenerative illness the symptoms of dementia gradually become worse over time (Ikonomovic and Abrahamson, 2017). Due to the nature of neurodegenerative illnesses, symptoms are less pronounced in the earlier stages and underlying pathological changes which cause dementia occur decades before any symptoms are seen (Forlenza et al., 2010). This means that a diagnosis is often achieved too late, after neural degeneration has reached an extent that treatments for the condition are not as effective, had the diagnosis been achieved in a timelier manner (Pantel, et al., 2004).

In the UK, the most used method of diagnosing dementia is the MMSE (Scheffels, et al., 2020). However, there are concerns with this assessment. Some argue that the MMSE should be retired due to issues with reliability, validity, and ethnocentricity (Carnero-Pardo, 2014), while other researchers have reported that the results of an MMSE evaluation can be influenced by levels of literacy, as well as cultural norms (Devenney and Hodges, 2017). This may be explained by reports that the MMSE was never originally intended to be used for achieving a dementia diagnosis (Folstein, et al.,1983).

Previous research has reported that confounding external factors such as age, gender, education ethnicity, and caffeine intake and others must be considered when evaluating neuropsychological performance (Jacova, et al., 2007; Fields, et al., 2011; Morais, et al., 2018; Walters and Lesk, 2015; 2016; Walters, 2015; Lesk et al., 2009). The overall motivation for the research in this thesis was to explore other methods that have the potential to be used in diagnosis in the future aiding accuracy of any cognitive assessment, that avoid many of these confounding factors.

10.3 Summary of Findings

It is vital to always maintain postural stability, as the process of maintaining balance is required for human functioning (Farcy, 2020). This point is reflected in literature which has found that impaired postural stability is associated with health conditions such as strokes, ear infections, hypotension, AD, and more (Winter et al 1990). Previous research has also demonstrated that deficits in postural stability can be seen in both AD (Visser, 1983) and in MCI (Shin et al., 2011). The relationship between postural stability and cognitive functioning within cognitively-healthy populations is less clear.

Chapter Five outlined novel relationships with postural control and cognitive functioning and it was revealed that greater standard deviations in AP sway and poorer cognitive test scores showed a significant relationship in a group of cognitively-healthy participants. ML sway was not found to be related to cognitive functioning, though this is not surprising given the side-by-side standing stance, which is required to stand on the WBB, which results in balance being controlled by the ankles, leading to greater deviations in AP sway (Balasubramaniam, et al., 2000). The findings of this study further previous findings regarding the relationship between cognition and postural stability. Sant'anna et al. (2019) reported that individuals with AD demonstrated greater sway velocity with reduced sway control when compared to controls in a study which utilised the WBB. Similarly, a meta-analysis from Mesbah (2019) revealed that older adults with mild-to-moderate AD showed less postural control when compared to cognitively- healthy controls. The findings of Chapter Five furthered these previous findings by identifying that within cognitively-healthy controls, the interaction between cognition and postural stability is still seen. Furthermore, the mean age group of participants in this study was twenty-five to thirty-one, and as Forlenza et al. (2010) stated that pathological changes occur in AD decades before symptoms can be seen, this finding is important.

Chapter Six explored this relationship further by assessing whether participation in sporting activities which have a posture element can influence performance on a series of cognitive assessments. Previous research has highlighted relationships between posture and cognitive functioning (Szturm, et al., 2013; Smith, et al., 2019; Rosenbaum, et al., 2017; Caron et al., 2020; Díez-Álamo, et al., 2019; Peper, et al., 2017), however, this previous literature has reported contradictory findings. Some researchers reported that standing posture influenced performance on a series of cognitive tasks (Rosenbaum, et al., 2017) whereas others did not replicate these findings (Caron et al., 2020). Furthermore, the relationship between posture-related sporting activities and their influence on cognitive functioning in cognitively-healthy populations remains unclear.

An online study was conducted which involved participants self-reporting their participation in sporting activities, followed by assessments of cognitive function. Results demonstrated that individuals who participated in a greater number of posture-related sporting activities performed better in assessments of memory than those who participated in fewer. However, there was no significant relationship between sporting activity participation and reasoning ability. Furthermore, no individual sporting activity demonstrated a significant relationship with scores on other cognitive assessments alone, nor did amount of time spent taking part. These findings may go some way towards explaining the contradictory findings of Rosenbaum et al. (2017) and Caron et al. (2020) as it may be the case that confounding variables, such as lifestyle choices, my produce conflicting findings if they are not considered during the data analysis process. These findings hold applications for further exploring cognitive brain health and physical activity, in particular those that have a posture related component. Furthermore, the findings support the results of the first experiment and extend the link between posture and cognition further. It is interesting that time spent taking part did not demonstrate a significant relationship with cognitive functioning. Further research is needed to establish exactly how much posture-related activity is indeed beneficial for effects on cognition. It is also interesting that no single posture-related activity demonstrated an effect. Whilst future research should look at individual sports in more profound detail, the findings do however suggest that it is the influence of posture overall that is the important variable of interest.

From here, this thesis turned to researching facial expressions of emotion; a separate factor which is not currently considered in dementia diagnoses but may hold the potential to provide a novel and useful non-invasive technique for its detection. Humans use facial expressions to convey a wide variety of emotions (Van Der Zant and Nelson, 2021), however, difficulties in expressing emotions have previously been associated with schizophrenia (Mandal et al., 1998), dementia (Asplund, et al., 1991; Seidl, et al., 2008), AD (Arroyo-Anlló et al., 2021), and autistic spectrum disorder (Drimalla et al., 2021; Keating et al., 2021). Similar to the literature relating to posture and cognition, previous research into facial cues and cognition has shown conflicting results. Some early findings have demonstrated that dementia patients produce more negative emotions than cognitively-healthy controls (Asplund, Jansson, and Norberg, 1995; Smith, 1995) whereas more recent research has reported that AD patients present fewer recognisable expressions at all (Seidl et al., 2008; 2012).

Prior to the study outlined in Chapter Seven, the relationship between cognitive functioning and facial expressions of emotions remained relatively unexplored. The findings of this study revealed that a greater frequency of negative facial expressions shared a significant, positive relationship with composite memory test scores. with no significant relationship seen between cognitive functioning and the facial expressions of surprise, happiness, anger, sadness, fear, or disgust. These results were surprising as previous research identified that AD patients either demonstrated a greater frequency of negative expressions of emotions (Asplund et al., 1995; Smith, 1995) or fewer recognisable emotions at all (Seidl et al., 2008; 2012). Due to the different methodologies used in these studies, it may be difficult to draw a direct comparison between the findings. The findings of this Chapter, however, are particularly important as Chapter Seven reports a novel finding in the field of facial expressions and its relationship with cognitive processing.

Following the research outlined in Chapter Seven, Chapter Eight continued research into exploring the relationship between facial cues and cognitive functioning by assessing the influence of blink rates on cognition. This study utilised the same participant cohort and video recordings as the study outlined in Chapter Seven, although Chapter Eight utilised different facial analysis software in order to measure blink rates. Early literature into the relationship between blink rates and cognitive functioning revealed a negative relationship showing that the greater the blink rate, the worse the cognitive performance (Holland and Tarlow 1972; 1975). More contemporary research has reported the opposite; that a higher blink rate resulted in greater cognitive performance (Kuwamizu, et al., 2020; Ortega, et al., 2021). The study of this chapter reported findings that participants who produced the bottom 25% of blink rates performed better on tests of cognition than the remaining 75%. These results were surprising as previous research has reported that MCI patients produce a lower blink rate than cognitively-healthy controls (Ladas et al., 2014), although due to methodological differences with previous studies, a direct comparison is difficult. It was concluded that blink rates may be a tangible marker to consider in cognitive assessments, however, there is a need to standardise the methodology of assessing blink rates for the sake of replicability.

Finally, Chapter Nine aimed to assess whether spatial memory as assessed by fully-immersive VR was related to scores on tests of cognition, and whether fully-immersive VR generated similar results to spatial memory assessments which used a standard PC screen. Assessing spatial memory is a complex task, as this form of memory comprises a series of cognitive functions which can act either in concert, or individually (Jacobs, 2003). Spatial memory assessments are often conducted using a PC screen; however, it was unclear whether new technologies which afford a greater capacity for naturalism may offer distinct and separate findings than previous studies which used less naturalistic methods.

This study was conducted by creating maze trials in fully-immersive VR, and comparing the results generated by this study to prior PC based literature assessing spatial memory. The results of Chapter Nine demonstrated that participants who took longer to complete the most difficult maze trial performed worse on tests of STM, LTM, associative learning, and a dual task assessment. This is similar to the findings of Lesk et al. (2014), who reported findings that the second most difficult level of a spatial memory task was related to scores on the CANTAB PAL (Paired Associates Learning) and the GNT. Based on the Chapter Nine results, a further logical area of research would be to see if more levels of increasing difficulty of the VR maze task would proportionally increase the strength of the witnessed relationship between maze escape times and cognitive functioning. Future study should look at how this should be implemented in a clinical setting. For example, establishing the best ‘difficulty’ level and testing this in older adults, in longitudinal studies, in those with cognitive impairment and assessing cognitive decline would be a logical way forward. Furthermore, if naturalistic methods of assessing spatial memory prove to provide conflicting results to PC tests, the validity of PC based spatial memory assessments should be considered.

10.4 Implications and Applications

Chapter Five outlined the findings that greater standard deviations in AP sway were negatively related to scores on tests of cognitive functioning in cognitively-healthy individuals. This was seen regardless of age or gender. Previous research has established that deficits in postural stability can be seen in both AD (Visser, 1983) and in MCI (Shin, et al., 2011), which is thought in some cases to be a transitional stage into developing dementia (Sullivan et al., 2019). The findings witnessed in Chapter Five appear to suggest that this relationship is found prior to any diagnosis of cognitive impairment. These findings hold potential implications for future cognitive assessments, as postural stability may be able to be considered as a novel, non-invasive and non-verbal factor which has the potential to improve the accuracy and reliability of cognitive assessments if they are used in tandem; for example, during a paper assessment of cognitive functioning, it is not unfeasible to suggest that a person simply stands on a FP during this period. Doing so would generate data on their postural stability which could be considered when assessing the results of a paper assessment of cognition. This is particularly important as there is only a six-point difference between normal cognition, MCI, and AD on test scores on the MMSE (Tombaugh, 2005).

Chapter Six furthered these findings with the use of an online study which utilised a self-report questionnaire in order to assess participants' sporting activity behaviour followed by memory and reasoning tests. It was found that participation in a greater variety of posture-related sporting activities was positively related to compound memory scores generated from the previously mentioned cognitive assessments. Previous research into posture and cognitive functioning has revealed contradictory findings, where some researchers reported that standing posture influenced performance on a series of cognitive tasks (Rosenbaum, et al., 2017) whereas others could not replicate these findings (Caron, et al., 2020). The results of this chapter suggest that there exists a relationship between posture and memory and that external factors, such as the variety of posture-related activities that an individual participates in, may have implications for their cognitive assessments. The first implications to consider for this study is that the findings from Chapter Five have been re-affirmed. It appears that a sensitive relationship exists between postural stability and cognitive functioning. These findings strengthen the results generated in Chapter Five, as this study strengthened the previous findings by supplying ecological validity that cannot be obtained through a standard lab-based assessment. The findings that that participation in a greater variety of posture-related sporting activities was positively related to compound memory scores generated from the previously mentioned cognitive assessments holds implications for lifestyle choices that can be recommended. The results suggest that participation in a variety of sporting activity may assist in the formation, maintenance, and consolidation of memory.

This thesis also found that a greater frequency of negative facial expressions displayed by a cognitively-healthy individual shared a significant, positive relationship with composite memory test scores. Previous research has shown conflicting results in displaying facial cues in individuals suffering from AD. Some findings have demonstrated that dementia patients produce more negative emotions (Asplund, Jansson, and Norberg, 1995; Smith, 1995) whereas others argue that AD patients present fewer recognisable expressions at all (Seidl, et al., 2008; 2012). However, there is little research regarding the facial expressions of emotion being displayed and their relationship with cognitive functioning within cognitively-healthy populations. The present findings that an increased frequency of expressions denoting a negative emotion is positively related to scores on tests of cognitive functioning holds implications both within diagnostic contexts and without. During cognitive assessments, if the individual consents, they could have their faces recorded and analysed, potentially in real-time, to assess their facial expressions of emotions while they are completing the assessment.

Similarly to this thesis' reported findings on postural stability, the facial cues findings outlined in Chapter Seven provide an additional, novel, non-invasive cognitive assessment tool which is not dependent on language ability. To further the findings reported in Chapter Seven, Chapter Eight analysed blink rates, another facial cue with the potential to be a non-invasive biomarker for cognitive ability. As mentioned above, previous literature into the relationship into blink rates and cognitive ability has reported contradictory findings, where older studies report a negative relationship and more recent studies report a positive relationship (Holland and Tarlow 1972; 1975; Kuwamizu, et al., 2020; Ortega, et al., 2021). The study outlined in Chapter Eight reported that participants who produced the lowest 25% of blink rates outperformed the remaining participants in a series of cognitive tests. As in Chapter Seven, the findings reported in Chapter Eight highlight another facial cue which has the potential to be utilised as a non-invasive biomarker for cognitive ability. If subsequent research mirrors the findings of the present study, there is potential for blink rates to be analysed alongside standard cognitive assessments.

Usually, cross-sectional studies do not consider an individual's postural stability, nor do they consider a participant's proclivity towards participating in sporting activities, or the facial expressions which are being displayed, or how often they blink. However, results suggest that each of these factors share some relationship with cognitive ability.

Finally, it was reported in Chapter Nine that greater maze escape time on the most difficult maze level was significantly negatively related to scores on tests of STM, LTM, associative learning, and positively related to score differences on the dual-task assessment. These results imply that spatial navigation using fully-immersive VR could accurately assess spatial memory, and that if these findings deviated from previous research, there would be implications for utilizing more naturalistic technologies in cognitive assessments. Previous research which utilised on-screen VR rather than fully-immersive VR from Lesk et al. (2014) reported that, in a similar experiment, of the five levels of increasing difficulty, level four significantly correlated with scores on the CANTAB PAL and the GNT. Given the different methodologies between this study and the Chapter Nine study, the results are difficult to compare. However, it is interesting to note that the results of the Chapter Nine study only managed to identify a relationship with the highest maze difficulty. It could be the case that the mazes developed for the Chapter Nine study were simply easier than the navigation tests used by Lesk et al. (2014). However, if future studies can identify that there is a difference between on-screen VR and fully-immersive VR, this will cast doubt on spatial memory test scores obtained through on-screen VR, as the results gained through fully-immersive VR are more naturalistic (Corriveau Lecavalier, et al., 2018).

10.5 Methodological Considerations and Future Directions

The aim of this thesis was to explore factors which are known to be related to dementia but are not yet utilised in a clinical context in the hopes of identifying potential non-invasive techniques for the detection and diagnosis of dementia, that avoid some of the external factors affecting neuropsychological assessment. The participants in the majority of the studies detailed in Chapters Five-Nine were mostly young adults, although some older adults took part in the study of Chapter Six. Future research should now move to investigate the findings in a large sample of older adults in order to generate normative data on individuals around the age that dementia is typically diagnosed. Moreover, the way in which the relationships reported within this thesis change over time are worth exploring. For example, the way in which these relationships change over the course of healthy cognitive ageing and/or cognitive decline could provide valuable insight into the mechanisms which underline the degenerative process. Additionally, future studies should investigate other forms of memory which were not assessed in the studies outlined in Chapters Five-Nine, such as sensory memory, procedural memory, or false memories.

Methodological considerations should be made regarding the ages of the participant cohort in all five studies presented in this thesis. An argument may be made that the participants who were in the higher age range of fifty or over may be showing early pathological changes regarding cognitive impairment. Were this to be the case, this may influence the findings. However, in each study in this thesis, age effects were analysed against scores on tests of cognition. All returned non-significant findings. Furthermore, Generally, it is standard to consider individuals aged 65+ as 'older individuals' (NHS, n.d.). Therefore, it is reasonable to assume the age demographics utilised in the studies throughout this thesis were appropriate for generating normative data.

Further methodological considerations should be made regarding the effects of caffeine on cognition. Walters and Lesk (2015) conducted a study to assess this relationship in thirty-six cognitively-healthy participants over the age of 60. The participants were tasked with completing a cognitive battery assessment. When controlling for caffeine, significant interactions were seen between caffeine, ToD and scores on the MMSE and the GNT. This would be useful to control for in future studies as Walters and Lesk (2015) have found caffeine to be a potential confounding variable for tests of cognition which is worthy of consideration. All studies detailed throughout Chapters Five-Nine analysed the effect of ToD on the findings, as previous research has reported ToD holds influence over cognition (Walters and Lesk, 2015). Moreover, ToD can hold influence over postural stability (Morelli et al., 2020), physical activity (Jago er al., 2005), and blink rates (Hove et al., 2021). It is not unreasonable to assume ToD effects may hold influence over spatial memory given the findings of Walters and Lesk (2015), although the specific relationship remains unclear. After a thorough literature search, no papers could be found regarding the influence of ToD on producing facial expressions of emotion. This highlights a need for further research. No significant ToD effects were seen in any study detailed in Chapters Five-Nine. Caffeine consumption was not controlled for in the studies in Chapters Five-Nine.

Future iterations of the studies outlined in this thesis studies should consider controlling for caffeine intake, as previous literature has identified relationships between caffeine intake and postural stability (Arsham et al., 2019), sporting performance (Pickering and Grgic, 2020), blink rates (Murari et al., 2018), and spatial memory (Nunes et al., 2018). After a thorough literature search, there is little on the effects of caffeine on the production of facial expressions of emotion. Rocha-Parra et al. (2021) found that the flavour of coffee held influence over the production of facial expressions, which is not fully relevant. However, this shows the absence of literature which requires further testing.

Considerations must also be made regarding the feasibility of applying the findings from Chapters Five-Nine in clinical contexts. Recording an individual's face during the diagnostic process may be a relatively easy inclusion as long as the participant consents. However, this may not be the case for all the non-invasive techniques which have been assessed. Assessing postural stability in a clinical environment would need careful administration, given the findings of Chapter Five report a negative relationship between postural stability and cognitive performance. Moreover, previous literature has shown that postural stability decreases as age increases (Brustio et al., 2021). Therefore, special care must be taken when asking older adults to stand on an elevated platform for several minutes. Similarly, attempting to implement fully-immersive VR into a clinical environment would be difficult. Even with fully-immersive VR becoming increasingly accessible (Mott et al., 2020), fully-immersive VR systems are still relatively expensive, and some require powerful computers in order to function correctly.

Furthermore, fully-immersive VR can induce motion sickness in some individuals (Farmani and Teather, 2018), and it is recommended in the Oculus Rift safety manual that individuals use fully-immersive VR for only a few minutes at a time if they have not used it before. Further research should explore the techniques detailed in Chapters Five-Nine within clinical contexts before the feasibility of their application can be stated for certain, as currently the studies lacked the necessary ecological validity. If ecological validity can be established for the findings reported through Chapters Five-Nine, it may hold implications for applying the findings in diagnostic contexts. The findings of the studies reported within this thesis may be capable of improving the accuracy of a dementia diagnosis as previous literature has reported that external factors may hold influence over the results of common neuropsychological assessments such as the MMSE, which can compromise the accuracy of their findings (Devenney and Hodges, 2017). These external factors include language dependence ethnicity, and education level (Devenney and Hodges, 2017). Moreover, assessing postural stability, facial expressions of emotion, and blink rates avoids visual and auditory impairments in the individual, which are further pitfalls of common neuropsychological assessments. Furthermore, the findings reported in Chapter Six that participating in a greater number of sports was related to improved memory performance may hold implications for lifestyle recommendations for older adults. If future research supports the current findings and it is the case that staying active, and in particular participating in posture-related activities, assists in maintaining memory functioning, then this could be recommended to help older adults maintain a higher quality of life for longer.

The findings of Chapter Five, i.e. that increased AP postural was negatively related to scores on tests of cognitive functioning could be expanded upon in a longitudinal study wherein the progression of cognitive impairment in individuals could be monitored over time, in order to assess whether the relationship between postural stability and cognition would be sensitive enough to predict decline over time. Chapter Five also reported a non-significant relationship between ML sway and cognitive functioning. This was attributed to the side-by-side stance which is required to adopt by the dimensions of the WBB as previous literature reports that balance is maintained by the ankles in a side-by-side stance, resulting in fluctuations in AP sway instead of ML sway (Balasubramaniam, et al., 2000). Future research could consider tasking the participants with standing in a series of different stances while their balance is assessed, in order to assess whether a front-to-back stance may show similar findings for ML sway. Furthermore, it is worth considering the placement off the WBB. In the Chapter Five study, the WBB was facing a window, several participants remarked that they felt it was helpful to have an object in the distance to focus on. Future studies should assess whether the relationship found between AP sway and cognitive functioning could also be found in differing lighting conditions such, as in darkness, and with varying focal points or distances.

Future research into postural stability and cognitive ability should also consider the findings of Chapter Six, that lifestyle choices such as participation in sporting activities can influence cognitive ability. Previously, a meta-analysis revealed that cognitive training can improve performance on dual-task management in older adults (Borel and Alescio-Lautier, 2014). This may explain the Chapter Six findings that there is a relationship between posture-related sports participation and scores on tests of cognition. Further research is warranted, however, before this can be stated for certain.

Future iterations of the Chapter Six study may consider assessing the memory capacity of sportspeople that participate in posture-related sports against non-sportspeople and sportspeople that participate in sports that have no posture-related component to explore the sensitivity of the relationship between posture-related sports participation and cognitive functioning. It appears that only individuals with an interest in sport participated in the online study, and as such, a control group of non-sportspeople was not generated. This would be necessary to generate a base level in order to compare against the sportspeople. Future research could also consider a greater number and variety of sports in order to generate a more robust understanding of the relationship between sporting activity, in particular those activities that have a strong posture element, and cognitive functioning. The study outlined in Chapter Six utilised a self-report questionnaire as part of the methodology. Therefore, the impact of social desirability must be considered. Social desirability is defined as the extent to which an individual projects a favorable view of themselves in social settings (Waltz et al., 2010), and has been identified as a long-standing problem in questionnaire research (Baumgartl et al., 2020). This holds implications for the accuracy and reliability of the findings.

Following the research into postural stability and cognitive functioning, the focus of the thesis pivoted onto a separate non-invasive technique which holds potential of assisting in a dementia diagnosis, facial cues. This research comprised of Chapter Seven which explored the relationship between facial expressions of emotion and cognition, and Chapter Eight which explored the relationship between blink rates and cognition. The findings of Chapters Seven and Eight are worth exploring further. Findings reported that individuals who demonstrated a greater frequency of negative facial expressions performed better in tests of cognitive functioning. If multiple iterations of this study witness this same relationship, it may hold implications for cognitive assessments in the future, in both clinical and non-clinical contexts. These results were surprising, given previous research has noted that individuals with dementia produce fewer faces that can be recognized as any facial expression (Asplund, et al., 1995), meaning that at some point during the transition from normal aging to dementia, individuals begin to produce fewer recognisable facial expressions. Future research should investigate this change, and aim to identify the point at which presentations of facial expressions of emotion begin to decline, and whether this is in also in line with cognitive decline. One potential method to do this is by assessing facial expressions in MCI patients, as this is widely believed to be a transitionary stage between normal aging and AD, the most common form of dementia (Sullivan et al., 2019; Lee et al., 2017).

Chapter Eight also revealed the unexpected results that individuals who produced the bottom 25% of blink rates performed better on memory assessments than the remaining 75% of participants. It was noted in Chapter Eight that it may be intuitive to assume the score difference may be due to the low blink rate group concentrating more, and therefore blink less. However, if this the case, it does not explain why other contemporary findings reported positive relationships between blink rates and cognition (Kuwamizu, et al., 2020; Ortega, et al., 2021). Future research should investigate the role that concentration plays, if any, in the relationship between blink rates and cognition. As this may need to be accounted for in future research, as it may influence the generated data. The software utilised in Chapter Eight was simply blink rate analysis software. Future studies could alter the software to set different parameters for half-blinks in order to assess if these changes influence results. This software was much simpler than the software used in Chapter Seven. Chapter Seven utilised computer learning software which required a bank of reference data in order to make determinations on the emotion that is being displayed by the participant. Future research should consider this and utilise different reference banks, to ensure the reported findings can be replicated. Moreover, each ethnicity may need their own reference bank in order to assess how this may influence the results over a wide variety of cultures and peoples. Furthermore, light levels were not controlled for in either Chapter Seven or Chapter Eight. Future studies should consider taking measurements at differing ToD as different light levels may influence the readings given by the software (Bacci et al., 2021).

A final consideration for future research into facial cues and cognitive functioning is that much of the previous research regarding facial cues and cognition began by exposing the participants to either positive or negative video stimuli (Asplund et al., 1991; 1995; Kumfor et al., 2019; Seidl et al., 2008; 2012). These studies did not utilize machine learning software, however. There is room to conduct a similar study using machine learning to analyse facial cues while participants are looking at these stimuli, and to explore whether contemporary technology show similar findings to older studies. Furthermore, these stimuli could be presented to participants prior to a cognitive battery assessment, in order to assess whether the stimuli hold any influence over sores on tests of cognition, as well as on the facial cues presented by participants.

Postural stability and facial cues are physiological factors which have been assessed for their applicability as a non-invasive technique for the detection and diagnosis of dementia. Following this research, this thesis then went on to explore the use of fully-immersive VR technology. The results seen in Chapter Nine reported a significant negative relationship between maze completion times and LTM, STM, and sores on an associative learning task, and a positive relationship between maze completion times and the difference between scores achieved on a dual task. Moreover, the results suggested an increased capacity for naturalism may influence results on assessments of spatial memory, as compared to on-screen VR. Future research could consider a direct comparison between fully-immersive VR and on-screen VR by having each participant complete both conditions. Although, in this study, special care must be taken to ensure the on-screen and fully-immersive mazes are of comparable difficulty while avoiding potential practice effects. Alternatively, a larger participant cohort could see independent groups study wherein half complete the maze study on screen, and the other half complete it in fully-immersive VR. Several participants noted that the earlier mazes were not difficult enough, which may explain the findings that only the most difficult maze reported a significant relationship between maze escape times and scores on tests of cognition.

Further studies should also investigate this relationship in more difficult fully-immersive VR mazes, or a greater escalation of difficulty between the trials. Also, as reported by Uddin et al. (2017), landmarks such as anchor points can improve participants' performance on spatial memory tasks. This could be implemented in future studies to see if these findings can be generalised from on-screen VR to fully-immersive VR.

Future studies may also consider having participants complete a practice maze. While it was the case in this study that participants had the opportunity to familiarise themselves with the virtual environment, they were not offered a maze to practice on. This may go some way towards explaining why the results of Chapter Nine noted that participants took longer to complete the first maze than the second on average, despite the second maze being more difficult than the first. Given the overarching aim to establish novel non-invasive techniques that could be implemented in detection and diagnosis of dementia, the limitations of fully-immersive VR must be considered. The side-effects of fully-immersive VR include disorientation and nausea (Farmani and Teather, 2018). This is referred to as cybersickness. In the Chapter Nine study, one participant reported feelings of cybersickness and the study was immediately terminated. Future research could consider additional precautions to maximise the comfort of the participant.

10.6 Conclusion

Achieving the greatest level of accuracy possible in cognitive assessments is of paramount importance. The results on tests of cognition can trigger the process for a diagnosis of dementia and clinical trial inclusion. Earlier diagnoses of dementia hold implications for reducing the economic burden, while ensuring the individuals with dementia can maintain the greatest quality of life possible for as long as possible (Petersen, 2009). This thesis has investigated a series of non-invasive techniques that avoid some of the external influences that are seen in current neuropsychological assessments. All techniques demonstrated a relationship with cognitive function in cognitively-healthy populations. Further research should look at these techniques in a large population of older adults and investigate how accurate the techniques are at assessing cognitive decline, with a view to implement them in clinical settings in the future.

Considerations should also be made regarding what information the five studies outlined in this thesis can offer while considered as a whole. Throughout the studies of this thesis, for all but one study, relationships were found for memory, but not the dual task. It may be the case that particular regions of the brain are more sensitive to the relationships explored throughout this thesis. The systems which are controlled by the temporal lobes, for example, are worth considering, as the Lateral Temporal System is responsible for the processing of visual information, WM, STM and retrieval of semantic information (Baker et al., 2018). Furthermore, the function of the Medial Temporal System involves spatial information processing, and is important for visuospatial processing and episodic memory (Baker et al., 2018). These particular areas of memory all being associated with the temporal lobes may be a potential reason for the relationships witnessed in this thesis, and is certainly worth further investigation.

Furthermore, the findings that lower AP sway and participation in a greater number of sports are both positively associated with memory performance, as witnessed in chapters Five and Six respectively, are worth considering in tandem. It may be the case, for example, that participation in these sporting activities results in improved postural stability, which interacts with postural sway. Future research may wish to consider multiple of these findings together in order to fully explore the results of the studies carried out within this thesis.

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Appendix 1: Cognitive Assessment Examples

Example 1 STM/LTM wordlist:

1. Musical
2. Regular
3. Limited
4. Opinion
5. Sensitive
6. Assistance
7. Quality
8. Advanced
9. Uniform
10. Poetry
11. Division
12. Benefit
13. Atmosphere
14. Commercial
15. Primary

Example 2 digit-span backwards:

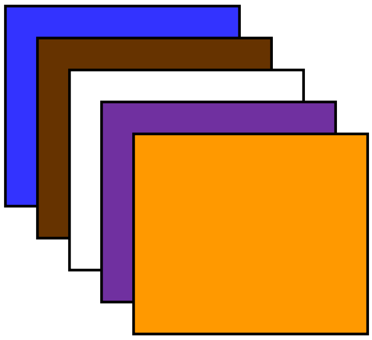
1. 138
2. 195
3. 4216
4. 2689
5. 24681
6. 52491
7. 351786
8. 481672
9. 2871564
10. 2179364
11. 67534891
12. 48965217
13. 413859627
14. 419637258

Example 3 Dual Task:

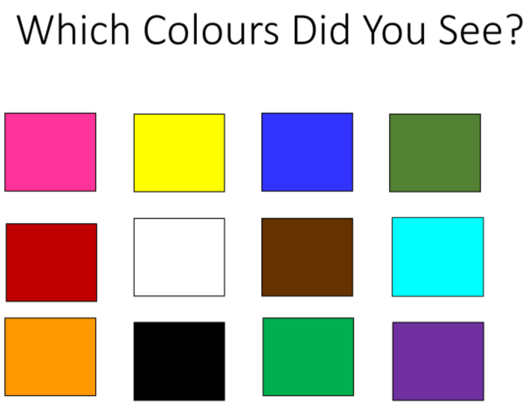
Letters heard:

1. B F H J L
2. X I F T J
3. F Z A D Q

Colours shown:

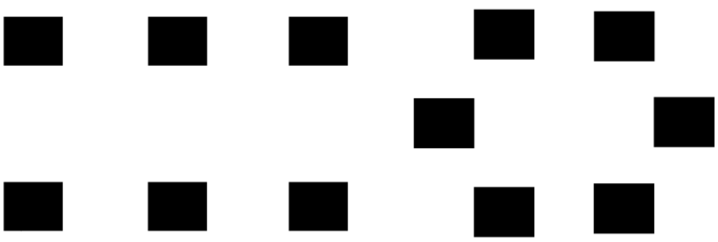


Colour Options:

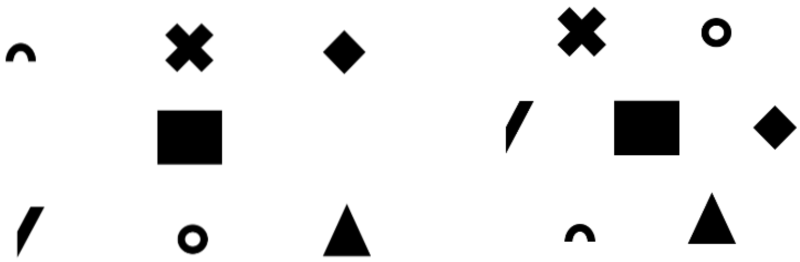


Example 4 Associative Learning:

Closed Boxes:



Open Boxes:



Example 5 Logical Reasoning:

1. You go to work on weekdays. today is a weekday. Therefore, you go to work. Does this make logical sense?
2. When you go to work, you wear a suit. You are wearing a suit. Therefore, you are at work. Does this make logical sense?
3. When you drive a car, you wear sensible shoes. You are not driving a car. Therefore, you are not wearing sensible shoes. Does this make logical sense?
4. You cannot walk your dog in the rain. It is not raining. Therefore, you can walk your dog. Does this make logical sense?

Appendix 2: Online Posture Questionnaire

An Online Study to Explore the Relationship between Posture and Cognition

Thank you for considering taking part in this study. Please read through the following statements and respond appropriately if they all of the statements apply to you. The purpose of this is to ensure that you are fully aware of the purpose of the research and are willing to participate

- I confirm that I am over 18 years of age.
- I have been informed of the purpose of the study.
- I understand that I am free to email the researcher to ask any questions I may have.
- I understand that I am free to withdraw from the study by closing the browser, and my data will not be used.
- I understand that I can withdraw my data after the study has concluded until December 15th 2019 without giving a reason.
- I understand that I will not have access to my scores.
- I confirm that I have had the opportunity to read Bristol Online Survey's privacy policy.
- I confirm that I have a good understanding of the English language.
- I understand that I will be tasked with completing a questionnaire about sports and other activities which are related to posture.
- I understand that I will be taking part in a cognitive assessment, which will test my short-term memory, reasoning ability, attention, and long-term memory.
- I understand that I am free to choose not to answer a question.
- I confirm that I am not suffering from dementia.
- I confirm that I am not suffering any diagnosed postural condition.
- I give my consent to take part in the research.

1 I have read all the above points and confirm I meet the criteria.

- No
- Yes

2 Please indicate your age group:

- 18-24
- 25-31
- 32-38
- 39-45
- 46-52
- 53-59
- 60+

3 Before we begin, please create a Confidentiality Code comprised of the first 3 letters of your favourite food followed by 3 numbers. We need this code in case we need to identify your data. For Example, if your favourite food is Pizza, and your numbers are 123, your Confidentiality Code would be 'Piz123'

Posture Questionnaire

Thank you for taking part in this study. The following questions are designed to get an understanding of your posture. This questionnaire asks you how often you participate in the following sports and activities, and how long you spend performing these activities. Please select the answer that applies to you. Filling in this section should take no longer than 10 minutes:

Participants were then asked the following questions:

4 How often do you participate in American Football?
5 How often do you participate in Ballet?
6 How often do you participate in Boxing?
7 How often do you participate in Cycling?
8 How often do you participate in Diving?
9 How often do you participate in Football (Soccer)?
10 How often do you participate in Gymnastics?
11 How often do you participate in Handball?
12 How often do you participate in Horse Riding?
13 How often do you participate in Irish Dancing?
14 How often do you participate in Martial Arts?
15 How often do you participate in Pilates?
16 How often do you participate in Rock Climbing?
17 How often do you participate in Clay-Pigeon Shooting?
18 How often do you participate in Skateboarding?
19 How often do you participate in Skiing?
20 How often do you participate in Snowboarding?
21 How often do you participate in Strength Training?
22 How often do you participate in Stretching?
23 How often do you participate in Surfing?
24 How often do you participate in Swimming?

Following each of these, participants were then asked to indicate how often they participated in this sporting activity with the following options:

- Every day
- 5-6 Times a week
- 3-4 Times a week
- 1-2 Time(s) a week
- Several times a month
- About once a month
- Several times a year
- About once a year
- Never
- Other

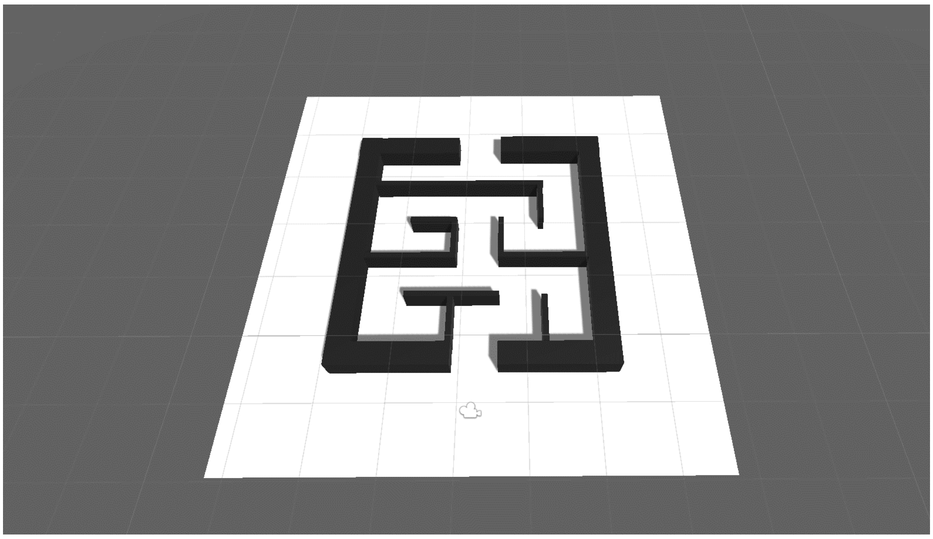
Following this, participants were then asked to indicate how much time in a single session they typically spend in a single session with the following options:

- Over 3 hours
- Up to 3 hours
- Up to 2 hours
- Up to an hour
- I do not participate in this activity
- Other

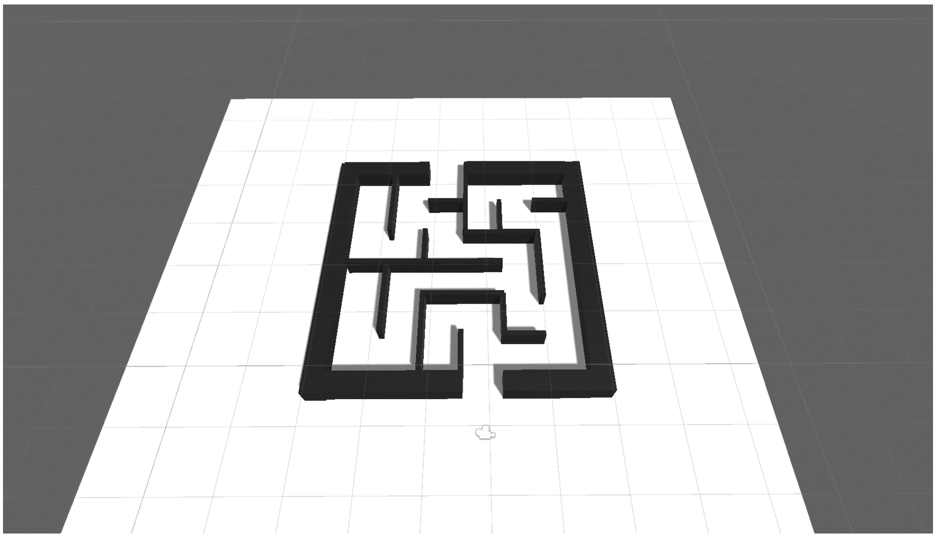
If 'Other' was selected, participants were asked to elaborate in a text box.

Appendix 3: Virtual Reality Mazes

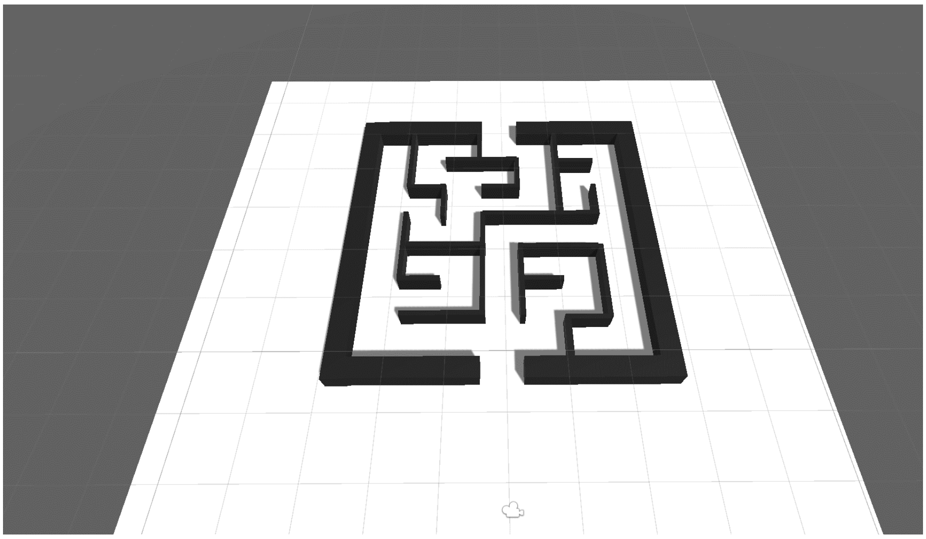
Maze 1:



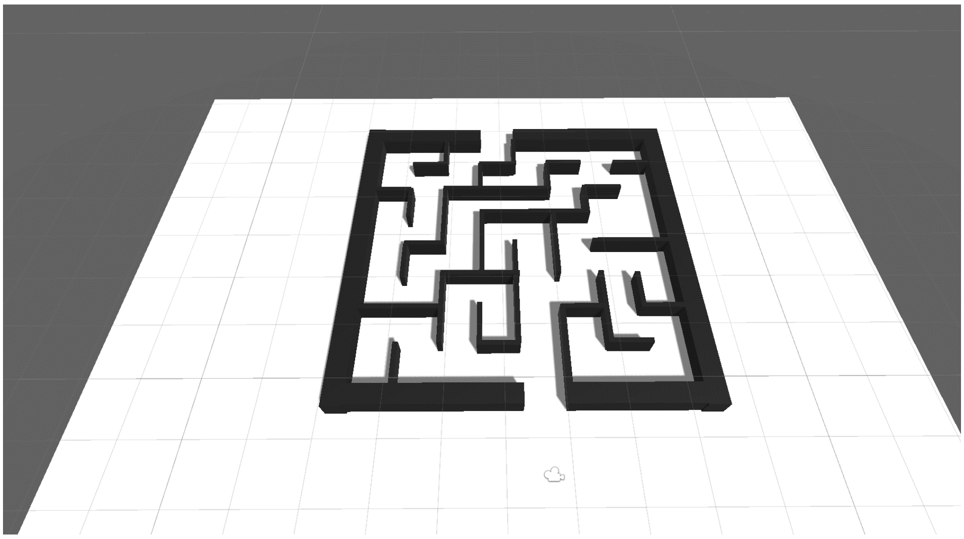
Maze 2:



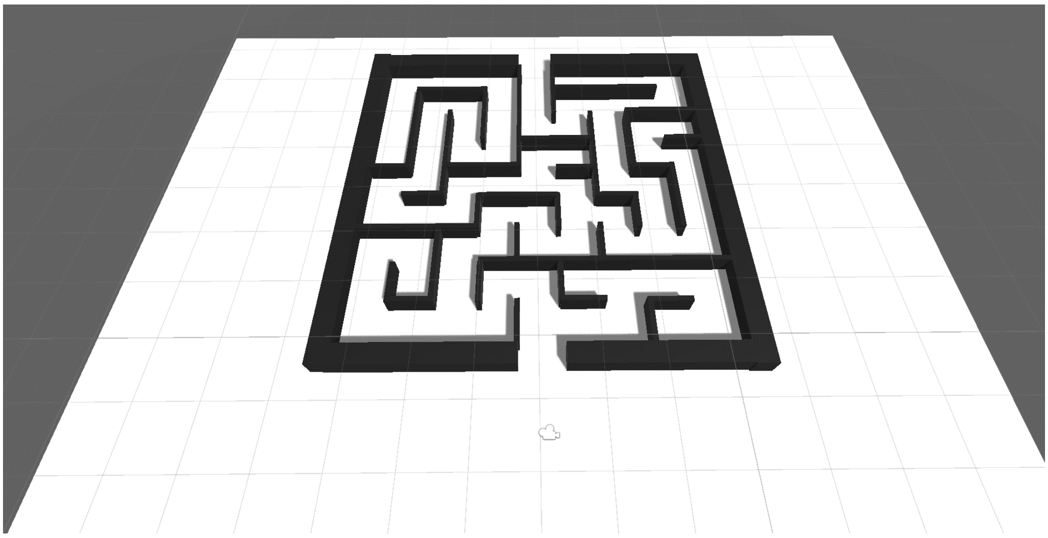
Maze 3:



Maze 4:



Maze 5:



Maze 6: