Factors affecting neuropsychological assessment in a group of South Asian older adults

FACTORS AFFECTING NEUROPSYCHOLOGICAL ASSESSMENT IN A GROUP OF SOUTH ASIAN OLDER ADULTS

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Abstract

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Keywords: South Asian older adults, cognition, Alzheimer's disease, mild cognitive impairment, early diagnosis, neuropsychological assessment, MMSE, RUDAS.

The accuracy of neuropsychological assessment is critical in the diagnosis of cognitive impairments in older adults. However, existing neuropsychological tests may not be suitable for minority populations. This thesis aimed to address this issue by recruiting cognitively-healthy South Asian older adults and assessing cognitive function in this group. Results showed that typically used assessments, despite being translated, were not suitable for this cohort. Furthermore, skills required for test completion such as mathematics and writing/hand dexterity (which are related to education levels) influenced test scores. Therefore, new assessments of general cognitive function and associative memory were developed to improve the accuracy of neuropsychological test scores. The new tests were not affected by education and they achieved high internal and test re-test reliability. Time of day (TOD) that testing takes place is also known to affect cognition. Interestingly, no TOD effects were observed in this cohort. It was hypothesised that engagement in the daily five Islamic prayers may have contributed to this lack of a TOD effect. However, the results did not confirm this. The thesis then looked at overall prayer engagement and cognition. Results showed that engagement in the daily five prayers and Quran recitation significantly increased scores on assessments of processing speed. This thesis demonstrates that accurately assessing cognition in South Asian older adults is challenging and that the cognitive tests used must be suitable for this cohort. Interesting findings emerged for prayer engagement which may have wider implications for the field of cognitive reserve.

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List of main abbreviations

10-CS - 10 Cognitive screener

3MS - The Modified Mini-mental State

6CIT - The 6-item cognitive impairment test

Ach - Acetylcholine

AD – Alzheimer’s disease

ADAT – Alzheimer’s Disease Awareness Test

ADI – Alzheimer’s Disease International

ADL – Activities of daily living

aMCI – Amnesic mild cognitive impairment

APOE – Apolipoprotein E

APP – Amyloid precursor protein

Aβ – Amyloid protein

BAME – Black, Asian and minority ethnic

BAMSE – Bangla Mini-mental State Examination

CANTAB – Cambridge Neuropsychological Test Automated Battery

CCG – Clinical Commissioning Group

CKS – Clinical Knowledge Summaries

CSF – Cerebral spinal fluid

CVLT – California Verbal Learning Test

DKQ – Dementia Knowledge Questionnaire

DR – Delayed recall

DSB – Digit span backwards

DSF- Digit span forward

DT – Dual task

EOAD – Early onset Alzheimer’s disease

GP – General practitioner

H-MoCA – Hindi Montreal Cognitive Assessment

HMSE - Hindi Mini-mental State Examination

HVLT – Hopkins Verbal Learning Test

LCS – Letter Comparison Speed

LOAD – Late onset Alzheimer’s disease

MANCOVA – Multivariate analysis of covariance

MANOVA – Multivariate analysis of variance

MCI – Mild Cognitive Impairment

MEQ – Morningness-Eveningness Questionnaire

MIS – Memory Impairment Screen

MMSE - Mini-mental State Examination

MoCA – Montreal Cognitive Assessment

MRI – Magnetic Resonance Imaging

naMCI – Non-amnesic Mild Cognitive Impairment

NbM - Nucleus basalis of Meynert

NFTs – Neurofibrillary tangles

NIA-AA - National Institute on Ageing and Alzheimer's Association

NICE – National Institute for Health and Care Excellence

NMDA - N-methyl- D -aspartate

ONS – Office for national statistics

PAL – Paired associative learning

PCS – Pattern Comparison Speed

PET – Positron Emission Tomography

RUDAS – Rowland Universal Dementia Assessment Scale

SALT – Spatial Associative Learning Test

SCN – Suprachiasmatic Nuclei

SDMT – Symbol Digit Modalities Test

SVPT – Snodgrass and Vanderwart's (1980) picture naming test

THIN – The Health Improvement Network

TMT A&B – Trial Making Black and White

TOD – Time of day

T-tau – Total tau

TYM – Test your memory

UNAS – Universal Neuropsychological Assessment Scale

WAIS-R - Wechsler adult intelligence scale revised

TD - Topographical disorientation

FCI – Financial Capacity Instrument

mAD – Mild Alzheimer's disease

p-tau – Phosphorylated tau

Chapter 1: Thesis overview

1.1. Introduction

According to the latest census data derived by the Office for National Statistics (ONS), there has been a significant increase in the number of South Asian older adults of Pakistani, Indian, and Bangladeshi origin residing in the UK (ONS, 2011). With the increase in international migration and an ageing population, the number of culturally diverse individuals suffering from age related conditions, such as Alzheimer's disease (AD), is also projected to increase (Blakemore et al., 2018; Kenning et al., 2017).

The primary presenting symptoms of AD are largely cognitive in nature (Roeck et al., 2019). Therefore, neuropsychological assessments are used to identify cognitive impairment, monitor the progression of impairment and to determine treatment effectiveness in clinical and research settings (Roeck et al., 2019; Montenegro and Argyriou, 2017).

However, research suggests that performance on commonly used neuropsychological assessments can be influenced by external factors such as age, education, and language even in the absence of any pathologically significant cognitive deficits (Cid et al., 2019; Paddick et al., 2017; Walters and Lesk, 2016). The influence of external factors on cognitive performance is not widely researched in South Asian older adults who are significantly underrepresented in the field of cognitive research (Blakemore et al., 2018; Kenning et al., 2017).

Considering the increase in the ageing population from a South Asian background, it is important to investigate the influence of external factors relevant to this population on neuropsychological performance. This is important because the accuracy of cognitive test scores will determine the quality of the diagnosis established. This can often be misleading if external factors present at the time of testing are not identified and controlled for (Walters and Lesk, 2016).

1.2. Overall aims of the thesis

This thesis aims to address the lack of data investigating factors influencing cognitive testing in South Asian older adults. This will be achieved by exploring a range of factors present at the time of testing to determine whether they exert any influence on neuropsychological test scores in a sample of cognitively-healthy South Asian older adults.

The factors which will be investigated include the influence of the language in which neuropsychological assessments are administered, the use of a battery of brief domain specific cognitive assessments with lower reliance on language and education, the influence of the type of skills required to complete the assessments, the time-of-day effect (TOD), and engagement in the Islamic prayer.

The influence of these factors will be investigated by asking participants to complete a battery of established neuropsychological assessments designed to measure a range of different cognitive abilities. The results will be discussed in the context of AD and Mild Cognitive Impairment (MCI) throughout.

Based on the research findings from the studies within this thesis, it is also aimed to develop a new assessment of general cognitive function and an assessment of visuo-spatial associative memory. These assessments are proposed as novel measures which aim to assess cognitive functioning more accurately in South Asian older adults. This is expected to be achieved by minimising the influence from linguistic and educational factors identified throughout the research studies conducted as part of this thesis. The use of both assessments will be evaluated and piloted in this thesis.

1.3. Overview of thesis structure

The present thesis consists of 11 chapters. The following section provides a brief overview of each chapter.

Chapter 1 provides an overview of the aims of the thesis and a brief summary of all the chapters in this thesis.

Chapter 2 provides a detailed overview of AD and MCI. It focuses on the areas of **(i)** incidence, **(ii)** diagnosis, **(iii)** symptoms, **(iv)** pathology, and **(v)** treatments.

Chapter 3 provides an in-depth overview of research on the South Asian community residing in the UK as this is the population of interest in this thesis. The chapter outlines the incidence of AD in this group and discusses the factors affecting their representation in cognitive screening and AD related services.

Chapter 4 describes and evaluates the battery of cognitive tests administered to the participants in this thesis by outlining the domains they assess, administration method and scoring system. This chapter also evaluates the adequacy of implementing these assessments to assess cognitive function in South Asian older adults.

Chapter 5 is the first experimental chapter which investigates the effects of the language that the cognitive tests are presented in on test scores in two assessments of general cognitive function. These are **(i)** the Mini-mental State Examination test (MMSE) (Folstein et al., 1975) and **(ii)** the Rowland Universal Dementia Assessment Scale (RUDAS) (Storey et al., 2004). The results showed that the sample of cognitively-healthy South Asian older adults scored poorly on both assessments when administered, both in English and in Urdu. The MMSE and RUDAS were also affected by education, with higher education levels correlating with increased test scores. This indicated that commonly used assessments of general cognitive function may not be adequate for use in South Asian older adults.

Chapter 6 is the second experimental chapter. Following on from the findings of the experiment in chapter 5, it was important to investigate the use of alternative assessments to determine their suitability for this cohort. This chapter aimed to explore **(i)** the cognitive performance of a sample of cognitively-healthy South Asian older adults on a battery of brief domain specific cognitive assessments claimed to have lower reliance on language and education; **(ii)** the influence of the type of skills required to complete the assessments on cognitive test scores and **(iii)** whether cognitive screening would be better when using a single assessment of general cognitive function, the MoCA, or when using the battery of several brief domain specific assessments. Population norms were used to calculate z-score transformed means for all the neuropsychological tests administered to compare scores on the different assessments using different scoring systems.

The results showed that participants performed below the population norms in all assessments, except for the adapted Trail Making Black and White (TMT A&B) (Kim et al., 2014). The findings also revealed that test scores were closer to the population norms in assessments measuring processing speed, and in assessments with a non-verbalised or non-spoken language skills component. Test scores were the furthest away from the populations means in assessments with a verbalised response component and use of mathematical and writing skills. Test scores were also found to be closer to the population means (but not above), and therefore better, on the single assessment of general cognitive function, the MoCA, when compared with the global cognitive z-scores on the battery of several brief domain specific assessments.

Overall, the results indicated that the poor performance on the battery of assessments administered may be more reflective of the present sample's lower levels of education and limited experience and familiarity with the testing situation, as opposed to reflecting pathologically significant impairments. The delivery method of the cognitive tests administered resembles school-based activities and tasks, which individuals with lower levels of education may not be familiar with. This may have potentially led the present sample of cognitively-healthy older adults to perform below the published population norms. The findings from this chapter further show that existing assessments, verbal and non-verbal, may not be suitable for this cohort calling for a need to develop new measures tailored for the needs of this group. This leads on to chapter 7 which developed two new assessments with the aim to improve the accuracy of cognitive screening in South Asian older adults.

Chapter 7 describes and evaluates two new assessments developed by the researcher for South Asian older adults. These tests are an assessment of **(i)**

general cognitive function, the UNAS and **(ii)** an assessment of visual spatial associative learning memory, the SALT. These assessments were developed by the researcher based on the findings from the first two experimental chapters of this thesis. They are proposed as novel measures of cognitive screening for populations from across diverse cultures and with lower levels of education. They have been developed with the aim to minimise the impact of external cultural, educational, and linguistic factors found to affect performance on neuropsychological assessments in South Asian older adults.

The important findings which emerged showed that both, the UNAS and SALT, were not affected by education and both assessments achieved a good level of internal and test re-test reliability. Test scores on the UNAS were also significantly higher, and therefore better, when compared with the more established assessment of general cognitive function, the MoCA, in the sample of cognitively-healthy South Asian older adults.

Therefore, the initial pilot of the UNAS and SALT indicates that these assessments may have reduced the educational and cultural bias present in existing assessments of cognitive function supporting further validation in more diverse and clinical samples.

Chapter 8 moves on to looking at the factor of time of day (TOD). TOD that the testing of cognitive functions occurs is known to affect scores on neuropsychological assessments (Walters and Lesk, 2015, West et al., 2002). The effect of TOD on cognitive performance, to our knowledge, has not previously been explored specifically in South Asian older adults or in other minority groups. Existing literature shows that older adults reach their peak cognitive arousal in the morning, and they should therefore be assessed during this time to optimise the accuracy of the scores obtained (Walters and Lesk, 2015; West et al., 2002). However, contrary to the existing findings, no TOD effects were observed in this cohort. It is not clear why the TOD effect was not replicated in this group of Muslim South Asian older adults. Chapter 9 seeks to investigate this further.

Chapter 9 extends the findings in the previous chapter by exploring whether the lack of a TOD effect in the cohort of Muslim South Asian older adults may be explained by the engagement of this group in a cognitively demanding praying practice which takes place across the day, the daily five Islamic prayers (Sayeed and Prakash, 2013). The interaction between engagement in the daily five Islamic prayers, TOD, and cognitive test scores was explored in a sample of Muslim South Asian older adults. However, no significant interactions were reported for the group of participants who confirmed engaging in the daily five prayers, neither in those who did not engage in this practice. Therefore, it could not be concluded that engagement in the daily five prayers was a contributing factor in the lack of a TOD effect observed in chapter 8. It is not clear what may have given raise to this lack of influence in both groups. However, the findings remain important as they indicate that the TOD effect may not consistently apply to all populations equally which requires to be studied further.

Chapter 10 is the last experimental chapter of this thesis. One of the salient characteristics of the sample in chapters 8 and 9 was that they all identified as being Muslims, and most of the participants engaged in prayer. Whilst the engagement in prayer did not seem to be responsible for the lack of TOD effects, based on the results in chapter 9, it led the researcher to wonder about its role and influence on cognition more generally. Considering that the Islamic prayer may be a cognitively demanding task, engagement in this practice has potential implications for cognitive reserve which refers to the brain's ability and flexibility in coping with neurocognitive changes (Montemurro et al., 2021; Devita et al., 2019). This motivated the present chapter to explore the influence of engagement in four different Islamic praying practices on cognition more generally. The results showed that participants who engaged in the daily five prayers and daily Quran recitation performed significantly better on assessments with a processing speed component. This is a novel and important finding which warrants further research due to the implications it has for the wider field of cognitive reserve.

Chapter 11 is the thesis discussion chapter which provides a summary of the key findings and their implications for the field of neuropsychological testing in ethnic minorities and other related disciplines. The chapter also offers directions for future research and an overall conclusion.

Chapter 2: Alzheimer's Disease and Mild Cognitive Impairment

2.1. Introduction

This chapter will provide a detailed overview of AD and MCI. Knowledge with regards to these conditions is necessary as the present thesis will aim to discuss the research findings from the experimental chapters in the context of implications for AD and MCI. The chapter will begin by providing some background information on AD by specifically focusing on incidence, symptomology, pathology, risk factors, diagnosis, and treatments. The second part of this chapter will introduce MCI which is often considered as the prodromal stage of AD (Silva et al., 2020; Petersen et al., 2014). This chapter aims to discuss the role of MCI as an early biomarker of future progression into AD and a potential target for the early therapeutic interventions to enhance treatment outcomes.

2.2. Prevalence and incidence of AD

The worldwide increase in life expectancy is leading to an increase in the ageing population, particularly in Western countries (Silva et al., 2019). In the UK, it is estimated that there are approximately 12 million individuals aged 65 years and over, and by 2030, it is expected that 21.8% of the general population will be aged 65 years and over (Age UK, 2019).

Consequently, because of economic reasons, individuals are gradually expected to work for longer and the UK government has already announced that state pension age is expected to increase to 68 years between 2037-2039 (Department for Work and Pensions, 2017).

This implies that older adults will be required to remain physically and cognitively-healthy for longer. However, ageing is associated with physiological decline which has physical, behavioural, and cognitive consequences (Bettio et al., 2017; Park and Reuter-Lorenz, 2009). Cognitive decline can manifest in normal ageing and in pathological conditions, such as neurodegenerative diseases like AD, which are common in the ageing population (Bettio et al., 2017). Consequently, with the increase in the ageing population, the prevalence of neurodegenerative diseases is also expected to experience a significant increase (Silva et al., 2019).

One of the most common neurodegenerative diseases worldwide is dementia (Voulgaropouloua et al., 2019). This is an umbrella term for a range of progressive diseases affecting the brain with the most common type being AD (Voulgaropouloua et al., 2019). It is estimated that there are currently 850,000 people in the UK living with dementia, and AD accounts for 63% of these dementia cases (Age UK, 2021). This figure is set to rise with the increasing ageing population, and it is expected to increase to one million by 2025 (Age UK, 2021).

In particular, the incidence of the different types of dementias is expected to increase in BAME communities who account for around 14% of the UK's general population (Blakemore et al., 2018). It is estimated that in the UK, approximately 25,000 people diagnosed with dementia are from BAME communities, and this figure is estimated to double by 2026 with the sharpest increase expected in South Asians of Pakistani, Indian, and Bangladeshi origin (Alzheimer's Society, 2019). This number is likely to be an underrepresentation as BAME communities, like the South Asian, face delays in receiving a dementia diagnosis and often encounter barriers in accessing the relevant services (Blakemore et al., 2018; Kenning et al., 2017; Mukadam et al., 2011). This is discussed in detail in chapter [3].

With the rise in the diversity of the UK's ageing population at risk of AD, increasing the understanding of AD in minority groups is imperative. This is particularly important considering that the symptoms of AD often lead to debilitating consequences in an individual's ability to engage in activities of daily living (ADL) (e.g., cooking, eating, walking, dressing) (Brewster et al., 2019).

Increased understanding of AD in minority groups also has the potential to contribute towards facilitating and improving access to specialised dementia services for people from across different cultures and reduce the disease burden on patients, carers as well as the healthcare system.

2.3. Background and history

AD was first discovered in 1906 by Dr Alois Alzheimer who followed the case of a female patient aged 51 years old presenting with symptoms of memory loss, language, and behavioural deficits (Grøntvedt et al., 2018). During autopsy, Dr Alzheimer found histological alterations in the brain which later became known as neurofibrillary tangles (NFTs) and senile plaques (Grøntvedt et al., 2018). Following extensive research, these have now become well-known pathological hallmarks of AD (Sandelius et al., 2019; Cox et al., 2016) and they are discussed in detail in section [2.6].

AD is commonly classified into two types, namely “early-onset” (EOAD) and “late-onset” (LOAD) (Reitz et al., 2020; Wattmo and Wallin, 2017). EOAD patients commonly exhibit AD symptoms before the age of 65, and this form is less common typically occurring in one to five percent of the total cases (Reitz et al., 2020; Wattmo and Wallin, 2017). LOAD is more common, and it usually occurs in patients aged over 65 years. Clinically, they are indistinguishable, however EOAD is generally associated with a more rapid rate of cognitive decline and faster progression into advanced stages (Reitz and Mayaux, 2014).

Despite the recent advances in AD research, it is often difficult to distinguish between normal age-related cognitive decline from decline caused by pathological abnormalities, such as AD (DeTure and Dickson, 2019). This remains a pressing challenge as AD is characterised by a long asymptomatic pre-clinical phase, and cognitively-healthy individuals may also suffer from this condition but may be unaware which often leads to delayed diagnosis (DeTure and Dickson, 2019).

There is an urgent need to develop measures which will facilitate the early detection of AD. This is particularly important because at the present time, there are no curative treatments available (Voulgaropoulou et al., 2019).

Therefore, increased understanding of pathological hallmarks and disease progression in different groups of people may enhance the development of potentially curative and/or more effective pharmacological treatments (Voulgaropoulou et al., 2019; DeTure and Dickson, 2019).

2.4. Symptoms and prognosis

AD is a progressive neurodegenerative disease which means that the symptoms gradually become worse in severity as more parts of the brain are compromised and damaged (Delpak and Talebi, 2020). AD is manifested in a combination of cognitive, behavioural, and psychiatric symptoms which are described next.

2.4.1. Cognitive and behavioural symptoms

AD largely manifests in the form of cognitive symptoms and one of the most evident symptoms first noticed is memory loss (Grøntvedt et al., 2018). People in the early stages of AD often experience changes in their episodic memory whereby free and cued recall abilities are impaired and individuals experience difficulties in remembering new information related to their everyday life/events (Grober et al., 2018; Dubois et al., 2007).

Other symptoms, such as disorientation and confusion are common, however the core symptoms in the early stages are usually memory related (Jimenez-Balado and Eich, 2021; Dubois et al., 2007). These symptoms gradually become worse overtime and diagnosis at the symptomatic onset is suboptimal as the underlying pathological changes take place many years before the visible presentation of symptoms (Carro et al., 2017; Roe et al., 2013; Forlenza et al., 2010).

In the more advanced stages of AD, patients begin to lose their ability to perform ADL, such as eating, dressing, and cooking (Brewster et al., 2019); mobility and transportation related activities (Graham-Phillips et al., 2016); and financial management (Triebel et al., 2010). The rate of decline is not fixed, and there is a large variation between the rate of progression from mild to the more severe symptoms (Grøntvedt et al., 2018). The rate of decline is often dependent upon a range of other risk factors such as family history, age, education levels, presence of other co-morbid conditions, genetic risk factors, amongst many other variables (Delpak and Talebi, 2020; Mielke et al., 2011; Rountree et al., 2013). Common AD risk factors are discussed in section [2.5].

In the UK, NICE provide guidance for health and social care procedures and they describe AD as being categorised into three stages: “mild”, “moderate” and “severe” (NICE, 2018).

The mild stage is described as symptoms, such as memory loss, feelings of disorientation and difficulty in coping with complex problems. The moderate stage is characterised by symptoms of severe memory loss, feelings of disorientation and finding it very hard to cope with everyday problems. The severe stage is characterised by symptoms of very severe memory loss, disorientation, and loss in the ability to communicate, make decisions or engage in simple tasks, such as eating or walking (NICE, 2018).

NICE (2018) suggest that the median survival time for those with a diagnosis of AD is estimated to be seven years from disease onset to death. Furthermore, in more advanced stages of cognitive impairment, patients tend to lose movement and they may become bed bound increasing their susceptibility for infections which often becomes a secondary cause of death (Todd et al., 2013). Todd et al. (2013) explored the causes of death in AD patients by examining the death certificates of 85 AD patients and 52 controls. The analysis of the data revealed that pneumonia was the most common underlying cause of death in patients with AD, and only 63.5% of death certificates of AD patients recorded the cause of death as being AD.

2.4.2. Psychiatric Symptoms

The symptoms of AD are not limited to cognitive deficits, but emerging research suggests that neuropsychiatric symptoms, such as depression, hallucinations, anxiety, and apathy are also common in people with AD (Cassano et al., 2019) with an overall occurrence ranging in between 39-49%

of cases (Zhao et al., 2016). The NICE (2018) dementia guidance also acknowledges the presence of such non-cognitive symptoms and recommends the use of antipsychotics and anti-depressants to manage these symptoms.

Ruthirakuhan et al. (2019) investigated the risk of developing AD in a sample of 4,932 patients diagnosed with MCI on a battery of neuropsychological assessments including the MMSE (Folstein et al., 1975) which is an assessment of general cognitive function. The sample was formed by patients who had symptoms of either depression or apathy, both, or no neuropsychiatric symptoms. Ruthirakuhan et al. (2019) found that 37% of their MCI participants developed AD after a median follow-up period of 23 months. Moreover, it was found that MCI patients with both apathy and depression, or apathy alone were at the greatest risk of conversion from MCI to AD. This is also consistent with research by Gallagher et al. (2019) who, in a sample of 1,965 older adults, found that the combination of MCI and recently active depression presented a significant risk factor for the progression from MCI to AD over a short median follow-up period of 27 months.

Hallucinations and delusions are also frequently reported in AD patients which have been found to be correlated with increased neocortical NFTs, hyperphosphorylated tau and disrupted serotoninergic signalling (Lanctot et al., 2017; Murray et al., 2014). These are pathological hallmarks of AD, and they are discussed in more detail in section [2.6].

It is also important to note that the presence of psychiatric symptoms and memory loss have been reported as causing stigma in the South Asian community (Blakemore et al., 2018; Uppal et al., 2014; Mackenzie, 2006). The South Asian community tends to associate these symptoms with “madness” and as a punishment from God/s which prevents and delays help-seeking behaviours, further contributing towards the lower dementia service uptake levels in this community (Hossain et al., 2018; Blakemore et al., 2018; Mukadam et al., 2011; Fontaine et al., 2007). This is discussed in more detail in chapter [3].

2.5. Risk Factors

There is a consensus that the cause of AD is multifactorial, consisting of a combination of genetic, lifestyle and environmental risk factors (Grøntvedt et al., 2018). Typically, the risk factors of AD have been classified as modifiable and non-modifiable (Grøntvedt et al., 2018). In the absence of curative treatments, there has been a growing interest in identifying modifiable risk factors and some of the most documented modifiable risk factors include cardiovascular diseases, MCI, obesity, physical inactivity, and low levels of education (Grøntvedt et al., 2018). These are briefly outlined in table one.

Table.1. Non-modifiable and modifiable risk factors associated with AD

Risk factors	Evidence
Non-modifiable	
Age	AD predominately affects older adults due to the unavoidable cumulative effects of degeneration of brain structures with increasing age (Sala Frigerio et al., 2019)
Gender	The risk of AD is higher in females compared to males (Delpak and Talebi, 2020). Life expectancy for women is longer compared to men and considering that age is one of the greatest risk factors in the development of AD, it places females at a higher predisposition to suffer from this condition (Mielke et al., 2018). Increased risk of AD in females has also been associated with reduced oestrogen levels with increasing age due to menopause (Bove et al., 2014).
Family history	Individuals who have a first degree relative diagnosed with AD are at a higher

	predisposition to suffer from AD (Cannon-Albright et al., 2019; Donix et al., 2012).
Genetics – APOE gene allele	The APOE gene is the strongest genetic risk factor associated with AD (Riphagen et al., 2020; Bales and Paul, 2019). It is located on chromosome 19 and exists in three common alleles, namely APOE2, APOE3 and APOE4. Possession of the latter (APOE4) carries an elevated risk of developing AD (Ling-Lin et al., 2020; Bales and Paul, 2019). APOE4 carriers demonstrate thinner entorhinal cortex, which is a brain region particularly susceptible to early AD pathology (Konishi et al., 2018; Fennema-Notestine et al., 2011) and have been found to have increased accumulation of amyloid plaques and NFTs (explained in section 2.6). The APOE gene is also a cholesterol carrier involved in the transportation of lipids (Hauser et al., 2011). As a result, it is closely associated with the development of heart diseases implying an overlap between AD and cardiovascular risk factors (Santiago and Potashkin, 2021).
Modifiable	
MCI	MCI is considered as the prodromal stage of AD and it has been associated with increased risk of conversion to AD

	(Jimenez-Balado and Eich, 2021; Berten et al., 2019; Michaud et al., 2017). MCI risk is discussed in more detail in section [2.9].
Lower levels of physical activity	Lower levels of physical activity have been associated with increased risk of developing AD (Norton et al., 2014). Physical activity has been associated with increased grey matter volume in the hippocampus which has been found to reduce the risk of cognitive decline characteristic of AD (Rosano et al., 2017).
Cardiovascular diseases	Cardiovascular risk factors, such as high blood pressure, heart disease and elevated cholesterol, have also been associated with increased risk of developing AD (Tini et al., 2020; Bruijin and Ikram., 2014). The mechanisms of this association are not yet clear; however, it is postulated that this could potentially be due to cardiovascular diseases and AD sharing similar risk factors, such as the involvement of the APOE4 allele and increased amyloid deposition which increase the predisposition to suffer from AD as well as cardiovascular diseases (Vijayan and Reddy, 2016).
Poor diet and obesity	Compelling evidence suggests that following a Mediterranean diet, which is high in the consumption of olive oil, fish and low in red meats, significantly reduces the risk of developing MCI and AD (Berti et al., 2018; Loughrey et al., 2017; Morris et al., 2015). On the contrary, a diet high in

	saturated fats, which raises the risk of obesity, has been found to increase amyloid load and the formation of plaques, subsequently increasing the risk of developing cognitive impairment and AD (Edwards et al., 2019).
Lower education levels	Lower levels of education have been associated with a higher risk of AD perhaps due to what has been termed as “cognitive reserve” (Grøntvedt et al., 2018). Cognitive reserve is a concept that states that education, as well as any other activities which are mentally stimulating (e.g., skilled occupations, bilingualism) are believed to contribute to the development of increased synaptic density which allows to withstand neurodegeneration for a longer period (Stern et al., 2020; Grøntvedt et al., 2018). This is particularly important in ethnic minorities in the UK, like South Asian older adults, who tend to have lower levels of education, and thereby are at an increased risk of developing more severe AD related pathology and symptoms (Blakemore et al., 2018). This is discussed throughout this thesis.

The above are only examples of some of the commonly identified risk factors in AD and the current literature identifies many more. It is important to note that modifiable risk factors are estimated to represent 35% of the AD risk implying that increasing focus on modifying and targeting these factors can potentially prevent up to one-third of all cases (Grøntvedt et al., 2018).

Moreover, postponing the symptomatic onset by only one year through modifiable preventative measures has the potential to reduce AD prevalence by 11% which would equate to a reduction in more than 9 million cases worldwide over the next 40 years (Grøntvedt et al., 2018). Consequently, leading to a major impact on health economics.

Further to the above, as it can been seen from the risk factors in table one, these appear to increase the risk of AD by predisposing individuals to pathological changes commonly identified in the development of AD. These are described in detail in the next section.

2.6. Pathology

The two main pathological hallmarks of AD are the combined presence of extracellular plaque deposits of β-amyloid peptide (Aβ) and NFTs of the microtubule binding the tau protein (Park et al., 2019; Forlenza et al., 2010).

These pathological hallmarks have received much support from the scientific community and their roles in AD are known as the amyloid cascade hypothesis and the phosphorylated tau protein hypothesis (Scholl and Maass, 2020).

The presence of Aβ and tau protein biomarkers are also recommended as a diagnostic criterion for AD in the research diagnostic guidelines set by the National Institute on Ageing Alzheimer’s Association (Jack et al., 2018; McKhann et al., 2011). Also, in UK clinical settings, NICE (2018) recommend the assessment of Aβ and tau in suspected cases of AD where diagnosis is uncertain through other measures by implementing neuroimaging techniques (NICE, 2018) which are discussed in section [2.7].

2.6.1. Amyloid Cascade Hypothesis

The amyloid cascade hypothesis is one of the mainstream explanations for the development of AD (Ly et al., 2020). It proposes that Aβ, which is cleaved from Aβ precursor protein (APP), is responsible for causing a chain of complex cascade events which lead to neural dysfunction and the atrophy observed in patients with AD (Teipel et al., 2020; DeTure and Dickson, 2019).

Aβ is a soluble neuro peptide formed by 39-43 amino acids and it is a large transmembrane protein which has been found to be involved in cell adhesion, synaptic plasticity, and learning (Barage and Sonawane, 2015). It is derived from two forms of secretase enzymes known as β-secretase and γ-secretase which predominately generate the formation of Aβ40 and Aβ42 types (Cohen et al., 2019; Barage and Sonawane, 2015). In non-demented older adults, Aβ is removed from APP by β- and γ-secretase and released extracellularly to the neuron where it is rapidly decomposed (Cohen et al., 2019). However, with ageing and particularly in the brains of individuals with AD, the ability of Aβ to decompose is significantly decreased leading to an accumulation of insoluble Aβ peptides in the brain (Walsh and Selkoe, 2020). In particular, the accumulation of Aβ42 induces Aβ fibril formations which develop into extracellular senile plaques known to cause neurotoxicity leading to neural atrophy and neurodegeneration characteristic of AD (Tolar et al., 2020; Grøntvedt et al., 2018). This pathology begins in the brain areas responsible for learning and memory, more specifically in the hippocampus and entorhinal cortex located in the temporal lobe, ultimately spreading, and diffusing across the entire cortex (Grøntvedt et al., 2018).

It has been reported that Aβ deposition can occur decades before the clinical onset of AD and the neurotoxicity caused by Aβ plaques is present in the brain years before any overt symptoms of cognitive impairment are manifested (Buchhave et al., 2012; Van Rossum et al., 2012; Roe et al., 2013). Therefore, indicating that Aβ deposition can be used as an indicator to warrant an early diagnosis.

For example, Buchhave et al. (2012) conducted a research study with the aim to assess amyloid and tau biomarkers to predict the future development of AD within a follow-up period of around nine years in patients with MCI. The data was gathered from a cognitively-healthy control group of 39 participants and 137 MCI patients. During the follow up period, 56 MCI patients remained stable (median age = 67 years); 57 progressed to AD (median age = 75 years) and 21 developed other forms of dementia. Cerebrospinal fluid (CSF) samples were obtained from participants at baseline to assess amyloid and tau levels and the samples were stored at -80°C to be analysed after the follow-up period was completed. MMSE test scores were used to assess cognition and calculate an annual change in cognitive functioning. The analysis of the data found that the presence of pathological CSF biomarkers (Aβ and elevated tau levels) predicted around 90% of the conversion from MCI to AD. Moreover, levels of Aβ42 were found to be entirely decreased at least five to ten years before the conversion to AD or other dementias. However, tau was found to be affected later in the disease progression. It was thereby concluded that altered Aβ levels precede tau related pathology, and this can be seen years before the conversion to AD or other dementias (Buchhave et al., 2012). Similar findings were inferred by Van Rossum et al. (2012) in a sample of 110 MCI patients. They found that based on CSF examinations of Aβ and MMSE test scores over an average follow-up period of two years, amyloid pathology in MCI patients was a strong predictor of conversion into AD.

Despite evidence supporting the role of Aβ formations in the development of AD, there are major critiques to this theory. For example, clinical trials implementing drugs aimed at reducing Aβ accumulations have demonstrated the potential to reduce Aβ production and accumulation, however despite this, no clinical improvements have been observed in patients with AD (Moussa, 2017; Kennedy et al., 2016; Salloway et al., 2014; May et al., 2011). In fact, most trials have required to be stopped due to either inefficacy of the treatment or severe and undesired side effects making the use of these drugs unfeasible (Cao et al., 2018).

The advances in amyloid imaging have also enabled researchers to measure these in the brains of healthy patients and these have reported that accumulations of Aβ are also present in cognitively-healthy individuals (Kametani and Hasegawa, 2018; Li et al., 2008; Edison et al., 2007). Moreover, some research has found that the accumulation of Aβ deposition in cognitively-healthy individuals is sometimes as extensive as in patients with AD (Jagust, 2016; Chetelat et al., 2013; Price et al., 2009; Fagan et al., 2009). This suggests that there is a lack of direct relationship between Aβ and cognitive function as plaques are also seen in the brains of cognitively-healthy individuals (Jagust, 2016; Jagust and Mormino, 2011). This implies that the presence of Aβ alone may not be a sufficient cause leading to AD.

Based on the inconclusive nature of the amyloid hypothesis, attention has been drawn to the possibility that Aβ exerts negative effects on the brain due to its interaction with the tau protein (Dani et al., 2019; Kametani and Hasegawa, 2018).

2.6.2. Tau and Neurofibrillary Tangles (NFTs)

Tau is a protein encoded on chromosome 12 and it is mainly found within neurons (Iqbal et al., 2010). Tau plays an important role in microtubule assembly and the maintenance of stability in neural microtubule networks (Blennow et al., 2020; Miao et al., 2019). However, in patients with AD, tau becomes hyperphosphorylated (Revett et al., 2013) forming paired helical filaments and straight filaments referred to as NFTs which impair the protein's ability to bind and assemble microtubules within the axon and dendrites (Schöll et al., 2016; Iqbal et al., 2010). Unlike Aβ, NFTs are more concentrated and restricted to brain structures in the medial temporal lobe, basal forebrain (nucleus basalis of Meynert), brainstem and olfactory areas which are regions known to influence cognitive functioning (Dallaire-Théroux et al., 2019).

The loss of tau's normal functioning and formation of NFTs leads to pathological disturbances in the brain which affect normal cellular functions (Neddens et al., 2018). Hyperphosphorylation promotes the aggregation of tau into intracellular NFTs which clump together within the neuron disrupting its normal functioning leading to the neurodegeneration observed in AD (Miao et al., 2019; Neddens et al., 2018).

Research also suggests that the interaction of Aβ with NFTs strongly predicts AD pathologies. For example, Dani et al. (2019) conducted a research study with the aim to investigate the relationship between NFTs and Aβ deposition in the cerebral cortex in patients with MCI and AD using Positron Emission Tomography (PET) imaging (described in section 2.7). Their sample was formed by 51 healthy controls, 13 amyloid positive MCI patients and 15 amyloid positive AD patients aged between 50-85 years. All participants were required to have at least eight years of education to give informed consent. MCI and AD status was determined based on MMSE test scores. The results of the data gathered revealed that tau aggregations into NFTs correlated with the levels of amyloid disposition, both in MCI and AD patients indicating that both pathologies may interact together in the development of AD.

Cognitive impairment has also been found to be more closely associated with NFTs and concentrations of total tau in CSF samples in MCI and AD patients independent of Aβ pathology (Weigand et al. 2020; Mielke et al., 2017; Okamura et al., 2015).

Weigand et al. (2020) conducted a research study with the aim to investigate the association between cognition, tau and Aβ as biomarkers in the pathology of AD in a sample of 523 AD patients and a subsample of 301 individuals without dementia. All participants underwent PET imaging as measures of tau and Aβ and were categorised as Aβ negative/ tau negative (A-/T-); Aβ positive/Tau negative (A+/T-); Aβ negative/Tau positive (A-/T+) or Aβ positive/Tau positive (A+/T+). The analysis of the results indicated that the A-/T- group and A+/T- had the best performance on neuropsychological assessments of memory, language, and EF. Moreover, cognitive performance in the A-/T+ was significantly poorer compared to the A-/T- group and this was observed in the presence of tau in the temporal medial lobe. Weigand et al. (2020) concluded that this indicates that the presence of tau pathology in the medial temporal lobe without cortical Aβ may be reflective of cognitive decline in early AD.

The above evidence suggests that tau pathologies may form earlier in the AD disease trajectory in MCI cases, and they are directly associated with global cognitive decline unlike Aβ. Considering that MCI is a precursor of AD (Petersen et al., 2014), the association between elevated plasma tau levels and cognitive decline makes tau an important early marker to be considered in the prodromal stage of AD.

2.6.3. Racial disparities in Aβ and tau levels

It is important to note that despite some evidence supporting the involvement of both, Aβ and tau in the development of AD, emerging evidence suggests that there are racial disparities in these biomarkers and most of the evidence to this effect is currently based on African American samples (Morris et al., 2019; Garrett et al., 2019; Howell et al., 2017).

Garrett et al. (2019) conducted a research study with the aim to explore racial differences in CSF tau and Aβ biomarkers. Their sample was formed by 152 African Americans and 210 White Caucasian participants with a mean age of 65.6 years. The African American sample was younger and had fewer years in education compared to the White Caucasian sample. One hundred and eighty-nine participants were identified as having MCI which was defined as scores of 26 or less on the Montreal Cognitive Assessment (MoCA) test which is an assessment of general cognitive function (Naseredine et al., 2005) and it is discussed in detail in chapter [4]. The authors note that the MoCA was used as opposed to the MMSE, however no explanation is provided for this choice. However, it is potentially due to the limitations of implementing the MMSE in ethnic minorities with lower educations levels which is discussed in chapters [4-5]. The results of the data gathered revealed that the prevalence of MCI was not statistically different between the two ethnic groups, however despite this, test scores on the MoCA were significantly lower in the African American group who had a mean test score of 23/30. Further to this, it was found that African Americans with MCI had significantly lower tau-based biomarkers and these were not explained by the degree or stage of the disease as reflected by hippocampal volumes assessed on Magnetic Resonance Imaging (MRI) (described in section 2.7) (Garrett et al., 2019). Consistent findings have been observed in further research by Howell et al. (2017) and Morris et al. (2019) in African American samples.

This suggests that the most established clinical biomarkers of AD (tau and Aβ biomarkers) may be influenced by race and ethnicity in people with similar levels of cognitive impairment (Garrett et al., 2019; Morris et al., 2019). This has important implications for the diagnostic process. If these differences are not accounted for and understood, they have the potential to affect the accuracy of diagnosis and the outcome of clinical trials which include minority samples. In particular, the presence of cognitive impairment, but lower tau levels may lead to clinical underdiagnosis of AD in African Americans. This emerging evidence suggests that molecular biomarkers of AD, such as tau, may be mediated by race dependent biological mechanisms. Therefore, race should be taken into consideration when using neuroimaging techniques to identify the biomarkers of AD in minority samples to ensure reliable and valid outcomes for people from across different backgrounds. This is particularly important considering that currently available neuropsychological assessment measures have not been widely validated in minority samples and they are influenced by external factors (Blakemore et al., 2018). This indicates that there is potential for minority groups to possibly be disadvantaged in obtaining an AD diagnosis both when implementing subjective and objective measures.

The present thesis focuses on subjective neuropsychological assessment measures and their adequacy in South Asian older adults as these measures are used in the initial stages of the disease presentation, whilst neuroimaging techniques are not as widely implemented in clinical settings (NICE, 2018). However, evidence of racial disparities in established AD pathological hallmarks in African American samples provides basis for further research to be expanded into other BAME groups at increased risk of AD, such as South Asian older adults. However, at present this is beyond the scope of this thesis

2.6.4. Neurotransmitter abnormalities

Changes in neurotransmitters have also been proposed to occur in the development of AD. Some of these are outlined in table two.

Table .2. Common neurotransmitter abnormalities in AD

Neurotransmitter	**Explanation**
Cholinergic hypothesis **(Acetylcholine (Ach))**	Cholinergic brain systems are those which are affected by the activity of the neurotransmitter Ach (Maurer and

	Williams, 2017). The limbic system is the largest brain pathway which receives cholinergic input, and it includes structures, such as the hippocampus, amygdala, anterior thalamus, hypothalamus, mamillary bodies, basal forebrain, septal area, orbitofrontal and para-hippocampal cortices (Pinto et al., 2011). Therefore, cholinergic transmission is critical for memory, learning, attention, and other higher end cognitive functions (Hampel et al., 2018). Most of the cholinergic innervation is initiated from the basal forebrain, with the hippocampus receiving its input from cholinergic neurons located in the medial septal nucleus and the vertical band of Broca whereas the remaining cerebral cortex receives their cholinergic input from the nucleus basalis of Meynert (nbM (Hampel et al., 2018). The cholinergic hypothesis states that cognitive dysfunction seen in AD patients results from disruptions in the activity of the neurotransmitter Ach (Klaassens et al., 2019; Pinto et al., 2011). This is argued as cholinergic neurons provide the main source of Ach in the cortex, and a decline in Ach levels has been directly associated with cognitive impairment (Maurer and Williams, 2017; Schmitz et al., 2016; Ferreira-Vieira et al., 2016) In particular,

	the number of cholinergic neurons has been found to be significantly reduced in the basal forebrain in patients with cognitive impairment and AD (Scheef et al., 2019; Ballinger et al., 2016; Schliebs and Arendt, 2011). Moreover, the NbM is also one of the earliest areas of the cholinergic system to be affected in AD and it shows a volume reduction, even in MCI cases (Kilimann et al., 2014; Grothe et al., 2010). In essence, the cholinergic hypothesis states that the denervation of cholinergic output leads to the development of clinical symptoms in AD, and this view is reinforced by the efficacy of Ach inhibitor drugs in the treatment of the cognitive symptoms of AD (Dumas and Newhouse, 2011; Furey, 2011). These are discussed in detail in section [2.8].
Serotonin	Serotonin functions as a neurotransmitter in the central nervous system and evidence shows that it plays a role in the development of psychiatric (depression, agitation, anxiety) and cognitive symptoms associated with AD (Francis et al., 2010). Evidence of this comes from the effectiveness of anti-depressant medication, such as citalopram in the alleviation of AD related symptoms (Wu et al., 2018; Porsteinsson et al., 2014)

	Moreover, NFTs and neuronal loss has been observed early in AD in the raphe nucleus which is responsible for most of the cortical serotonergic innervation further supporting its involvement in the development of AD (Francis et al., 2010). Lower serotonin transporter binding has also been observed in MCI cases in cortical, limbic, sensory, and motor areas which correlate with cognitive impairment (Peña-Bautista et al., 2020; Smith et al., 2017). This may be explained due to the association of serotonin with Aβ. Serotonin is involved in reducing amyloid plaque load; however, AD patients exhibit reduced serotonin receptors which consequently increases Aβ production leading to neuronal atrophy and subsequent cognitive decline (Sangubotla and Kim, 2018; Larsson and Markus, 2017)
Glutaminergic Systems	Glutamate is a major excitatory neurotransmitter present in the nervous system and glutamate receptors are located throughout the brain and spinal cord in the glia (Zhang et al., 2016). They play an important role in synaptic plasticity involving memory and learning (Zhang et al., 2016). Therefore, glutaminergic systems play a role in cognition and excessive glutaminergic activation has been associated with the development of

	AD (Danysz and Parsons, 2012; Wang and Reddy, 2017). Lower hippocampal concentrations of glutamate receptors have been observed in AD patients and decreased ability in glial neurons to remove excess glutamate from the synaptic cleft leading to overexcitability and toxicity (Wang and Reddy, 2017). This excitotoxicity is observed to promote neuronal death and it is argued to be a potential underlying mechanism of neurodegeneration observed in AD (Wang and Reddy, 2017). This is supported by the effectiveness of drugs, such as memantine, which acts as a glutamate receptor antagonist, in managing cognitive symptoms in AD (McShane et al., 2019; Wand and Reddy, 2017). The use of memantine as a glutaminergic receptor antagonist is discussed in section [2.8].

2.7. Diagnosis

Currently, the diagnosis of AD takes place when the brain has already suffered severe degeneration and the symptoms begin to impact the individual's autonomy and ability to engage in everyday life (Belleville et al., 2019).

The first point of contact for individuals who are concerned about having AD is their general practitioner (GP) (Age UK, 2019). The GP will conduct the initial assessment and if necessary, refer the patient to a specialist for a more detailed assessment with the aim to establish a diagnosis following standardised guidelines (Age UK, 2019).

2.7.1. The NICE diagnostic guidelines

In the UK, guidance on the diagnosis of different types of dementias, including AD, is provided by the NICE "Dementia Assessment and Diagnosis" Guidelines (2018). NICE (2018) recommend that the diagnosis of dementia should only be established once a comprehensive assessment has been undertaken which considers the following:

- Full patient history on cognitive, behavioural, and psychological symptoms and their impact on everyday life from the patient and if possible, from someone who knows the patient (e.g., family member).

- The NICE (2018) guidelines recommend the use of the "Informant Questionnaire on Cognitive Decline in the Elderly" (IQCODE) or the Functional Activities Questionnaire" (FAQ) to supplement history taking from someone who knows the patient with suspected dementia.

- Physical examination and blood analysis to rule out probability of other conditions that could cause cognitive decline.

- Full review of current prescriptions, including over the counter drugs, to minimise medication use which may have adverse effects on cognitive functioning.

- Use of brief cognitive tests to evaluate the patient's current cognitive abilities using validated measures such as:

    - The 10-point cognitive screener (10-CS);
    - The 6-item cognitive impairment test (6CIT);
    - The 6-item screener;
    - The memory impairment screen (MIS);
    - The mini-cog;
    - Test your memory (TYM);

- The above recommended assessments measure a range of different cognitive functions, and test scores are used to determine the level of cognitive impairment. It is also important to note that the guidance recommends the use of verbal episodic memory assessments in cases where AD is suspected. The guidance describes episodic memory as information relating to recent or past events and experiences, as opposed to factual knowledge, skills, or habits (NICE, 2018). However, no specific assessment is recommended from the list above, questioning the practical applicability of this advice.

Following the above, NICE (2018) recommend that if reversible causes of cognitive decline are not identified (e.g., depression, delirium, sensory impairment, or cognitive impairment associated with medicines) and dementia continues to be suspected then the patient should be referred to a specialist diagnostic service, such as a memory clinic or community old age psychiatry service. However, if rapidly progressive dementia is suspected, NICE (2018) recommend that the patient is referred to a neurological service with access to tests such as CSF to rule out the possibility of other conditions.

2.7.2. Neuroimaging techniques

With the advances in imaging techniques, the NICE (2018) guidelines recommend the use of PET, MRI, and CSF examinations to check for the presence of tau and Aβ pathologies in limited cases where AD is suspected, but not confirmed by the means of other measures described above. These assessments are described next.

2.7.2.1. MRI

MRI is a non-invasive imaging technique which uses powerful magnetic fields and radio frequency pulses to generate detailed images of the brain’s structure and it is a commonly used technique to identify brain atrophy and neurodegeneration associated with AD and MCI (Moscoso et al., 2019; Jack et al., 2018). In research, MRI scanning has been used to classify AD with a sensitivity (true positive rates) and specificity (true negative rates) of approximately 80% and above (Farina et al., 2020; Beheshti et al., 2017). In MCI cases, the estimates are more varied, but they range between 50%-90% (Farina et al., 2020; Beheshti et al., 2017). One of the most established biomarkers observed in MRI imaging is the atrophy of the medial temporal lobe which is strongly associated with cognitive decline (Jack et al., 2018; Cohen et al., 2019). Moreover, atrophy in the medial temporal lobe is also the only neuroimaging marker included in the diagnostic criteria for AD by the National Institute on Ageing and Alzheimer's Association (NIA-AA). NIA-AA is a research association which aims to provide a common framework for researchers to communicate their research observations (Jack et al., 2018).

It is important to note that the areas of atrophy identified in MRI scans can overlap with other dementias, and therefore relying on MRI measures alone may not be sufficient to confirm an AD diagnosis (Johnson et al., 2012). MRI scans cannot directly detect pathological hallmarks of AD, i.e., amyloid plaques and NFTs, and cerebral atrophy detected by MRI scans is non-specific and may overlap by degeneration caused by other diseases and different types of dementias (Johnson et al., 2012). Moreover, with regards monitoring disease progression, volume changes in neuronal loss as detected by MRI scans can also be produced by other factors such as ageing, and therefore its use as a measure of progression is also currently obscure (Walsh et al., 2020; Johnson et al., 2012).

Therefore, MRI assesses structure, but it cannot assess function, which is measured at a more sophisticated level by PET scans (Johnson et al., 2012).

2.7.2.2. PET

PET scans allow to measure concentrations of molecules in the brain, such as Aβ and NFTs, which are the most established biological hallmarks of AD (Cohen et al., 2019; Zhang et al., 2017). However, PET scans are more expensive and invasive when compared to MRI scans as these require for a ligand to be injected which emits a small amount of radiation (Salvatore et al., 2018; Johnson et al., 2012). Evidence shows that Aβ and NFTs observed in PET scans correlate with cognitive decline in AD, and increased pathology correlates with increasing clinical severity (Ten et al., 2019; Maass et al., 2017).

Therefore, considering that AD is characterised by cerebral atrophy, Aβ load and NFTs, it is proposed that the combined use of MRI and PET scanning offers the most accurate diagnostic techniques to identify AD as opposed to the use of either of the modalities alone (Zhang et al., 2017). MRI scanning would allow to visualise cerebral volume loss in critical areas and provide three-dimensional images of brain structures, while PET scanning provides metabolic and molecular information which together can be used to identify AD related atrophy and monitor progression into the different stages (Zhang et al., 2017).

2.7.2.3. CSF

CSF is a fluid which circulates throughout the brain and ventricles and it is one of the most established fluid biomarkers for cerebral Aβ and tau pathology (Cohen et al., 2019). CSF examination involves a lumbar puncture to take a sample of CSF with the aim to analyse Aβ and total tau (T-tau) concentrations (Hansson et al., 2019).

Reduced Aβ42 and high tau concentrations in CSF samples are highly associated with AD, particularly in its earlier stages (Ashton et al., 2018; Olsson et al., 2016; Petersen et al., 2009; Forlenza et al., 2010). Evidence also indicates that amyloidosis is reflected in CSF earlier than detected in PET scans (Lewczuk et al., 2017; Palmqvist et al., 2016). Therefore, suggesting that CSF sampling may be more accurate in detecting early pathology associated with AD when compared to MRI and PET scans. Moreover, CSF sampling is significantly cheaper and more accessible when compared to PET scans (Hansson et al., 2019). Despite CSF sampling being a reliable early indicator of Aβ and tau burden, the procedure is more invasive than MRI and PET scans (Johnson et al., 2012). Its implementation is accompanied with increased risk of side effects, such a backache, headache and patients are required to remain under observation following the procedure before being discharged home (Johnson et al., 2012; Ashford et al., 2006).

Although the above-mentioned neuroimaging techniques offer the opportunity to accurately measure biological hallmarks of AD without influence or bias from external factors such as language, culture, or education levels, all these procedures are costly and they require highly trained professionals to carry out the procedures (Johnson et al., 2012). Moreover, MRI and PET scans expose people to radiation and may not be suited for repeated testing.

It is also potentially due to the above drawbacks that the NICE (2018) guidelines do not recommend the routine use of neuroimaging techniques for all suspected cases of AD. The guidance states that these measures are only to be used in suspected cases of AD after cognitive screening has taken place. The guidance further states that MRI, PET and/or CSF should only be used if it will help to diagnose the dementia subtype and, where knowing about the subtype would change the disease management approach. Therefore, AD diagnosis is typically based on a combination of behavioural and neuropsychological measures, whilst the use of more objective neuroimaging techniques remains restricted. However, neuropsychological tests often have limitations in that they rely on subjective judgments, can be influenced by external factors, such as education and culture, and they are less sensitive to the early stages of the disease (Cassani et al., 2018). Nonetheless, neuroimaging techniques are widely implemented in AD research and clinical trials and there are increasing efforts to identify non-invasive brain markers before the onset of the cognitive and behavioural symptoms of AD (Jack et al., 2018; Varghese et al., 2013).

2.7.3. Limitations of the NICE diagnostic guidelines

Despite the advances in neuroimaging techniques, neuropsychological testing plays a central role in the assessment and identification of conditions like AD (NICE, 2018; Anderson et al., 2017). In fact, the NICE (2018) dementia guidelines state that cognitive tests should be performed in primary care settings in all patients who are suspected to have dementia before progressing into any further evaluation. This is potentially because as previously discussed, the presenting symptoms of AD are largely cognitive in nature (Roeck et al., 2019). Therefore, this makes cognitive or neuropsychological assessments the most appropriate screening measures to identify cognitive impairment. Consequently, considering that the findings from neuropsychological assessments are likely to play a role in further evaluations and specialist referrals, it is vital for these assessments to be reliable and valid to infer an early and accurate diagnosis. However, neuropsychological assessments as recommended by NICE (2018) are often affected by external factors which have the potential to bias results and mislead diagnosis if not controlled and accounted for, particularly in ethnic minorities (Blakemore et al., 2018).

Considering the limitations of existing neuropsychological assessments and the restricted use of objective neuroimaging measures in clinical settings, it is important to validate existing assessments in minority underrepresented groups and identify external factors which can bias test scores with the aim to enhance the accuracy of diagnosis. This will be the focus of the present thesis with reference to South Asian older adults residing in the UK who are identified at high risk of developing AD (Blakemore et al., 2018; Kenning et al., 2017). However, they remain largely underrepresented in AD research and service use (Blakemore et al., 2018; Kenning et al., 2017). This is discussed in more detail in chapter [3].

2.8. Treatments

Since 2003 no new AD drugs have been approved, and there are no approved disease modifying drugs for the treatment of AD (Cummings et al., 2019). As previously discussed, the two established pathological hallmarks of AD include the presence of senile plaques composed of Aβ and NFTs composed of hyperphosphorylated tau protein which are accompanied by neuronal atrophy and synaptic degeneration (Teipel et al., 2020). Currently available treatments do not target AD pathology and they only provide symptomatic benefits aimed at slowing down the progression of cognitive decline (Hansson et al., 2018).

The available treatments can be divided into two categories, namely Acetylcholinesterase inhibitors (AChE) and N-methyl-D-aspartate (NMDA) antagonists which are discussed next.

2.8.1. Acetylcholinesterase (AChE) inhibitors

NICE (2018) recommend the use of AChE inhibitors as the primary option for the management of mild to moderate cases of AD. Currently, there are three types of approved AChE inhibitors available which include donepezil, rivastigmine and galantamine (NICE, 2020; Li et al., 2019). These drugs work by inhibiting the action of the acetylcholinesterase enzyme which is responsible for the degradation of acetylcholine at the neuronal synaptic cleft (Tricco et al., 2018; Zambrano et al., 2019). The action of these medications leads to increased levels of acetylcholine which improves communication between neurons and improves memory and cognitive performance (Tricco et al., 2018; Zambrano et al., 2019).

NICE (2018) recommend that the treatment with AChE inhibitors should be started with the drug that incurs the lowest acquisition cost. However, the guidance further states that alternative drugs can be prescribed if the first choice based on cost is not adequate due to adverse effects, medical comorbidity, or possibility of interaction with other drugs (NICE, 2018).

The recommended dose varies with each drug and the side effects are a common factor impacting usability and compliance. The most common side effects typically observed in patients taking AChE inhibitors are gastro related, such as nausea and vomiting, diarrhoea as well as headaches and sleep disturbances and these become notably worse with increased dosages (Zambrano et al., 2019; Atri, 2011; Mimica and Presecki, 2009).

Amongst the three AChE’s currently available, galantamine is reported to have the most side effects followed by rivastigmine (Lockhart et al., 2009). Further to this, despite the side effects, an extensive review by Tricco et al. (2018) exploring the findings of 142 studies consistently found that all three AChE inhibitors improved cognition better than the placebo treatments.

2.8.2. N-methyl-D-aspartate (NMDA) antagonists

NMDA antagonists inhibit the binding of glutamate which is elevated in patients with AD leading to neuronal toxicity (Liu et al., 2019; Farrimond et al., 2012). Consequently, this leads to a gradual loss of synaptic function reducing communication between neurons and ultimately leading to the neural atrophy observed in AD patients which correlates with clinical decline in cognition (Liu et al., 2019).

Currently, memantine is the only available and approved NMDA receptor antagonist for the treatment of AD (McShane et al., 2019). NICE (2018) recommends the use of memantine in AD patients who are intolerant to AChE inhibitors, or are at a severe stage of AD.

An early clinical trial by Winblad and Poritis (1999) demonstrated improved symptoms in patients with AD as assessed on the MMSE following three months with a ten mg dosage of memantine. Reisberg et al (2003) in a sample of 181 patients with moderate to severe AD reported a significant improvement in their ability to engage in ADL on a daily dose of 20 mg. More recently, McShane et al. (2019) conducted a review exploring the use of memantine in a total of 10,000 participants taking part in 144 trials. Many of the studies reviewed had implemented the MMSE to assess the severity of symptoms. McShane et al. (2019) found that the clinical benefits of memantine were greater in moderate to severe cases of AD and this was irrespective of people also taking AChE inhibitors simultaneously. Moreover, they found that the beneficial effects of memantine were not observed in people with mild AD. Therefore, suggesting that NMDA antagonists are only beneficial in more advanced stages of AD.

In conclusion, there are only two types of drugs approved for the treatment of AD, and these are only effective in providing symptomatic relief as opposed to targeting the pathological hallmarks of the disease. However, many clinical trials are currently investigating the potential of new drugs targeting the pathological hallmarks of AD (Cummings et al., 2019).

2.9. Mild Cognitive Impairment

The process of degeneration in AD is argued to begin many years before the clinical presentation of symptoms of cognitive impairment (Carro et al., 2017). MCI has been proposed as the stage between healthy cognitive ageing and dementia which is marked by cognitive decline which does not impair daily living (Bertens et al., 2019; Petersen et al., 2014). It is estimated that the annual conversion rate from MCI to AD is between three to 15% compared to one to two percent in the general population (Michaud et al., 2017).

MCI is categorised as amnestic MCI (aMCI) when memory is the primary domain affected and non-amnestic MCI (naMCI) when other non-memory related domains are affected, such as language and/or executive function (EF) (Csukly et al., 2016; Petersen et al., 2014; Dubois et al., 2014). MCI can be further classified as single domain MCI whereby only one domain is affected or multiple domain MCI whereby more than one cognitive domain is impaired (Petersen et al., 2014). However, not all MCI cases develop into AD, some remain stable whilst others return to normal cognition (Roberts et al., 2014). It is unclear how MCI progresses into AD, and it is possible that specific MCI subtypes may be more associated with the progression to AD. Evidence suggests that individuals with multiple domain aMCI are at a greater risk of progressing from MCI to AD (Michaud et al., 2017; Busse et al., 2006; Alexopoulos et al., 2006).

For example, Michaud et al. (2017) explored the clinical and demographic characteristics associated with the risk of MCI in all its subtypes and their progression into AD. The data was gathered from the National Alzheimer's Coordinating Centre which included data from a sample of 8,691 participants with normal cognition at baseline with an overall mean follow-up time of four point three years. MCI status and cognition were assessed on the MMSE and the Global Dementia Rating scale. The analysis of the data gathered revealed that 16.3% of the sample (mean age = 76.44) developed MCI, of which 15.8% progressed to develop AD over an average period of four point three years. Moreover, it was also found that multiple domain aMCI patients were significantly more likely to progress into a full dementia diagnosis compared to single domain aMCI patients. Therefore, this supports the view that MCI, and in particular multiple domain aMCI is an important early indicator of cognitive decline and development of AD.

Despite evidence suggesting that MCI may be a critical factor in the development of AD, there are challenges which act as a barrier in the identification of MCI. As previously discussed, CSF biomarkers of tau and amyloid plaque load are reliable indicators of early prodromal AD pathology, however the administration of these assessments is restricted to clinical trials and their use is costly and invasive for routine use in clinical settings (Olsson et al., 2016). Consequently, the identification of cognitive impairment in MCI is inferred through test scores on neuropsychological assessments (Petersen et al., 2014). One of the most commonly used assessment to detect cognitive impairment in research settings is the MMSE, a test of general cognitive assessment. However, assessments like the MMSE are not sensitive enough to detect MCI (Arevalo-Rodriguez et al., 2015; Mitchell, 2009) and they are ethnocentric in nature further limiting their use in the growing ethnic minority population residing in the UK (Blakemore et all., 2018; Kenning et al., 2017). Therefore, considering the importance of early diagnosis as a measure of improving treatment outcomes, it is vital that researchers and clinicians have access to sensitive tests which will facilitate the identification of subtle cognitive changes associated with MCI.

For example, Insel et al. (2018) conducted a research study with the aim to explore cognitive decline and brain injury in individuals progressing from preclinical AD to MCI and AD in the presence or absence of amyloid load. Their sample was formed by 75 older adults who had progressed into MCI after a median follow-up period of four years in the Aβ+ group (n=40; mean age = 78 years) and three years in the Aβ- group (n= 35; mean age = 75 years). Aβ status was determined through amyloid PET scans and CSF concentrations. MRI scanning was also implemented to assess cortical volumes. Cognitive functioning was assessed on a battery of cognitive assessments which included the MMSE. The analysis of the results demonstrated that Aβ+ and Aβ- individuals had similar progression time to

MCI, however Aβ+ individuals experienced a significantly faster rate of decline on tests of memory, EF, processing speed and language and had elevated levels of CSF tau at baseline. On the other hand, Aβ- individuals who progressed to MCI demonstrated increased depressive symptoms and faster accumulation of white matter lesions. Based on these findings, Insel et al. (2018) concluded that the progression of MCI is characterised by distinctive physiological features and identifying these has potential to facilitate early diagnosis and treatment of AD, particularly in clinical trials aimed at halting the progression from a pre-clinical to prodromal (MCI) stages.

The above findings are promising for the early detection and management of AD, however their applicability in clinical settings is currently limited as the NICE (2018) guidelines do not recommend the routine use of neuroimaging techniques. Moreover, currently NICE do not have any guidelines with regards to the diagnosis of MCI, and in research settings the cognitive assessment of MCI largely relies on neuropsychological assessment test scores (Petersen et al., 2014). Therefore, to enhance the early detection of AD during the MCI stage, it is crucial that the commonly used neuropsychological assessments are valid and reliable in detecting the most subtle changes in cognition.

This is particularly important as it is argued that the lack of success of anti-amyloid drug trials is largely attributed to the fact that when this pathology is clinically detected, it has reached a far too advanced stage which cannot be reversed (Walsh and Selkoe, 2020). Therefore, the early detection of cognitive deficits at the MCI stage has potential to improve therapeutic outcomes which is crucial considering that despite vast amounts of efforts by the research community, no new drug treatments have been approved for AD since 2003 (Cummings et al., 2019).

2.10. Chapter Summary

AD is a complex neurodegenerative disease which is progressive in nature and it is associated with numerous pathologies and cognitive and behavioural profiles. Currently, there are no curative treatments available, and the structural brain degeneration characteristic of AD is said to occur many years before any tangible symptoms are observed (Jimenez-Balado and Eich, 2021). This makes the early detection of AD difficult, delaying treatment. MCI has been proposed as the prodromal stage of AD and evidence suggests that many MCI cases progress to a full AD diagnosis (Petersen et al., 2014). Therefore, this suggests that early diagnosis is required at the mild stages to halt the detrimental pathological changes associated with AD.

However, neuroimaging techniques are not routinely recommended for use in the diagnosis of AD. As a result, AD diagnosis is typically inferred through a combination of behavioural and neuropsychological assessment measures. These tests have limitations in that they rely on subjective judgement, can be influenced by external factors, such as culture and education, and they are less sensitive to changes in the early stages of the disease. The consequences of this are likely to be worse in minority populations, particularly in the growing South Asian older adults residing in the UK, who are currently underrepresented in cognitive research and clinical settings despite being identified as being at a higher risk for developing AD. Therefore, the next chapter of this thesis will discuss the raise in the South Asian older adults in the UK, their incidence and susceptibility to AD and describe common barriers preventing their access to an accurate and timely AD diagnosis.

Chapter 3: AD and the South Asian community in the UK

3.1. Introduction

As discussed in chapter [2], the UK is experiencing an increase in the ageing migrant population, and, at the time of writing, the latest available statistics show that there has been a particular increase in the BAME population (ONS, 2011). It is estimated that 14% of the UK's population is formed by BAME groups and 8% (therefore over 50%) of this population is aged 60 years or over (ONS 2018, 2011). Estimating the current proportion of BAME population in the UK is challenging because the annual population estimates produced by the ONS do not include data on ethnicity (Age UK, 2019). Most of the data on ethnicity trends in the UK's population is derived from the 2011 census data which is currently the most recent and reliable source of information on ethnic populations residing in the UK (Age UK, 2019). The current census is taking place now in 2021, however the data from this was not available at the time of writing.

More specifically, amongst the BAME groups, South Asians of Pakistani, Indian, and Bangladeshi origin (see figure one for map of South Asian countries) represent the largest minority group constituting 5% of the general population in the UK (ONS, 2011). The increase in the ageing population in this group is argued to be attributed to the large number of individuals who migrated to the UK between 1950 and 1970 for work purposes (Lievesley, 2010; Hossain et al., 2018).

Figure .1. Geographical location of South Asia

Initially, the wave of migration from these communities was more prominent in males who were encouraged to come to the UK by the economic opportunities in the textiles and manufacturing industries (Hossain et al., 2018). Individuals from this first wave of migration from South Asian countries were family oriented and would turn to “biraderis” (kinship network) for help in all aspects of their life (Akhtar, 2014). They were hesitant to integrate into the British society as they arrived with the mindset that they would earn sufficient money and then return home (Akhtar, 2014). In 1962 changes to immigration law restricted migration from Commonwealth countries, such as Pakistan, India and Bangladesh which prompted male members in the UK to bring their wives and children to the UK and avoid being affected by the ban (Akhtar, 2014). This led to mass migration from South Asian countries, particularly from India, Pakistan and Bangladesh in the 1960’s creating a large South Asian diaspora in the UK (Akhtar, 2014). Based on the timing of this migration trend, a large percentage of this population is now likely to be ageing (Blakemore et al., 2018).

As discussed in chapter [2], with the increase in international migration and an ageing population in the UK, the number of culturally diverse individuals suffering from age related neurodegenerative conditions, such as AD, is also projected to increase (Blakemore et al., 2018; Hossain et al., 2018; Mukadam et al., 2013). The sharpest increase in the incidence of AD is expected in South Asians of Pakistani, Bangladeshi, and Indian origin (Blakemore et al., 2018).

The increased risk of AD in this group is likely to be attributed to the higher rates of AD and dementia risk factors in this community which include hypertension, diabetes and cardiovascular diseases which were discussed in chapter [2] (Adelman et al., 2011).

Despite the increase in the prevalence of AD in the South Asian community in the UK, this group remains largely absent from dementia services and is underrepresented in cognitive research (Waheed et al., 2020; Blakemore et al., 2018). With this distinct lack of research in the rapidly growing South Asian ageing population, improving awareness and recognition of AD in BAME groups is a public health priority to promote the effectiveness of cognitive screening measures, diagnosis, and treatment to prevent the detrimental psychosocial and clinical/medical consequences associated with AD (Wang, 2012; Blakemore et al., 2018).

3.2. AD risk in the UK-based South Asian population

Current incidence figures are likely to be underrepresented as AD has been classified as a hidden problem in the South Asian community (Hossain et al., 2018; Wilkinson, 2003). This is attributed to the differences in the perception of symptoms based on cultural factors which often affect help seeking behaviours (Hossain et al., 2018; Mukadam et al., 2015).

Blakemore et al. (2018) conducted an extensive review of research studies which explored dementia in UK-based South Asians of Pakistani, Indian, and Bangladeshi origin. As part of their inclusion criteria, they reviewed studies which included UK-based South Asians diagnosed with dementia, family carers and healthcare professionals working with South Asian patients. The research studies were identified by searching on the following databases: Cochrane Register of Controlled Trials, MEDLINE, PsychINFO, Embase and Cochrane database of systematic reviews. Twenty-seven studies were identified which met the above-mentioned inclusion criteria. Blakemore et al. (2018) found that over the years, there has been very limited research exploring the prevalence of AD in the South Asian population residing in the UK. Moreover, Blakemore et al. (2018) found that most of the prevalence related studies reviewed comprised of very small sample sizes and they were outdated with the last one identified as being published in 2004 by Haider et al. (2004).

Prevalence data is therefore currently scarce. Despite this, South Asian individuals have been identified as having a higher likelihood of experiencing an early onset of AD and they are at a greater risk of developing cognitive impairment compared to their White British counterparts (Mukadam et al., 2019; Hossain et al., 2018; Adelman et al., 2011). This is argued based on their higher susceptibility to suffering from diabetes and hypertension which are considered co-morbid conditions and risk factors in the development of AD (Mukadam et al., 2019; Uppal et al., 2014; Barnes and Yaffe, 2011).

For example, Barnes and Yaffe (2011) carried out a literature review exploring the prevalence of AD worldwide and identified seven potential risk factors which included: diabetes, mid-life hypertension, mid-life obesity, smoking, depression, low educational achievement, and lack of physical activity. More recent research further supports the involvement of these factors in the development of AD and other dementias as outlined in chapter [2] (e.g., Christopher et al., 2019; Rosano et al., 2017). Diabetes, depression, smoking and low educational achievement are common in the South Asian community and these factors have been identified as principal risk factors in the development of AD (Hossain et al., 2018; Uppal et al., 2014).

For example, statistical data suggests that individuals from the South Asian community are up to six times more likely to develop diabetes which also increases their risk of developing cardiovascular diseases (Diabetes UK, 2019). It is not entirely known what leads to this increased predisposition. However, it is argued that lifestyle choices potentially mediated by culturally determined dietary and exercise patterns and genetic factors may contribute towards the increased risk of diabetes in the South Asian community (Diabetes UK, 2019). Further to this, the highest rates of self-reported smoking are found in individuals from Pakistani and Bangladeshi backgrounds, with Bangladeshi individuals also having the highest incidence of tobacco consumption compared to the rates in other ethnicities within the UK (Hossian et al., 2018).

Many of the South Asian older adults of Pakistani, Indian, and Bangladeshi origin in the UK have also been identified as having lower levels of education which further increases their predisposition to suffering from AD (Blakemore et al., 2018; Mukadam et al., 2013), and this is discussed in detail throughout the experimental chapters of this thesis.

3.3. Importance of early diagnosis

Currently, there are no disease modifying or curative treatments for AD, and existing medications are only effective in temporarily alleviating and slowing down the progression of cognitive symptoms in mild to moderate stages of the disease (Livingston et al., 2017). Therefore, early diagnosis is currently a national priority to facilitate a timely access to treatment interventions (Mukadam et al., 2011).

It is argued that this has potential to allow people to make informed decisions and choices with regards to their future living/care arrangements as well as making relevant financial and legal arrangements for when they no longer have the cognitive ability to make sound decisions (Sagbakken et al., 2018). Timely diagnosis is also argued to offer caregivers the opportunity to plan their caring arrangements in advance (Sagbakken et al., 2018). More competent caregiving interventions in the mild and moderate stages of AD are argued to delay institutionalisation which can assist in saving costs in the long-term, both by patients and the healthcare system (Sagbakken et al., 2018).

AD and other dementias are also considered as the most important health problem in economic terms as they cost the UK economy approximately £26 billion per year (Alzheimer’s UK, 2021). The increased financial burden of AD on health services may be partly explained due to the cognitive impairments associated with AD leading to poorer outcomes in the self-management of other conditions, such as diabetes and cardiovascular diseases (Sagbakken et al., 2018). This has potential to increase the risk of institutionalisation, thereby further adding to the economic burden. Increasing awareness of the importance of early diagnosis has potential to not only improve the quality of care received by those affected, but it can also reduce the overall financial burden on health services (Kirson et al., 2016). Moreover, therapeutic interventions are most effective in improving cognitive function and treating psychiatric symptoms, such as depression, when implemented early in the disease course (Guest et al., 2020; Dafsari and Jessen, 2020).

Based on the importance of early diagnosis, several Western countries have introduced campaigns to increase awareness of the different types of dementias, including AD (Livingston et al., 2017). In the UK, The National Dementia Strategy was launched in 2009 (Department of Health and Social Care, 2009). The main aim of this strategy was to deliver quality improvements to dementia services by offering support and guidance to health and social care professionals to facilitate early diagnosis (Department of health and social care, 2009). The launch of this campaign led to increased diagnosis rates and prescription of dementia medication (Donegan et al., 2017; Mukadam et al., 2014). Further to this, this strategy also identified that BAME groups were at increased risk of an earlier onset of dementia and that the needs of ethnic minority populations with dementia may be different to those of the majority of the population calling out for a need to develop specifically tailored approaches (Department of Health and Social Care, 2009). However, despite this, a review of a further campaign titled "Dementia 2020 Challenge" which was introduced in 2015 found that there is a lack of progress in diagnosing and reducing the risk of dementia in BAME communities (Department of Health and Social Care, 2019).

A recent piece of qualitative research further aimed to explore the timeliness of access to memory services between older White Caucasian and South Asian patients who were defined as Pakistani, Indian and Bangladeshi (Ogliari et al., 2020). Ogliari et al. (2020) implemented a longitudinal design to explore their aims in a sample of 3654 White British and 32 South Asian older outpatients from the Nottinghamshire Healthcare NHS Foundation Trust who were aged 65 years and above. Ogliari et al. (2020) aimed to explore whether South Asian adults would be less likely to receive a timely access to memory services once referred when compared to White Caucasian patients. A secondary aim of their research was to explore the effects of age, deprivation, and gender on access to rapid response mental health services. The research findings indicated that South Asian patients were less likely, when compared to White Caucasian patients, to achieve a timely access to dementia services which was defined as 90 days from the referral date. However, no gap was observed in the timing of access when the patients identified their first language as being English. Therefore, these findings indicate that despite the benefits of timely access to memory services and diagnosis, there are ethnic disparities amongst those who do not speak English in the timely access of dementia services following referral. This is particularly alarming considering that South Asians underuse dementia services and those who do, often present to services at a later stage of the disease (Ogliari et al., 2020). Moreover, many South Asian older adults do not speak English (Blakemore et al., 2018).

The above suggests that despite the launch of campaigns aimed at improving early diagnosis and reducing the inequality in dementia diagnosis and care, BAME communities appear to remain somewhat disadvantaged.

3.4. Representation in clinical and research settings

South Asian older adults have lower service uptake levels within the memory and dementia services (Hossain et al, 2018; Blakemore et al., 2018; Cooper et al., 2010). In contrast, service use for conditions with physical symptoms is argued to be equivalent to the rest of the population (Giebel et al., 2015; Livingstone et al., 2002).

The underuse of dementia services may arise from a general lack of information regarding the pathways to access appropriate services due to factors, such as lower education levels and linguistic barriers (Blakemore et al., 2018). The traditional linguistic and cultural preservation of attitudes and beliefs in ethnic minority older adults may also act against accessing the necessary services in a timely manner (Tillmann et al., 2019; Mukadam et al., 2015). South Asian older adults often associate the symptoms of AD with the idea of “madness” because of the lack of an obvious physical aetiology

(Mukadam et al., 2015). Consequently, this reduces help seeking behaviours further contributing towards lower service uptake (Mukadam et al., 2015).

It is argued that South Asian older adults tend to access dementia related healthcare services in response to a crisis (Mukadam et al., 2019), which often tends to occur when the disease course has reached an advanced stage and family members can no longer cope with the increased care burden (Leroi et al., 2019; Blakemore et al., 2018).

Nonetheless, some research does suggest that the rates of diagnosis and referrals to memory clinics are improving in ethnic minorities residing in the UK. Cook et al. (2018) investigated whether referrals to memory services in London were reflective of the ethnic diversity of the population in this city. The data on referrals was gathered by requesting 32 Clinical Commissioning Groups (CCG) to provide ethnic distribution data for their memory services for people aged 65 years and over. Data was received from 19 out of 32 CCGs in London which indicated that the percentage of people from BAME groups referred to memory services was significantly higher than expected based on the percentage of the ethnic population. In particular, the highest rates of referrals amongst BAME groups were observed in people from African Caribbean and Indian backgrounds. However, ethnic minorities originating from China, Pakistan and Bangladesh were amongst the most underrepresented populations in the memory services. Despite this, Cook et al. (2018) found that the overall number of referrals from BAME groups to memory services in London was higher than expected. It was thereby concluded that these findings suggest that there have been improvements in the awareness of dementia and help-seeking behaviours in BAME groups.

Although these results are encouraging, it is important to note that the above findings may not be reflective of the UK's general population as London is more ethnically diverse which was also acknowledged by the authors (Cook et al. 2018). Moreover, data was only analysed for people aged 65 years and over and considering that dementia onset in ethnic minorities tends to be at a younger age (Mukadam et al., 2019; Adelman et al., 2011), implies that the above findings may not be entirely accurate. More importantly, the data suggesting that Pakistani and Bangladeshi individuals were amongst the least represented BAME groups further supports the argument that some South Asian older adults continue to be underrepresented in dementia service utilisation.

Moreover, following the introduction of the “National Dementia Strategy” in 2009, there was an increase in the number of people diagnosed with dementia (Mukadam et al., 2014). Evaluations of the implications and effects of this policy have failed to explore the rates of diagnosis in ethnic minority populations (Mukadam et al., 2018). It is unclear whether such policies offer any positive outcomes in contributing towards improving access to early diagnosis and service use in ethnic minorities.

Recent research also indicates that when individuals from BAME backgrounds do access the relevant health services, they are less likely to be prescribed with treatments that offer symptomatic relief (Jones et al., 2020). Jones et al. (2020) conducted a research study with the aim to explore the prescription of anti-dementia, psychotropic and anticholinergic drugs in minority ethnic people in the UK. They analysed data from UK primary care electronic records from the Health Improvement Network (THIN). The final analysis included data from 53,718 people with dementia and 1,648,889 people without dementia aged between 50-105 years of age. The analysis of the data revealed that compared to the White Caucasian groups, South Asians with dementia were less likely to be prescribed with anti-dementia drugs when these were likely to be indicated as adequate by the relevant guidelines. South Asians and Black ethnic minorities were also found to be more likely to be prescribed with antipsychotic drugs for a longer time relative to White Caucasian people. This suggests that there are potential racial disparities in dementia prescribing pointing towards care inequalities within the dementia services.

Currently there is a lack of research in the field of AD and dementia recruiting South Asian samples (Blakemore et al., 2018). Moreover, the limited research available in BAME groups is predominately carried out in the USA where the target populations have been African Americans, Chinese, Koreans, Latinos and Hispanics (Adelman et al., 2011; Mukadam et al., 2011). Moreover, Boer et al. (2007) conducted a systematic review of qualitative research investigating the impact of dementia and patients' perspectives in the Netherlands. Fifty studies internationally met the inclusion criteria for the review, however none of these studies represented the South Asian group.

Therefore, this leads to little insight into UK-based evidence on the needs of the growing South Asian ethnic minorities and little to no guidance with regards to the problems they may face when accessing the relevant services and how to counter these problems (Waheed et al., 2020).

More recently, as previously discussed, Blakemore et al. (2018) conducted an extensive review of the research literature investigating dementia in the UK-based South Asian population. However, the review identified 27 studies of which only two aimed to validate the use of the commonly used cognitive screening test, the MMSE, in a South Asian sample (Lindesay et al., 1997; Rait et al., 2000) and the review failed to identify a single clinical trial exploring the effectiveness of interventions for dementia in the South Asian population. The remaining studies identified in the review largely focused on perceptions, knowledge, and attitudes of the South Asian community towards dementia as opposed to validating the screening and diagnosis of cognitive decline (Blakemore et al., 2018).

The lack of research exploring AD and dementia in the UK South Asian population indicates a neglect of 5.3% of the UK's population (Blakemore et al., 2018). This has implications for research and healthcare settings. Neuropsychological assessments developed through research in non-UK based ethnic minorities and the subsequent diagnostic and care pathways cannot extend across all ethnic minority groups. Different countries have different types of ethnic minorities and healthcare settings, and therefore what is valid for ethnic minorities in the USA, may not be the case in the UK (Waheed et al., 2020; Khan and Tadros, 2014). Therefore, the lack of UK-based research and representation of the South Asian population questions the feasibility of implementing existing diagnostic pathways and interventions prior to carrying out an assessment with regards to their acceptability and effectiveness in this group of individuals.

3.5. Cultural and linguistic barriers

The lower representation of UK-based South Asians in research and clinical settings may be explained by a range of cultural and linguistic barriers which are discussed next.

3.5.1. Lack of general knowledge about AD

The current literature suggests that there is a general lack of awareness about AD as a form of dementia within South Asian and other ethnic minority older adults residing in the UK (Hossain et al., 2018; Mukadam et al., 2015).

Many older adults from ethnic minorities perceive symptoms, such as memory loss and other cognitive deficits as a normal part of aging (Kenning et al., 2017; Nielsen and Waldemar, 2016). For example, Nielsen and Waldemar (2016) conducted a research study with the aim to compare knowledge and perceptions of dementia and AD amongst four ethnic groups in Denmark. Their aims were assessed implementing the Dementia Knowledge Questionnaire (DKQ) which was supplemented with two questions from the Alzheimer's Disease Awareness Test (ADAT). Survey data from 260 participants was analysed. The sample was formed by native Danish (n= 100); Polish immigrants (n = 47); Turkish immigrants (n= 51) and Pakistani immigrants (n= 62). Nielsen and Waldemar (2016) found that there was a particular lack of knowledge regarding dementia and AD in Turkish and Pakistani immigrants who viewed these conditions as a normal part of aging, or as a form of insanity which was stigmatised. This is also consistent with research by Ayalon and Arean (2004) who found that Latino and Asian adults held stigmatising views against AD and were more likely to view AD as part of ageing. This means that even when symptoms of cognitive decline are detected by the South Asian community, these may not be perceived as problematic or something to warrant medical assessment (Hossain et al., 2018; Blakemore et al., 2018; McCleary et al., 2012).

In the UK, Purandare et al. (2007) conducted a research study with the aim to explore the knowledge of dementia in South Asian older adults residing in

Manchester in comparison to Caucasian older adults. Their sample was formed by cognitively-healthy attendees of three day-care centres. The sample was requested to complete the DKQ which was professionally translated into Guajarati and Urdu. A total of 257 out of 281 DKQ's were returned from the three day-care centres. Out of 196 South Asian respondents, 191 reported their ethnicity as "Indian" and as a result, the remaining five respondents were excluded to make the analysis homogenous. The final sample of Caucasians was formed by 55 respondents. The analysis of the data revealed that knowledge of the basic aspects of dementia was significantly poorer in Indian older adults when compared to the White Caucasian sample. Moreover, it was found that Indian older adults were less aware with regards to dementia affecting an individual's personality, speech, and reasoning. It was thereby concluded that Indian older adults in the UK had limited knowledge of dementia and this was likely to be one of the main reasons for their absence from dementia services (Purandare et al, 2007).

The above is consistent with more recent research by Uppal et al. (2014) who conducted focus groups with the aim to explore knowledge of dementia in a sample of 28 Indian Sikh participants aged between 18-55 years residing in the UK. Uppal et al. (2014) found that many participants claimed that they had never come across dementia. Moreover, those who did, were surprised to learn that dementia can affect an individual beyond memory loss. Specifically, Uppal et al. (2014) found that their participants were less aware with regards to dementia having the potential to lead to social withdrawal and impairments in the ability to engage in everyday activities.

A review by the "All-Party Parliamentary Group on Dementia" (2013) identified that there is no word for dementia in any of the South Asian languages. This creates challenges in helping individuals understand the condition as the lack of words implies that dementia is often not recognised as a concept (Hossain et al., 2019). This creates barriers in people's ability to understand or discuss about a condition which does not have a linguistic existence and the symptoms of which are often perceived to be derogatory (Hossain et al., 2019).

Turner et al. (2005) also reported differences in attitudes towards care. They found that South Asian older adults reported that care was to be provided within the family, and as a result they were less likely to present to health services to seek for professional help as this was not deemed necessary (Turner et al., 2005).

In line with the above, Lawrence et al. (2008) conducted a qualitative piece of research with the aim to explore caregiving ideologies in dementia carers. Their sample consisted of 32 carers of people with a dementia diagnosis from Black Caribbean, South Asian (countries not specified) and White British ethnic groups. The analysis of the data revealed that most of the South Asian carers held a traditional ideology whereby they believed that care of older adults was expected from younger family members. This was perceived as a noble and virtuous act (Lawrence et al., 2008). However, with this ideology, challenges arise when we consider that poor knowledge about dementia may not only be restricted in older adults, but some evidence shows that carers often also show little awareness (Blakemore et al., 2018; Adamson, 2001).

Adamson (2001) interviewed 12 South Asian carers of Pakistani and Indian origin which included spouses, daughters, daughters-in-law, sons, and granddaughters of people with dementia in the UK. Six carers were aged 40 years or over and the remaining of the six carers were aged under 40 years of age. The analysis of the data revealed that a significant number of family carers did not have knowledge of the symptoms of dementia before an official diagnosis was established. Adamson (2000) further found that carers often associated the symptoms as being part of other issues including diabetes, isolation and social withdrawal with old age, depression, and anxiety (Adamson, 2001). Additionality, it was also found that carers' religious beliefs also contributed to their understanding of dementia symptoms and in particular, Pakistani carers pointed out that dementia was perceived as a punishment from God resulting from the individual's wrong doings in the past and not because of an illness (Adamson 2001; McCleary et al., 2012).

In addition to this, the lack of knowledge also leads some carers to believe that people with dementia, or AD are deliberately being difficult as opposed to acknowledging that the issues may be explained by a disease pathology (Mukadam et al., 2015).

It is further interesting to note that a literature review by Kenning et al. (2017) found that the lack of dementia knowledge was not limited to patients and carers in the South Asian community, but there was a widespread lack of knowledge within the healthcare system in the UK and particularly amongst GPs. They found that there was a recurrent theme in nine out of 28 studies reviewed whereby GPs reinforced the normalisation of memory loss as part of ageing. Consequently, lowering the concern of carers whilst failing to adequately establish a timely diagnosis (Kenning et al., 2017). This was found to result from poor specialised training leading to a lack of awareness about dementia screening (Kenning et al., 2017).

The evidence discussed supports the view that many South Asian older adults often lack knowledge with regards to dementia (Blakemore et al., 2018; Kenning et al., 2017; Uppal et al., 2014; Lawrence et al., 2008). Moreover, it also indicates that the care of people showing symptoms of AD and dementia is often preferred to be provided by family because of traditional cultural ideologies (Kenning et al., 2017; Adamson, 2001). Traditional cultural views within the South Asian community often also lead to marked differences in the perception of symptoms as being a punishment from God/s which has the potential to prevent access to formal healthcare systems (Hossain et al., 2018; Kenning et al., 2017). The varying cultural views and perceptions often lead to stigma further preventing help-seeking behaviours in this cohort.

3.5.2 Cultural perceptions and stigma attached to AD

The current literature suggests that the cultural understanding of AD and stigma attached to it plays a major role in reducing help-seeking behaviours in some divisions of the South Asian community, delaying diagnosis and treatment (Blakemore et al., 2018; Mukadam et al., 2011; MacKenzie, 2006).

For example, Mackenzie (2006) conducted a qualitative study to gain an insight into the cultural differences in the understanding of dementia amongst

South Asian and Eastern European carers in the UK. This was investigated in a sample of 11 Pakistani carers, five Indian carers, four Polish carers and one Ukrainian carer. Mackenzie (2006) found that there was a widespread stigma against dementia amongst South Asian carers which was primarily rooted in religious ideologies. Care was identified as a religious obligation by all Pakistani and Indian carers. However, although caring for an older relative was perceived as acceptable, all forms of dementia were classed as a mental illness with spiritual explanations giving rise to stigma. Carers and their family members with dementia were stigmatised and seen by the wider community as being cursed and/or possessed by evils. They believed that dementia was caused because the affected person had failed to be good in his/her religious duties and was now being punished by god/s which brought shame to the whole family (Mackenzie, 2006).

Furthermore, Giebel et al. (2016) conducted a research study with the aim to assess the differences in the perception of dementia between South Asian people of Indian and Pakistani ethnic backgrounds who consulted a GP about their dementia related symptoms and between those who did not. Their sample was formed by 33 South Asians aged 65 years and over. Eighteen of the participants had not consulted a GP about their memory problems and 15 had. Perceptions of dementia were assessed on the Barts Explanatory Inventory for Dementia. Cognition was assessed using the MMSE and the clock drawing test. Depression was assessed on the Geriatric Depression Scale. The results of the analysis revealed that on average, participants who did not consult a GP about their memory problems scored 22.6 points on the MMSE, whilst those who did consult a GP scored 20.3 points. Moreover, Giebel et al. (2016) found that the group of Pakistani and Indian participants of Muslim and Hindu faith who failed to consult a GP were significantly more likely to see their memory issues as given by God/s, and consequently believed that medical interventions would be inappropriate as they saw acceptance of faith as an alternative to treatment. Moreover, higher levels of diabetes, heart diseases and depression were found amongst those who did not consult a GP, which as discussed in chapter [2], are risk factors in the development of AD.

Regan (2016) conducted a case study of a Pakistani Muslim man referred to as “Mr Q” who was accessing UK health and social care services for people with dementia. The main aim of the case study was to establish what motivates an individual from an underrepresented group to access dementia services despite having a supportive family and strong religious and community links. Through the case study, Regan (2016) found that Mr Q only accessed dementia care services as a last resource and out of desperation. He did not wish to access support from family or religious establishments due to fear of embarrassment and losing his honour. Moreover, he did not wish for the people in his community to find out about his diagnosis due to fear of being stigmatised, but he did not experience any issues sharing about his physical illnesses with other people in the community. As a result of this, he had isolated himself and withdrawn from the wider community leading to loneliness (Regan, 2016).

It is further found in the literature that the stigma attached to all forms of dementia in the South Asian community also causes interference with the family or carers’ ability to participate in wider community activities leading to increased risk of isolation amongst family members and carers (Kenning et al., 2017; MacKenzie, 2006; Jutlla, 2011).

Loneliness and isolation have also been identified as factors which predict and contribute towards cognitive decline (Sundström et al., 2019; DiNapoli et al., 2014; Read et al., 2020; Evans et al., 2018). It is claimed that the mechanism by which isolation and loneliness contribute to poor cognitive outcomes relates to the lack of social stimulation on the brain which reduces its resilience to age related damage and cell atrophy leading to cognitive decline (Evans et al., 2018). This implies that isolation may potentially be a further risk factor in the development of cognitive impairment in South Asian older adults.

It is also important to highlight that whereas stigma exists against carers as well as patients, if a family member is unable to act as a carer for an ill relative, then this also leads to a potential source of stigmatisation in the South Asian community (Hossain et al., 2018). Regardless of the presence of any type of illness, caring for an aging member of the family at home is favoured and seen as a virtuous deed (Lynch, 2019). Carers from a South Asian background are under pressure from their wider community to look after older family members and seeking any sort of external help is reported as casting shame upon the family's honour (Lynch, 2019). This, therefore, further contributes towards the lack of professional help-seeking behaviours in this group of individuals.

It would thereby be correct to say that reduced help-seeking behaviours mediated by cultural norms prevent early interventions and treatment, increasing the burden on patients, carers, and the wider healthcare system (Blakemore et al., 2018; Cooper et al., 2010). Therefore, unarguably, to improve the early diagnosis of dementia in the South Asian population it is firstly imperative to increase dementia awareness and knowledge which is important work, but it is beyond the scope of the present thesis. Moreover, it is equally important to develop culturally sensitive services to improve the healthcare system's ability to engage this group of individuals in formal healthcare. This can be achieved by creating simple methods which are valid across cultures and can be easily administered by primary health care workers (Blakemore et al., 2018). This would make access to dementia services more equitable for those who are identified at high risk for poor outcomes due to the ethnocentric nature of dementia diagnosis.

3.5.3. Language barriers and literacy

The assessment of AD in South Asian older adults is challenged by the lack of culturally adapted assessment tools, lack of understanding of the English language and likelihood of lower literacy levels (Blakemore et al., 2018; Hossain et al., 2018; Kenning et al., 2017). This is an issue because many of the neuropsychological assessments commonly used are widely influenced by linguistic, educational, and cultural factors which negatively affect the ability to accurately identify cognitive impairments in ethnic minorities (Babulal et al., 2019; Blakemore et al., 2018; Hossain et al., 2019) (see chapters [4-5]).

It is estimated that in the UK, only 35% of South Asian older adults aged over 65 years can speak English, and only 21% are able to read and write in English with most older adults relying on their first language which tends to be Urdu

(Khan et al., 2014). This creates challenges for this group of individuals when accessing mainstream health services and completing diagnostic tools which tend to be in English, lack cultural relevance and require a certain level of education to complete (Hossain et al., 2018).

South Asian older adults in the UK are also identified as amongst the least educated BAME groups (Blakemore et al., 2018) and this has direct implications on the completion of neuropsychological assessment tests used in the diagnosis of AD (Blakemore et al., 2018; Hossain et al., 2018). For example, according to data obtained by UNICEF (2019), even at the present time there are over 11 million children who do not have access to education in South Asian countries and there is a general failure in the population to master the basic foundations of numeracy and literacy skills.

Moreover, lower education levels in South Asian older adults often make it challenging to accurately determine their age and education level which are important factors to account for when administering neuropsychological assessments to evaluate cognitive functioning (Blakemore et al., 2018; Nielsen et al., 2011). South Asian older adults are often unaware of their exact date of birth, and the one recorded in their official documents may not always be accurate. A report by UNICEF (2019) highlighted that the lack of birth registrations has been a major issue in South Asian countries, particularly India and Pakistan, and although the governments of these respective countries are addressing this issue, many children continue to go unregistered at birth. If this issue persists in the present time, it is likely that a large proportion of older adults who migrated in the 1960's and 1970's were not aware of their exact ages. In addition to this, education systems vary between low, middle, and high-income countries (ADI, 2014). Therefore, even if the UK-based South Asian older adults attained an education in their home country, this is unlikely to be comparable due to system and quality differences (ADI, 2014).

This has implications when analysing neuropsychological test scores and accurately determining the effects of age and education. It is a common practice in clinical and research settings to control for the effects of age and education on test scores to infer an accurate analysis and to develop normative data to compare different populations (Lam et al., 2013; Ostrosky-Solís et al., 2007). Therefore, this implies that age and education related effects on test scores in South Asian older adults cannot always be implied with accuracy.

3.6. Improving research in the South Asian community

Information gathered from research guides the development and conceptualisation of cognitive assessments. However, assessments developed from research which fails to adequately represent the needs of ethnic minorities like the South Asian older adults has increased potential to lack internal and external validity, which in turn can lead to false positive and/or false negative test scores (Waheed et al., 2020). Therefore, current AD diagnostic pathways developed through research which is not ethnically generalisable cannot reasonably be extended across people from different cultures.

It is well established in the literature discussed in this chapter that the South Asian community are often reluctant to seek professional help for AD related symptoms because they tend to hold traditional cultural perceptions (Uppal et al., 2014). However, Cook et al. (2018) found that there has been an increase in the rates of referral to memory clinics in ethnic minority groups which may be explained by the launch of a number of campaigns since 2009 aimed at improving awareness and the early diagnosis of dementia. Although the numbers were not exceptionally high in proportion to the increased prevalence, this does provide some indication that awareness of AD and dementia is increasing in ethnic minorities which is leading to higher rates of service utilisation. This makes it imperative to conduct research exploring the cultural effectiveness of current diagnostic measures to ensure that the increased number of people presenting to use dementia services are not discouraged at this stage by the inadequacy of the current assessment measures. There is little value in only focusing on improving awareness of AD if the current care pathways are not well equipped to manage the assessment of cognitive impairments in minority group with reliability and validity.

As discussed in chapter [2], the initial diagnosis of AD is relied upon test scores on neuropsychological assessments, but these are widely affected by external factors in Caucasian samples (Blakemore et al., 2018). However, there is little to no research on the influence of external factors on cognitive test scores in the UK South Asian older adults (Blakemore et al., 2018). Therefore, this warrants further exploration to bridge the current gap in the literature.

The present thesis aims to contribute novel information towards the limited AD and cognitive research base within the South Asian community in the UK. It aims to achieve this by exploring the effects of external factors present at the time of testing on cognitive test scores. To our knowledge, and at the time of writing, this thesis' research was the first to implement commonly used neuropsychological assessments to determine their adequacy of use in minority South Asian older adults and to assess the influence of external factors on test scores. Exploring and identifying external factors which may bias neuropsychological test scores has important implications for early diagnosis by offering a potential to reduce the barriers which compromise the equality of AD diagnosis. This will be discussed in more detail throughout the next chapters of this thesis.

3.7. The present study population

As previously discussed, the present thesis aims to explore the use of neuropsychological assessments in the ageing South Asian older adults residing in the UK, specifically in Bradford and London. The existing literature defines the ageing South Asians in the UK as originating from Pakistan, India and Bangladesh based on a history of mass migration in the 1960's and 1970's. Following this, the present thesis also aimed to explore its aims and objectives in this population. The South Asian older adults in the UK as well as sharing many similarities, are also a heterogeneous group with diverse cultures and faiths (Ogliari et al., 2020). Therefore, it was particularly important to recruit a heterogeneous group of South Asian older adults to allow for the findings to be generalisable to the wider UK-based South Asian community. However, following the process of recruitment, the present sample is predominately formed by a high percentage of older adults originating from Pakistan and 100% of the sample identified as being Muslim.

The above may be attributed to the fact that the recruitment of participants was predominately conducted in the city of Bradford. Based on ethnicity and religion data outlined in the “Intelligence Bulletin” published by the City of Bradford Metropolitan District Council (2017), Bradford has the largest proportion of people from Pakistan in England. Moreover, Pakistanis constitute the largest ethnic minority group in Bradford accounting for 20.4% of the total population whilst Indians and Bangladeshis only account for two-point six percent and one percent, respectively. With regards to religion, the bulletin outlined that since 2001, Bradford has experienced a decline in the number of people identifying as Christians and a significant increase in the number of individuals identifying as Muslims. Muslims represent the second largest faith group in Bradford with 24.7% of the population identifying as Muslims. On the other hand, the proportion of the population identifying as Hindus, Buddhists and Sikhs was zero-point nine percent, zero-point two percent and one percent, respectively. The report also highlighted that the proportion of Bradford’s population identifying as Muslims was higher compared to national data, and when excluding the inner and outer boroughs of London, Bradford had the second largest number of Muslims in England. Therefore, the large number of Pakistani and Muslim participants in the present thesis appear to be reflective of the demographics of the South Asian population residing in Bradford.

Therefore, although the present sample is formed by individuals from Pakistan, India and Bangladesh, the latter are only represented in a smaller percentage of the overall sample. Consequently, the final findings may only be reflective of the South Asian population in Bradford and may not be generalisable to the wider non-Muslim South Asians across the UK.

3.8. Summary and conclusion

The UK is currently experiencing an increase in the prevalence of AD and other dementias in BAME groups (Ogliari et al., 2020). Specifically, there is an increase in the ageing South Asian population who represent the largest ethnic minority group in the UK (Ogliari et al., 2020; Blakemore et al., 2018). With this increase, the prevalence of AD and dementia is expected to increase in South Asian older adults (Blakemore et al., 2018). However, despite the increased prevalence and risk factors, South Asian older adults face many disparities in accessing diagnostic services (Ogliari et al., 2020). Currently, AD care and diagnosis is often fragmented, uncoordinated, and unresponsive to the needs of the growing South Asian older adults due to cultural differences in the perception of dementia and challenges within the healthcare system's diagnostic pathways (Ogliari et al., 2020; Blakemore et al., 2018).

Nonetheless, recent evidence indicates that the number of people from ethnic minority backgrounds accessing dementia services is increasing (Cook et al., 2018). Therefore, it important to ensure that the current diagnostic measures are adequate to meet the needs of the increasing ethnic minorities seeking professional help. However, there is limited to no research in the UK investigating the use and cultural adequacy of existing neuropsychological assessments which are the first step into the assessment of cognitive impairments associated with AD and other dementias (NICE, 2018).

The next chapter of this thesis will begin by outlining a battery of commonly used neuropsychological assessments and evaluate their use in South Asian older adults.

Chapter 4: Neuropsychological testing: Review and methodology

4.1. Introduction

AD is an age-related neurodegenerative disease and as it progresses, it leads to impairments in memory, attention, language, EF and subsequently affects the ability to engage in ADL (Kriebel-Gasparro, 2020; Delpak and Talebi, 2020). Considering that the primary presenting symptoms of AD are largely cognitive in nature, neuropsychological assessments are the most appropriate and commonly used screening method to infer an AD diagnosis (Roeck et al., 2019; Montenegro and Argyriou, 2017). These assessments involve the use of questions and tasks aimed at measuring an individual's cognitive functioning (Koll et al., 2020). Test scores on neuropsychological assessments allow to identify people exhibiting clinically significant symptoms based on impairment cut-off scores developed through the average scores of a normative reference group (Koll et al., 2020; Chapman et al., 2010). Individuals identified as having a clinically significant cognitive impairment can then be referred to adequate specialist services for a more in-depth evaluation to establish a diagnosis and determine the feasibility of treatment interventions (Koll et al., 2020; Montenegro and Argyriou, 2017; Iracleous et al., 2010).

The use of neuropsychological assessments is widely preferred because these screening instruments are often cheap, quick to administer and offer a non-invasive method to assess and manage individuals presenting with symptoms of cognitive impairment in time constrained primary care settings (Roeck et al., 2019; Razak et al., 2019).

Several general cognitive tests are currently available and obtaining a test score allows to screen for underlying cognitive impairments and to distinguish impairment caused by AD from normal age-related cognitive decline based on normality cut-off scores (Torres et al., 2019; Sheehan, 2012). However, single test scores in isolation are not sufficient to infer a diagnosis (Harvey 2012, NICE, 2018). In clinical settings, health professionals integrate scores obtained on neuropsychological assessments with a wider collection of information obtained through detailed history taking, blood tests and neuroimaging techniques to adequately determine whether further evaluation and pharmacological interventions are required (NICE, 2018; Tosi et al., 2020; Roeck et al., 2019). Test scores are also used in research settings to compare different populations, determine suitability for inclusion in research trials (Karas et al., 2019; Gauthier et al., 2013) and to monitor the progression of symptoms and effectiveness of treatments in clinical or controlled experimental trials (Sheehan, 2012).

At the present time, based on the NICE (2018) guidelines, a comprehensive assessment of cognitive functioning in clinical cases is delivered at a stage when patients first begin to experience tangible signs of cognitive decline which leads patients (or their carers) to seek medical help. However, neuropsychological assessment at this stage is often challenging because as discussed in chapter [2], the underlying pathological changes associated with AD tend to take place many years before the presentation of its symptomatic onset, and such changes are currently irreversible (Slot et al., 2019; Rajan et al., 2015). Therefore, the earlier phases of AD offer a critical opportunity where prognostic and therapeutic interventions may result most effective in delaying, or potentially even preventing further disease progression (Yassine, 2017).

Moreover, a wide range of neuropsychological assessments have been developed in high income Western countries largely implementing Caucasian samples, and these therefore may not necessarily be appropriate for people from diverse backgrounds due to variations in literacy levels and cultural practices (Cid et al., 2019; Blakemore, 2018; Paddick et al., 2017; Mukadam et al., 2011). It is further argued that existing cognitive measures lack rigorous psychometric validation across people from different cultural groups and settings (Magklara et al., 2018; O'Driscoll and Shaikh, 2017; Rosli et al., 2016). If external factors present at the time of testing are not identified through research and controlled for, they can affect the interpretation of test scores (Cid et al., 2019; Walters and Lesk, 2016; Lesk et al., 2009). This has the potential to lead to an erroneous diagnosis in minority groups because they were not the target population when these assessments were initially conceptualised and developed (Blakemore et al., 2018).

Considering that neuropsychological assessments play a central role in the diagnosis of AD; it is remarkable that research exploring their sensitivity and specificity for the identification of cognitive impairment in South Asian older adults is sparse. Given the growing cultural diversity of the UK's ageing population (Blakemore et al., 2018), it is important that neuropsychological assessments account for cultural factors in testing. This is important to ensure that minority groups are not being discriminated by the ethnocentric nature of these assessments and potentially missing out on the benefits of early diagnosis as discussed in chapter [3].

The current chapter will now explore a range of commonly used neuropsychological assessments by providing a detailed description of these assessments and the potential issues or benefits these may have when implemented in minority populations, such as the South Asian older adults.

The assessments which will be discussed in this chapter include the cognitive battery of tests implemented to participants throughout this thesis to explore its aims and objectives.

4.2. Assessments of general cognitive function

Assessments of general cognitive function are usually implemented at the patient's first point of contact (e.g., their GP) and their use is preferred because they are quick and easy to administer with an average administration time of ten to 15 minutes (Age UK, 2021; Iracleous et al., 2010).

Assessments of general cognitive function allow to measure different cognitive domains enabling to determine the presence and severity of global cognitive impairment (Feldman et al., 2008). Scores which are below the normality cut-off points allow the identification of individuals who may require further detailed assessment using alternative screening methods to establish a diagnosis, such as blood test analysis and the use of neuroimaging techniques (NICE, 2018). Assessments of general cognitive function tend to have a lower sensitivity in detecting mild stages of cognitive impairment, and as a result, their efficacy in identifying earlier stages of dementia and AD is low (Revett et al., 2013; Magklara et al., 2019).

Examples of such tests include the MMSE (Folstein et al., 1975), the MoCA (Nasreddine et al., 2005) and the RUDAS (Storey et al., 2004). These are discussed next.

4.2.1. The Mini-mental State Examination Test (MMSE)

The MMSE was developed by Folstein et al. (1975) and it has now been over 40 years since it was first published. It remains one of the most widely administered tests to assess cognitive decline in the ageing population in research and clinical settings (Karas et al., 2019; Piersma et al., 2018). The MMSE was originally distributed free of charge, however it subsequently acquired copyright and clinicians and researcher must now obtain permission and pay a fee to use the test (Feldman et al., 2013).

The MMSE consists of 19 components taxing the domains of orientation, registration, attention and calculation, word recall, naming, repetition, comprehension, writing and construction through an 11-item questionnaire which is completed using a pen and paper (Folstein et al., 1975). It takes approximately ten minutes to complete and a maximum score of 30 points can be obtained. The interpretation of the scores varies, however the most common cut-off score for impairment which was initially suggested by the authors is a score of 24 or less out of 30 (Folstein et al., 1975). However, NICE (2018) proposed alternative cut-off scores for AD as follows: 21-26 (mild AD); ten to 20 (moderate AD); ten to 14 (moderately severe AD) and less than ten (severe AD). It is important to note that this scoring system incorporates a score of ten to 14 both in the moderate AD and moderately severe AD stage. Therefore, it is unclear how a score between ten and 14 would be categorised.

NICE has in the past recommended the use of the MMSE and the above cut-off points to determine eligibility for treatment in cases of AD (Davey and

Jamieson, 2004). However, a judicial review found this practice to be discriminatory based on disability and or/race because many individuals may not speak English as their first language, and as a result may struggle to complete the MMSE. Therefore, compromising their access to treatment interventions. This led NICE to update their guidance to incorporate culture and language as confounding variables to be taken into consideration when assessing cognitive decline and interpreting tests scores (NICE, 2018). Although NICE (2018) updated their guidance by acknowledging the importance of accounting for culture and language in the assessment of AD, they have yet failed to provide any specific guidance with regards to how this can be achieved. Therefore, clinicians may not have any available guidance to assist them in testing ethnic minority patients with varying levels of education and presence of other cultural and linguistic factors. This is relevant for the South Asian older adults residing in the UK, as they tend to have lower levels of education and poor proficiency in spoken English (Blakemore et al., 2018; Hossain et al., 2019).

Further to the above, the MMSE has been identified as lacking reliability in detecting mild cases of cognitive impairment and research has suggested that individuals with early AD or MCI can often score within the cognitively normal range (Van Patten et al., 2019; Breton et al., 2019; Perneczky et al., 2006). This is argued to be partly attributed to the lack of items measuring higher cognitive functions such as EF (Pinto et al., 2019; Trzepacz et al., 2015).

For example, Van Patten et al. (2019) conducted a research study with the aim to explore the psychometric properties of the MMSE and of the Modified Mini-mental State (3MS) in the assessment of MCI. The 3MS incorporates the same items as the MMSE, however it includes an additional four items covering the domains of long-term memory, verbal fluency, abstract thinking, and delayed recall. It also extends the scoring range from 30 points to 100 points. Van Pattern et al. (2019) administered the MMSE and the 3MS to a sample of 87 cognitively-healthy controls and 206 participants with a diagnosis of MCI. Participants were aged 55 years or above, referred from a teaching hospital in America, and 98.4% of the sample was Caucasian. The analysis of their findings revealed that the MMSE correctly identified 11.7% of patients with MCI compared to 65.5% in the case of the 3MS. Based on this, Van Pattern et al. (2019) concluded that the MMSE was not sensitive enough to detect MCI in their sample, and adapted tools like the 3MS are more appropriate to detect MCI and infer an early diagnosis.

This is further supported by an earlier piece of research by Freitas et al. (2013) who conducted a study with the aim to validate the use of the MoCA (discussed in section 4.2.2 of this chapter) as an assessment of AD and MCI. Their sample was formed by two clinical groups with a diagnosis of MCI (n = 90) and AD (n = 90) who were matched to a control group by age, sex, and education. The MMSE and the MoCA were administered to the sample as measures of general cognitive function and comparisons between test scores on both assessments were established. The analysis of the results demonstrated that the MoCA had superior psychometric properties compared to the MMSE, as well as higher diagnostic accuracy to differentiate between MCI and AD. Moreover, it was found that at the optimal cut-off score (below 22 for the MoCA and below 17 for the MMSE), the MoCA demonstrated significantly superior values when compared to the MMSE for sensitivity, specificity, positive and negative predictive values, and classification accuracy. The MoCA was also found to be more sensitive as a measure of cognitive decline overtime.

The limitations of the MMSE in detecting MCI reduce its benefits as a diagnostic tool to infer an early diagnosis. This is of particular concern considering that South Asian older adults are not always able to access dementia services in a timely manner (Blakemore et al., 2018; Mukadam et al., 2011). As such, if cognitive screening measures used to infer a diagnosis are not sensitive to MCI this can further delay diagnosis in minority groups. Alternative assessments like the MoCA are argued to be better equipped to detect cognitive impairment in the early stages compared to the widely used MMSE.

Further to the above, the MMSE has been found to be affected by variables such as age, education, culture, and language whereby older participants and those with fewer years of education and poorer grasp of the English language tend to perform poorly on the MMSE (Pinto et al., 2019; Magklara et al., 2018).

The above is of particular importance as it suggests that using the MMSE may disadvantage some non-Caucasian populations whose first language is not English, or if they are culturally unfamiliar with the context of the items in the assessment.

To address this issue, the NICE guidelines had incorporated a note to suggest that the scores on the MMSE should not be used in isolation to make a clinical decision and cultural and linguistic factors should be taken into consideration (NICE, 2018). However, no guidance was provided with regards to how this should be achieved. Therefore, the practical applicability of this guidance note is debatable.

Further to this, the MMSE was omitted for use in the most recent update of the “Dementia Assessment and Diagnosis” guidelines (2018) due to financial and time related issues in primary care settings. However, its use did not appear to have been entirely ruled out. NICE have a section titled “Clinical Knowledge Summaries” (CKS) which provides practitioners with concise and accessible summaries on evidence based best practice guidelines. This part of NICE’s CKS guidance has a sub-section titled “cognitive assessment tools” and within this sub-section the MMSE was listed as the first recommended assessment of cognitive function despite the guidance no longer recommending its use. This discrepancy between the information on the CKS and the guidance was put to NICE through an email. A response was received from the Communications Executive at NICE who confirmed that the discrepancy was correct, and that the CKS on dementia was not duly updated when the reviewed dementia assessment guidelines were published in 2018. The email also confirmed that they will arrange for the CKS’s to be amended at the earliest possible. It is important to highlight that the email was sent in June 2020, and the subsequent correction was not made until October 2020. With the reviewed CKS, although the recommendation to use the MMSE was omitted, the guidance now recommends the use of the MoCA which is also an assessment of general cognitive function like the MMSE (Nasreddine et al., 2005) and is discussed in more detail in the next section of this chapter.

Moreover, most contemporaneous literature continues to implement the use of the MMSE to identify cognitive decline (e.g., Donaghy et al., 2020; Hildre et al., 2020; Banning et al., 2020; Bradburn et al., 2019; Wang et al., 2019). Therefore, despite the limitations of the MMSE, it remains widely used in research settings.

The limitations of the MMSE restrict its use in multicultural populations which is problematic in the UK which is formed by a large ageing BAME population as illustrated by the latest data from the ONS (ONS, 2011) (see chapter [2-3]). However, there is a large gap in the literature in the UK which investigates the use of neuropsychological assessments like the MMSE in the South Asian population (Blakemore et al., 2018). Consequently, there is a lack of normative data in this group which limits the ability to compare test results with other studies implementing this test which will be discussed in detail in chapter [6]. Therefore, based on the continuing widespread use of the MMSE, particularly in research settings, the current thesis will be exploring its use in an underrepresented population.

Further to the above, it is also important to note that the MMSE was selected as a choice of general cognitive assessment because when this thesis was proposed and the initial literature research was carried out, the NICE (2011) guidelines were widely recommending the use of the MMSE to diagnose dementia and AD despite the literature recommending against its use. In any case, although the current NICE (2018) guidelines no longer recommend its use as a diagnostic tool in primary care settings, they continue to recommend the use of other short assessments of general cognitive function which have been conceptualised following assessments like the MMSE, and therefore this topic remains relevant (Pink et al., 2018). Moreover, as previously discussed, the use of the MMSE only appears to have been ruled out in time constrained primary care settings, and the use of another similar assessment, the MoCA, continues to be recommended in the CKS guidance by NICE (2020).

4.2.2. The Montreal Cognitive Assessment (MoCA)

The MoCA is an assessment of general cognitive function developed as an alternative brief screening test to enable first-line clinicians to detect MCI, which often goes undetected when using the MMSE (Gupta et al., 2019; Freitas et al., 2013; Nasreddine et al., 2005).

The MoCA, like the MMSE, was also developed to be a quick cognitive screening tool which assess the domains of attention, concentration, EF, memory, language, visuo-constructional skills, conceptual thinking, calculation, and orientation (Nasreddine et al., 2005). The total possible score on the MoCA is also 30 points, with higher scores reflecting better performance. Nasreddine et al. (2005) have suggested a normality cut-off score of 26 out of 30 as opposed to 24 out of 30 in the MMSE to allow for cases of MCI to be detected.

The MoCA has also been reported to have good internal consistency and test re-test reliability (Markwick et al., 2012). This is argued to be facilitated by its enhanced and more thorough testing of EF and memory which are domains found to be sensitive to decline in the early stages of cognitive impairment (Aguilar-Navarro et al., 2018; Dubois et al., 2007; Blackwell et al., 2004).

The MoCA has also been found to be an effective screening measure to identify MCI which implies that it has the potential to facilitate early diagnosis (Nasreddine et al., 2005).

Initial validation with this regard was explored by Nasreddine et al. (2005) when they first developed the MoCA. They conducted a research study with the aim to develop the MoCA based on the clinical experience of one of the authors and to assess its ability to detect MCI. Their sample was formed by 94 patients with MCI, 93 patients with mild AD and a cognitively-healthy control group of 90 participants. All participants were tested on the MoCA and the MMSE to establish comparisons between both screening measures. Implementing a normality cut-off score of 26 points out of 30, Nasreddine et al. (2005) found that the MMSE had a sensitivity of 18% in detecting MCI compared to 90% sensitivity observed in the MoCA. In the mild AD group, the MMSE showed a sensitivity of 78% compared to 100% sensitivity in the MoCA. It was concluded that the MoCA was more superior in detecting MCI compared to the MMSE. This has been further validated by Damian et al. (2011); Freitas et al. (2013); Markwick et al. (2012); Bergeron et al. (2017). However, most of the studies discussed have been conducted in Caucasian samples or samples where ethnicity has not been noted.

One of the few studies in the South Asian population was carried out by Gupta et al. (2019) who aimed to evaluate the validity and reliability of the translated Hindi version of the MoCA (H-MoCA) and the ability of the original version to detect MCI in a group of older adults residing in India. The H-MoCA was a translated version of the original MoCA which incorporated three modifications. The title of the first (trail making) and seventh item (subtraction) were simplified, the title and instructions of the fifth item (memory) were also simplified and the word “church” was replaced by “mandir (Hindu temple)” to make it more relevant for the testing population. Gupta et al.’s (2019) sample was formed by 30 adults aged 55 years and over. As part of the inclusion criteria, participants were required to speak and understand English and Hindi to complete both, the H-MoCA and the original English version of the MoCA. The results revealed that the H-MoCA had good internal consistency, high test re-test reliability and it was also found to be a valid and reliable tool to detect MCI in a sample of Indian older adults. However, although the findings are positive, some caution is required when interpreting these. The results do not necessarily imply that the translated H-MoCA is culturally more appropriate to detect MCI. This is argued because the study only catered for those individuals who were able to speak and understand English, however as discussed in chapter [3], a large proportion of South Asian older adults in the UK have a poor grasp of the English language, and thereby these findings are not generalisable to the wider South Asian older adults residing in the UK. Also, the authors do not specify how language proficiency was measured, therefore it is also not clear whether all participants spoke English to the same level. Moreover, the Hindi translated version of the MoCA is not a direct translation as items and instructions were modified, which limits the cross-comparability between the original MoCA and the adapted H-MoCA.

Further to the above, the scoring of the MoCA allows to award two additional points to participants with 12 or less years in education (Malek-Ahmadi et al., 2015). However, the efficacy of this is questionable in some groups like the South Asian older adults. As discussed in chapter [3], the level and quality of education varies between low to high income countries (ADI, 2014), therefore it is unlikely that the education adjusted points developed in Caucasian samples will be comparable and applicable to most of the South Asian older adults.

Moreover, Gagnon et al. (2013) conducted a piece of research to investigate the impact of the suggested education correction on the sensitivity and specificity of the MoCA. Gagnon et al. (2013) recruited their sample from geriatric clinical and research programmes in Ontario. Their sample was formed by 25 patients with dementia, 39 patients with aMCI and 30 cognitively-healthy controls who completed the MoCA and underwent a psychiatric and neurologic evaluation to rule out other cognitive impairments. Moreover, all participants were proficient in English which they used for work purposes or for social interactions. The results indicated that the MoCA had high sensitivity and specificity in identifying MCI when scores were unadjusted for education. However, when scores were adjusted for education, this reduced the ability of the MoCA to detect MCI cases. Therefore, Gagnon et al. (2013) concluded that the adjustment of scores based on education leads to detrimental effects on the sensitivity of the MoCA. With loss of sensitivity this also increases the potential for false negatives in samples where education related adjustments are necessary, such as in the South Asian older adults in the UK.

The MoCA has also not been widely studied in minority groups and a wide range of studies have been limited to predominantly Caucasian samples (Milani et al., 2018). Research studies which have incorporated minority samples have concluded that the initially established cut-off score of 26 is relatively high and has a likelihood of labelling cognitively normal minority individuals as being cognitively impaired due to factors such as lower education levels and poor language comprehension (Sink et al., 2015; Rossetti et al., 2017). For example, Sink et al (2015) found that when using a cut-off score of 26 points in an African-American cohort, 90% of cognitively-healthy participants were positively screened for cognitive impairment whilst Rossetti et al. (2017) also found that 80% of their sample of cognitively-healthy African-Americans fell below the threshold of 26 points. This suggests that the MoCA may require further re-evaluation with regards to its applicability and performance in less educated minority populations.

4.2.3. The Rowland Universal Dementia Assessment Scale (RUDAS)

The two most widely used assessments of general cognitive function, the MMSE and the MoCA, have not been widely validated in minority populations and they can be biased by education and culture (Custodio et al., 2019). Considering this, the RUDAS was conceptualised and developed for use in ethnically diverse minority populations (Storey et al., 2004).

The RUDAS consists of a six-item questionnaire developed with a multicultural community in Australia, and unlike the MMSE, it does not have copyright issues attached (Storey et al., 2004). Like the MMSE and the MoCA, the RUDAS is also scored out of 30 points and scores of 22 points or less are considered to imply probable cognitive impairment and a call for further evaluation (Storey et al., 2004). This represents a lower cut-off score than the MMSE and the MoCA. The administration time of the test is approximately ten minutes, and the items address a range of cognitive domains which include memory, language, praxis, and visuo-construction skills (Storey et al., 2004). Thus, the RUDAS, like the MoCA is also effective in assessing frontal lobe activity (EF) which is not accounted for by the MMSE (Custodio et al., 2019).

Scores on the RUDAS also do not appear to be biased by language (Limpawattana et al., 2012). The RUDAS can be directly translated into other languages (for example Nepali, Spanish, Turkish) without having to change the format or structure of any of the items (Nielsen et al., 2012; Storey et al., 2004). This implies that when translated, the RUDAS is more reliable compared to the MMSE and the MoCA as the items do not lose contextual meaning when adapted for non-English speakers (Nielsen et al., 2012; Storey et al., 2004). Moreover, Nielsen et al. (2013) carried out a research study which aimed to compare the RUDAS with the MMSE as a screening tool to detect early signs of dementia in a culturally diverse sample. The research was conducted in Denmark in a sample of 137 patients (34 with an immigrant background) from a Danish memory clinic. Participants from an immigrant background originated from Middle Eastern countries, Asia, America, and Africa. All participants were tested using the MMSE and the RUDAS. Nielsen et al. (2013) found that the diagnostic accuracy of the RUDAS was similar to the MMSE. The best cut-off scores for sensitivity, specificity and accuracy were of 24 out of 30 on the RUDAS and 25 out of 30 on the MMSE. More importantly, it was also found that the RUDAS was not affected by immigration related factors, such as culture and language. Therefore, Nielsen et al. (2013) concluded that the RUDAS had high specificity in detecting cognitive decline and it was less affected by culture, making it more valuable for use in multicultural older adults. Similar findings have also been implied by Chayaa et al. (2016) and Wong et al. (2012). More recently, a review of 26 studies implementing the RUDAS also found that this assessment has good diagnostic accuracy for identifying dementia, has limited the bias in people with lower levels of education and it has limited the need for cultural and linguistic adaptions (Nielsen et al., 2020).

However, one of the apparent issues with the RUDAS is that it fails to measure for time orientation (O'Keeffe et al., 2011). This is relevant as it has been found that an inability to correctly identify the year, month or time is a sufficient and sensitive indicator of the early stages of AD which should encourage further and more detailed cognitive screening (O'Keeffe et al., 2011). Therefore, this questions the ability of the RUDAS to accurately detect MCI.

Also, although the RUDAS is generally more appropriate compared to the MMSE, it has been found to be affected by education (Basic et al., 2009; Storey et al., 2004; Nielsen et al., 2012). For example, Nielsen et al. (2012) carried out a research study with the aim to compare performance on the RUDAS and the MMSE in a sample of 76 cognitively-healthy adults aged 50 years and over. The sample was formed by Turkish immigrants residing in Denmark. The results of the data gathered revealed that participants, on average, scored higher on the RUDAS when compared to the MMSE. However, both the MMSE and the RUDAS, were significantly affected by education, whereby fewer years in education led to a significant decline in test scores.

This is consistent with research by Iype et al. (2006) who administered the RUDAS and the MMSE to a sample of 116 Indian Malayalam speaking participants. Their research was conducted in Kerala (India) and the sample was formed by 58 participants with a dementia diagnosis based on the DSM-IV criteria. The sensitivity and specificity of both assessments was explored and the correlation between test scores and education was also assessed. It was found that the RUDAS had similar levels of sensitivity as the MMSE, but better specificity. However, the RUDAS was found to have an education bias, whereby fewer years in education correlated with poorer test scores.

Considering that the RUDAS is also affected by education, further validation, and potential adaptions are required for its implementation in older adults from minority backgrounds residing in the UK.

The review of the literature as part of this thesis revealed that the RUDAS, to the best of our knowledge, has not been tested in a population of South Asian older adults residing in the UK. Therefore, this presents with a potential to further explore its use in an underrepresented BAME group which has not been the focus of previous research in the UK.

4.2.4. Summary: Assessments of general cognitive function

Brief assessments of general cognitive function are a preferred first-line method to assess cognition as they offer a quick and non-invasive method to determine an individual’s overall cognitive functioning and to monitor the progression of future cognitive decline (Roeck et al., 2019; Montenegro and Argyriou, 2017).

The MMSE is one of the first and most used cognitive screening measures, however, it has poor sensitivity in detecting early stages of AD and MCI particularly in older and less educated individuals (Van Patten et al., 2019; Casey et al., 2019; Perneczky et al., 2006). The MoCA was developed with the aim to improve the diagnosis of AD in MCI stages (Nasreddine et al., 2005). It has been found to be more superior compared to the MMSE in identifying MCI, however it is also affected by education levels (Larouche et al., 2016; Gagnon et al., 2013).

The RUDAS was developed as an alternative assessment which claimed to be free from the educational and culture bias associated with the MMSE (Storey et al., 2004). It has been found to be more culturally appropriate compared to the MMSE and the MoCA (Nielsen et al., 2012); however, test scores on the RUDAS are also affected by education levels (Nielsen et al., 2012; Iype et al., 2006). This questions the widespread use of assessments like the MMSE, MoCA and the RUDAS in less educated samples from across different cultural backgrounds.

4.3. Brief domain-specific neuropsychological assessments

The remainder of this chapter will now outline and discuss a battery of domain specific neuropsychological assessments administered as a part of the experiments in this thesis. The use of these domain specific assessments is important to explore in the current sample as some of these shorter cognitive assessments place lower reliance on language and education, and they may prove to be more suitable to be implemented in less educated populations, like the UK based South Asian older adults. Their use is currently not reported in this group of people.

4.3.1. Word Recall

Word recall tests involve the assessment of short-term memory by requiring individuals to recall a list of words presented to them orally immediately after the list has been presented (immediate recall), or after a predetermined time interval (delayed recall (DR)) (Cerami et al., 2017; Cherry et al., 2002). There are a wide range of measures available in clinical and research settings to measure memory recall (Cerami et al., 2017). These assessments are often formed by a list of ten to 16 words and include standardised assessments like the California Verbal Learning Test (CVLT) (Delis et al., 1987) and the Hopkins Verbal Learning Test (HVLT) (Brandt and Benedict, 2001) which are often used to diagnose and monitor MCI and its progression to AD (Cerami et al., 2017). Word list tasks are also part of some assessments of general cognitive function such as the MMSE, MoCA and the RUDAS. The word recall element in such tests tends to be shorter (three to five-word), and therefore makes them quicker to administer (Cerami et al., 2017).

Word recall assessments are particularly important as the presence of an early and significant memory deficit has been proposed as the core criterion to support a diagnosis of AD (Vallet et al., 2016; Baldwin and Farias, 2009; Dubois et al., 2007). Moreover, impaired memory performance has been identified as one of the best hallmarks of future progression to AD (Cerami et al., 2017; Sarazin et al., 2007). For example, one of the early pathological changes observed in AD patients involves the entorhinal cortex and the hippocampal structures disconnecting the Papez Circuit which plays a vital role in the formation of episodic memory (Cerami et al., 2017). Subsequently, this disconnection has been found to negatively impact the ability to consolidate new information, resulting in impaired performance on delayed recall tests (Squire et al., 2004; Cerami et al., 2017).

Moreover, assessments of memory are a vital aspect in the early diagnosis of AD (Cerami et al. 2017). This is argued as the presence of impaired memory on objective neuropsychological assessments is required to meet the definition of MCI (Cerami et al. 2017). Test scores on cognitive assessments of DR are also considered as one of the most reliable methods to predict the conversion from MCI to AD (Cerami et al. 2017; Quaranta et al., 2018; Gainotti et al., 2014; Sarazin et al., 2007). Evidence also indicates that $A\beta_{1-42}$, the most toxic form of the amyloid peptide (see chapter [2]), triggers AD pathology by accelerating the rate of memory decline (Shallie et al., 2020; Sasmita et al., 2018; Ferrerira et al., 2015).

The above is also in agreement with previous studies, such as those by Teng et al., (1989) and Cherry et al. (2002) who found that patients with AD found it difficult to complete assessments of word recall when compared to a cognitively-healthy control group. Cherry et al. (2002) administered a word recall test to 35 patients who met the clinical criteria of probable AD and 38 cognitively-healthy older adults using a ten-item word recall task. The findings demonstrated that participants with probable AD recalled significantly fewer words compared to the healthy sample. Similar findings were observed by Chaves and Camozzato's (2007) who investigated word recall in 44 participants diagnosed with mild AD following the criteria set by the DSM IV and two cognitively-healthy control groups formed by 341 participants. Participants were assessed on the MMSE and a word recall list formed by ten words. The results indicated that patients with AD had a word span of three out of ten words. On the other hand, cognitively-healthy young adults on average scored six out of ten and older cognitively-healthy participants scored five point five out of ten. These differences were statistically significant, therefore implying a significant memory impairment in patients with AD (Chaves and Camozzato, 2007).

Clinical advances in the diagnosis of AD have also found that deficits observed in assessments of DR are associated with hippocampal abnormalities observed through PET and MRI scans, presence of β amyloid plaques and increased levels of the tau protein in CSF which predict the conversion from MCI to AD with high diagnostic accuracy (Dubois et al., 2014; Sperling et al., 2011; Hort et al., 2010).

Therefore, based on the evidence suggesting that memory impairments are a salient aspect in the identification and progression from MCI to AD, it is imperative for the battery of assessments being used in this thesis to incorporate an assessment of delayed recall. Standard assessments such as the CVLT or the HVLT were not implemented in this thesis due to financial constraints. A word recall test formed by 15 words was created using the MRC psycholinguistics database (https://websites.psychology.uwa.edu.au/school/MRCDatabase/uwa_mrc.ht

m) by controlling for word length, familiarity and frequency to ensure standardisation in all of the words generated. This method enabled the researcher to generate a list of words which was linguistically and culturally relevant to the South Asian sample by ensuring that the words generated had a direct translation in Urdu.

4.3.2. Digit Span

Tests of digit span assess attention and working memory which is defined as the temporary retention and manipulation of information (Aumont et al., 2019) and it is a component of the Wechsler Adult Intelligence Scale Revised (WAIS-R) (Wechsler, 1981).

Digit span tasks involve the presentation of numerical sequences which vary in length and the task is commonly comprised of two parts, namely digit span forward (DSF) and digit span backward (DSB) (Wahlstrom et al., 2016). In DSF, a series of numbers are presented to participants with a starting sequence length of three numbers which increases to a maximum sequence of nine numbers, and participants are required to repeat back the sequences in the same order (e.g., 123 will be repeated as 123). The DSB stage of the test requires for the sequence of numbers to be repeated in reverse order (e.g., 123 will be repeated as 321). The string length of the numerical sequences is increased with each trial and the test is terminated when the individual is unable to repeat two sets of a certain length in the same order. The scores on the DSF and DSB consist of the number of digits in the last correctly recalled set.

Although both the DSF and DSB are assessments of working memory, DSF is better considered as a measure of attention whilst DSB is argued to be a qualitatively different task which relies more on working memory (Holdnack, 2019). Moreover, AD patients often demonstrate a normal DSF span despite suffering from severe memory impairments (Cherry et al., 2002; Reynolds, 1997). In contrast, performance on DSB is affected by procedural learning through exposure to DSF which helps participants to gain an insight into the nature of the task, and thereby its processing is of a more complex nature when compared to DSF (Holdnack, 2019).

It is also apparent that DSF shares similarities with assessments of immediate word recall as in both assessments, participants are asked to recall and repeat a series of digits or words and the scoring system determines how many words or digits were correctly recalled following a single presentation (Cherry et al., 2002).

Cherry et al (2002) carried out a series of experiments implementing word and digit recall tasks and concluded that AD patients performed better on digit recall compared to word recall. They argued that this was potentially explained by the fact that digits are shorter in length (one or two syllables) and thereby easier to organise and remember when compared to words. In contrast, words can be much larger in length, have emotional valence, and vary in familiarity level. Consequently, these different attributes potentially make the processing of words much more complex, particularly for people suffering from AD due to the higher demands on brain processes (Cherry et al., 2002). Cherry et al. (2002) further found that patients with AD performed significantly worse on both, the DSF and DSB compared to the control group, with performance being better on DSF which is likely to be explained due to the lower demands of DSF on long term stores which are argued to be less deficient in AD patients (Cherry et al., 2002).

Moreover, Lortie et al. (2012) explored the use of a short cognitive battery incorporating an assessment of digit span, clock drawing task and the Dementia Rating Scale with the aim to assess their ability in detecting MCI in a sample of ten participants with an established diagnosis of MCI. The research findings indicated that the digit span test was a good predictor of MCI. The same was not found with regards to the other two assessments implemented. This is consistent with research by Kurt et al. (2011) who found that impaired digit span scores in older people are predictive of the conversion from subjective memory complaints to MCI over an average follow-up period of six point six years.

Currently there is a lack of studies which have investigated the use of this test in a minority population, like the South Asian older adults in the UK. Therefore, it will be interesting and novel to implement and explore the adequacy of the digit span test in this cohort.

4.3.3. Letter (LCS) and Pattern Comparison Speed (PCS)

The LCS and PCS are assessments of processing speed (Salthouse and Babcock, 1991). LCS requires participants to state whether two strings of letters are the same or different whilst the PCS uses patterns. In LCS, participants are presented with two strings of three, six or nine letters and are asked to state whether they are the same or different. In PCS, participants are presented with two geometric shapes (patterns) and asked to state whether these are the same or different. This is a timed task whereby participants are given a maximum of 20 seconds to compare as many pairs as possible. The total number of correctly identified responses within the given time limit is scored.

The PCS and LCS are important assessments to incorporate in a battery of neuropsychological assessments as processing speed is argued to slow down with normal ageing (McCabe and Hartman, 2008); however, a disproportionate rate of decline has been observed in patients with MCI and AD (Lu et al.,2017; Haworth et al., 2016; Baek et al., 2016). Despite this, assessments of general cognitive function, like the MMSE do not assess processing speed (Hoops, 2009).

Baek et al. (2016) conducted a piece of research with the aim to validate an adapted MMSE which incorporated an additional item assessing processing speed in a sample of Korean participants. The results revealed that the adapted MMSE had a higher sensitivity and specificity in discriminating between participants with normal cognitive function from patients with MCI and AD (Baek et al., 2016). Therefore, further supporting the use of assessments of processing speed, like the PCS and LCS, to detect early cognitive impairment.

Lusting et al. (2006) investigated the use of the paper and pen version of Salthouse and Babcock's (1991) PCS and LCS to explore processing speed in cognitively-healthy younger and older adults. Their sample was formed by 312 young adults and 239 older adults. They found that, as expected, older adults performed poorer both, on the PCS and LCS. They argued that this may be explained by the older adults' inability to ignore distracting stimuli caused by the paper versions of the PCS and LCS whereby a large number of letters and patterns are presented on a single piece of paper slowing down reaction times. Lusting et al. (2006) also reported higher error rates in both groups as the string length increased, with performance on the PCS being significantly worse in older adults. It is expected that these results would be even more heightened in people with an AD diagnosis, however the current research literature on this area using the PCS and LCS is very limited.

To the best of our knowledge, there is no evidence in the current literature that the PCS or LCS have been implemented and explored in South Asian older adults, or other BAME groups in the UK. However, based on the above-described characteristics of the PCS and LCS, this appears to be fairly free from a cultural bias and as such it has potential for further exploration in minority samples, particularly considering the importance of processing speed in AD and MCI.

4.3.4. Symbol Digit Modalities Task (SDMT)

The SDMT (Smith, 1968) is a symbol substitution task which measures processing speed and EF (Gonzalez et al., 2007). It is implemented as a paper and pen copy and requires participants to substitute geometric symbols for numbers from a key (Pascoe et al., 2018). After a practice session, participants are given 90 seconds to complete as many grids as possible by writing the correct number underneath each corresponding symbol. The scoring is inferred from the total number of correctly identified numbers matched to the corresponding symbols. A higher score implies better cognitive functioning.

The SDMT has been found to be minimally biased by education and language making it suitable to be implemented with minority populations with lower levels of education and fluency in the English language (Lopez et al., 2008; Fleisher et al., 2007).

Further to the above, Lopez et al. (2008) conducted a research study in the USA with a Hispanic sample of 106 patients diagnosed with AD in accordance with the DSM IV criteria. The sample was aged 50 years or over and had an average of ten point eight years in education. Lopez et al. (2008) aimed to assess the effectiveness of AD treatment using Donepezil in a 12-week trial. Treatment effectiveness was assessed using baseline and treatment completion test scores on the MMSE and SDMT. The analysis of the data obtained revealed that tests scores on both, the MMSE and SDMT, showed significant improvement following a 12-week treatment programme. This indicated that the SDMT may also serve as a useful tool to monitor cognitive functioning overtime.

Fleisher et al. (2007) also conducted a research study in a sample of 539 patients with aMCI with the aim to explore the best predictive measures for the conversion from MCI to AD. Amongst the large battery of assessments implemented to test this aim, participants were assessed on the MMSE, SDMT, DSB and delayed recall. The research findings indicated that test scores on SDMT were amongst the three assessment scores which best predicted the progression from aMCI to AD over a period of 36 months. Therefore, providing some support for its use as a tool to infer an early diagnosis of AD.

However, as with the assessments discussed earlier, the SDMT has not been widely used in MCI and AD research or studied in South Asian older adults. In any case, the limited evidence discussed above with regards to the characteristics of the SDMT appears to suggest that it has minimal linguistic, cultural, and educational bias. Therefore, it may have the potential to be implemented in minority populations. This is argued because like the PCS and LCS, although the SDMT involves the use of numbers and symbols, no numerical knowledge or mathematical skills are required to complete the assessment. It is, however, important to acknowledge that there is potential for some educational bias. Although an understanding of numbers and symbols is not necessary to complete the test, a lack of familiarity with these may potentially influence performance in a group of participants who have lower levels of education. However, this has not previously been explored and therefore, it will be valuable to evaluate the use of this assessment in a sample of South Asian older adults.

4.3.5. Trail Making Black and White Part A&B (TMT A& B)

The Trail Making Black and White A&B (TMT A&B) (Kim et al., 2014) test is an assessment measuring processing speed and EF (Osterman et al., 2010) and it is a cultural adaption of the original Trail Making Test A & B (Reitan and Davison, 1974). It is scored as the time taken to complete both part A and B.

The original trail making test has been implemented in the current AD literature to identity MCI and mild stages of dementia (Pena-Casanova et al., 2014). Moreover, it is commonly administered in English speaking countries with high prevalence of education, however its use is limited in cultural contexts due to the use of the English alphabet in part B of the test (Zhao et al., 2013).

The original trail making test consists of components A and B, both of which assess different cognitive domains. Part A is a primary measure of processing speed and part B also taxes EF (O'Rourke et al., 2011). Part A requires an individual to connect randomly distributed numbers inside a circle in ascending order. Part B consists of both numbers and alphabetical letters, and participants are required to alternate between a number and a letter and connect these in ascending order.

With regards to the original version, Ewers et al. (2012) explored its use in a sample of 81 patients diagnosed with MCI and 101 cognitively-healthy controls. Their research findings indicated that part B of the assessment was a single best predictor of subsequent conversion from MCI to AD which was also found by Samtani et al. (2012).

Brown et al. (2011) also found that part A of the original trail making test, i.e., the processing speed component, was significantly associated with more severe cognitive impairment in a sample of 394 aMCI patients who were compared to a cognitively-healthy control group of 229 participants and 193 patients with mild AD. Chapman et al. (2011) further argued that the EF component of part B may serve as a potential tool to identify an early conversion from MCI to AD. Therefore, evidence indicates that the trail making test has useful psychometric properties to assist in the early identification of cognitive impairment (Brown et al., 2011).

Nonetheless, despite the above benefits of the original trail making test, it has been found to be affected by age and education levels, whereby with increasing age and fewer years in education participants take longer to complete the assessment and this challenge is more notable on part B (Hashimoto et al., 2006). It is fair to argue that this is potentially caused due to the verbal/linguistic component in the alphabetical aspect of the test (part B) which places less educated, illiterate, and non-English speakers at a disadvantage due to the lack of familiarity with the items within the assessment (Kim et al., 2014; Hashimoto et al., 2006).

Due to the above limitations, an alternative trail making test known as the Trial Making black and white A&B (TMT A&B) was developed by Kim et al. (2014) and tested in a lower educated Korean sample. The TMT A&B is psychometrically similar to the original version. Part A remains the same as in the original version. The main difference is presented in the conception of part B whereby the English alphabet has been removed and replaced with black and white circles. Part B presents a sequence of two sets of numbers ranging from 1-25 in each colour inside a circle (black and white) and participants are required to connect the numbers in ascending order by alternating between black and white circles.

Kim et al. (2014) explored the use of the new TMT A&B in a sample of 138 Korean older adults (31 = cognitively-healthy control; 55 = MCI; 52 = AD). Participants were tested on the new TMT A&B as well as on the original version. The findings revealed that the new TMT A&B was as reliable and effective as the original in assessing cognitive impairment. Also, it was found that participants were more likely to not complete the original TMT A&B when compared with the adapted version. Participants with lower education levels performed significantly better on the adapted version of the assessment when compared to the original. Therefore, the authors concluded that the new adaption of the trail making test is more appropriate for populations with lower levels of education and lack of familiarity with the English language which are characteristics similar to the target population in this thesis (South Asian older adults) (see chapter [3]).

This is a relatively new assessment which has not be widely validated, however some studies have suggested that the adaption of the TMT is more reliable and has reduced the education bias present in the original version (Kim et al., 2014; Han et al., 2019). Moreover, the attempt to make the assessment more relevant to those who lack familiarity with the English language implies that its implementation may be more advantageous, compared to the original assessment, in culturally diverse populations. This is because despite the adaption, it has retained many of its psychometric properties (Han et al., 2019; Kim et al., 2014).

Therefore, the adapted TMT A&B was implemented in this thesis as opposed to the original TMT A&B. Permission was obtained directly from the authors to implement this assessment. Further to this, like the other assessments discussed earlier, there is currently very limited (if not at all) data on the use of the original or the adapted TMT A&B in South Asian older adults which has further guided the use of this measure in the present thesis.

4.3.6. Dual Task

Dual task (DT) is a paper and pen assessment which primarily measures EF and working memory (Baddeley et al., 1991). It consists of an A4 paper representing a string of connected empty boxes. The first part of the assessment involves participants being timed for one minute during which they are required to place a cross in each box following the direction of the strings (Baddeley et al., 1997). During the second part, participants are required to repeat the first task, however they are required to simultaneously remember and repeat the strings of numbers based on their digit span score whilst also placing a cross in each box, hence completing two tasks at once. In both parts the participant is timed for one minute. The scoring is based on the difference between the number of boxes crossed between the first and the second time (DT T1-T2) and the dual task ratio (DTR) which is calculated as the ratio of boxes crossed to the number of strings remembered.

Assessments involving DT are of value when investigating cognitive deficits as they allow the assessment of both attention and EF, which have been reported to be amongst two of the first non-memory related impairments to appear in individuals diagnosed with AD (Festa et al., 2010; Amieva et al., 2004). Research investigating the involvement of attention deficits in AD using DT has consistently shown that AD patients perform significantly worse on assessments requiring the engagement in simultaneous tasks relative to healthy controls (Ramsden et al., 2008; Sebastian et al., 2006; Logie et al., 2004; Baddeley et al., 2001). When considering these findings, it has been argued that dual task deficits in AD may be mediated by an inability to coordinate processing across attentional networks which dual-task assessments allow to identify (Baddeley et al., 2001; Logie et al., 2004).

There is a consensus that when two tasks are being performed concurrently, there will be a decline in performance due to the increased cognitive demands of dividing attention between two tasks (Whitson et al., 2018; Nebes et al., 2001). It has been claimed that this decline in cognitive performance is more pronounced in patients with AD when compared to cognitively-healthy controls (Della Sala and Logie, 2001, Baddeley et al., 1986, 1991).

However, there are some conflicting findings with regards to the use of DT assessments in the early detection of AD. For example, Lonie et al. (2009) conducted a piece of research with the aim to explore whether DT assessments are a sensitive measure of AD, particularly in the early phases of the disease. The paper and pen version of the DT and the original TMT A&B were implemented in a sample of 33 patients diagnosed with aMCI; ten patients diagnosed with early-stage AD; 21 cognitively-healthy controls and 17 controls with depressive symptoms. All participants were matched for age and intellectual abilities. From the analysis of the data gathered, Lonie et al. (2009) found that AD patients were particularly impaired on part B of the TMT, however no differences in test scores on DT were observed in any of the groups being assessed. Based on this, the authors concluded that DT assessments are not sensitive enough to detect early cognitive decline. However, some caution is required when interpreting these discrepancies as different methodologies are often used in the implementation of DT tasks. For example, previous research with regards to the use of DT by Baddeley et al. (2001) used a total test duration of 120 seconds and found the assessment to be a useful indicator of AD, whilst Lonie et al. (2009) implemented a shorter time of 90 seconds. Therefore, direct comparison between different data sets implementing DT assessments cannot be inferred due to lack of standardisation leading to methodological differences.

Further to the above, older adults and individuals with age-related neurodegenerative conditions like AD are more affected by deficits in DT performance due to the ageing process leading to degeneration of neural circuits (Kahya et al., 2019; Kelly et al., 2012). This subsequently leads to not only cognitive performance deficits, but also motor deficits which are much more studied in the current literature. Such studies have suggested that reduced ability to allocate attentional resources to two simultaneous tasks results in increased risk of falls and loss of independence in older adults with age related conditions such as AD (Kahya et al., 2019; Wajda et al., 2017; Festa et al., 2010). This, therefore, may also contribute towards reduced ability to engage in ADL.

Therefore, there is some literature supporting a decline in DT performance in people with neurodegenerative conditions. However, this is not widely studied with regards to diagnosing AD and particularly, there is very limited information with regards to performance on DT in ethnic minority samples. Further to this, Della Stella (2010) also reports that there is a lack of published normative data for DT which may be due to the limited research using this assessment in minority samples.

4.4. Chapter Summary

Neuropsychological testing remains critical in the diagnosis of cognitive impairments characteristic of conditions like AD and other dementias (Roeck et al., 2019; Montenegro and Argyriou, 2017). It provides an objective and structured approach to measure complex cognitive functions which allows to differentiate between normal age-related cognitive decline from clinically significant decline (Roeck et al., 2019; Montenegro and Argyriou, 2017). Subsequently, this can guide diagnosis and treatment planning. Neuropsychological testing using brief cognitive assessments is also recommended by NICE (2018) to identify cognitive decline in primary care settings.

Assessments of general cognitive function are often used in research and clinical settings as these allow to tax a range of different cognitive domains providing an insight into global cognitive functioning (Feldman et al., 2008). Examples includes assessments like the MMSE (Folstein et al., 1975), the MoCA (Nasreddine et al., 2005) and the RUDAS (Storey et al., 2004) which are widely used in research and clinical settings across the globe to detect AD and MCI. These assessments are widely influenced by external factors such as age, education, culture, and language (Cid et al., 2019). This has implications for the interpretation of test scores, and the education and culture related bias limits their use in multicultural populations due to increased risk of false positives.

The present chapter has also considered the properties of a battery of short domain specific assessments of cognitive function which place lower reliance on the understanding of the English language and education related knowledge to complete. This battery includes an assessment of DR, PCS, LCS, DSF, DSB, SDMT, TMT A&B and DT. This battery of cognitive assessments taxes multiple cognitive domains like the assessments of general cognitive function, however it is proposed that it will allow to measure each domain in more detail and with reduced bias from factors, such as education and language making it potentially more appropriate for populations like the South Asian older adults. Also, the evidence discussed indicates that these assessments target domains known to be affected early in the development of AD. To our knowledge and at the time of writing, there were no studies in the current literature investigating the adequacy of these assessments to measure cognitive performance in UK-based South Asian older adults.

The next chapter of this thesis will begin by investigating the influence of the testing language on test scores on two assessments of general cognitive function, the MMSE and the RUDAS. Following this, a range of other factors and their influence on test scores will be investigated by implementing the short domain-specific battery of cognitive assessments discussed in this chapter.

Table one below summarises the assessments mentioned in this chapter and the main cognitive domains they assess.

Table .1. Summary of neuropsychological tests by main cognitive domains assessed

Cognitive Domain	**Assessment**
General Cognitive Function	MMSE
	MoCA
	RUDAS
Short-term Memory	DR
Working Memory	DSF
	DSB
	DT
Processing Speed	PCS
	LCS
	TMT
	SDMT

Executive Function	SDMT
	TMT B
	DT
	RUDAS

Chapter 5: The influence of the testing language on cognitive performance

5.1. Introduction

Performance on cognitive assessments can often be affected by external factors, such as education, language, and culture (Cid et al., 2019; Paddick et al., 2017). The influence of these external factors is likely to be more heightened in minority populations, like South Asian older adults, as they were not the target population when the assessments were initially conceptualised and developed (Blakemore et al., 2018). This chapter will explore the language that the tests are administered in as a factor which may affect performance.

South Asian older adults who migrated to the UK tend to have poorer proficiency in the English language and a significant number have lower levels of education (see chapter [3]) (Blakemore et al., 2018). This may lead to overestimations regarding the degree of cognitive impairment due to lower scores on conventional neuropsychological tests routinely used at primary care settings (Goudsmit et al., 2018).

Despite the limitations of existing cognitive assessments in minority groups, these have not been widely validated in South Asian older adults (Blakemore et al., 2018) or other similar BAME groups (Nielsen et al., 2013).

This chapter aims to address this issue by investigating the use of the MMSE and the RUDAS in a sample of South Asian older adults and explore whether the language in which the assessments are administered in (English or Urdu), has any influence on test scores.

5.1.1. Suitability of the MMSE in South Asian older

The MMSE is a widely used assessment of general cognitive function in research and clinical settings (see chapter [4]) (Pinto et al., 2019). However, a review by Blakemore et al. (2018), which was discussed in detail in chapter

[3], only identified two studies which investigated the validity and reliability of the MMSE in South Asian older adults residing in the UK.

One of the studies reported was conducted by Lindesay et al. (1997) who piloted the use of the Gujrati version of the MMSE. Lindesay et al.'s (1997) sample was formed by 149 UK based Gujratis (Indians) and 148 White British participants. Cognitive performance was assessed on the original English version or the Gujrati version of the MMSE. Data analysis revealed that test scores on the MMSE were significantly lower in the Gujarati sample. It was found that the Gujarati group had an independent effect of cultural bias in three orientation items (day, year, and street) because when these items were removed from the analysis, there were no significant differences between the two groups in mean test scores after adjusting for age and education.

Rait et al. (2000) also implemented the MMSE in a UK based South Asian sample of Pakistanis and Gujratis of Indian origin aged 60 years and above. The MMSE was translated into participants' native languages using professional translators. The research findings suggested that the MMSE was only appropriate to be implemented with this group of participants when adjusted and lowered cut-off scores were used, particularly when aiming to identify MCI.

More recent research by Raina et al. (2015) investigated the use of the MMSE in a sample of 2000 participants from the Northwest of India aged 60 years and over. Their results revealed that participants found it particularly challenging to correctly draw a pentagon (one of the testing items within the MMSE), because of their lower literacy levels (Raina et al., 2015). Ardila et al. (2010) conducted an extensive review investigating the impact of illiteracy on cognitive performance and found that even scores of 14/30 on the MMSE, which is ten points under the normal cut-off score for impairment, can still be considered as normal in illiterate and culturally different populations.

As well as limited research within the UK, there is also very limited data on the validation of assessments like the MMSE within South Asian countries

(Blakemore et al., 2018), and most of the available data largely originates from India as seen from the evidence discussed above.

Awan et al. (2015) conducted the first, and currently the only (to our knowledge) validation study of the MMSE in Pakistan and noted that this assessment is often used by neurologists in the country.

Awan et al. (2015) translated the MMSE into Urdu with the aim to validate its use in a native Pakistani population. During the process of translation, the reading and writing items were modified due to unsuitability for illiterate participants. Awan et al.'s (2015) sample was formed by 400 participants of which 25% had a clinical diagnosis of dementia and 75% of the sample was formed by a cognitively-healthy control. Ten-point five percent of the sample was illiterate, 28% of the sample had formal education up-to grade ten (secondary school), and the remaining of 61.5% of the sample had graduated or obtained a masters qualification. Data analysis revealed that the mean Urdu MMSE scores were lower in the dementia group (18.5 points) compared to the control group (26.8 points). Moreover, participants with no, or lower levels of education scored significantly lower compared to those with higher levels of education. Awan et al. (2015) also assessed the sensitivity and specificity of optimal cut-off scores for the Urdu MMSE, and education-based cut-off scores varied with scores below 15 yielding the best sensitivity and specificity for the diagnosis of dementia. Awan et al. (2015) concluded that the Urdu MMSE may be an adequate tool for use in the Pakistani population, however it is affected by education, and for a country with high illiteracy levels, different education-based cut-off scores are necessary.

It is important to note that over half of the sample implemented by Awan et al. (2015) was highly educated. This is not representative of the South Asian older adults residing in the UK which may also explain the high average MMSE scores in the control group. Moreover, Awan et al. (2015) adapted two items on the MMSE which may have also led to improved performance in the cognitively-healthy cohort. This further reflects the inadequacy of using unadapted versions of the MMSE with less educated populations.

There are several studies in which authors have implemented translated and culturally adapted versions of the MMSE. Kabir and Herlitz (2000) developed a modified MMSE, known as the Bangla Adaption of the Mini-Mental State Examination (BAMSE), which incorporates cultural modifications in all items to meet the needs of their sample. Some of the modifications included the omission of the question asking for the current year, the registration words "apple, penny and table" were replaced by "mango, flower, and fish" and the calculation item was also simplified to account for people with lower literacy levels. Comparisons were made between test scores on the adapted BAMSE and the English MMSE. Test scores on the BAMSE were less affected by age and education compared to test scores on the MMSE. It was concluded that the culturally adapted and translated version was more valid, and useful when testing illiterate populations. However, all items from the original MMSE were modified and adapted. This challenges the comparability of scores on the BAMSE across studies implementing the MMSE as the BAMSE could be considered as a new test which may not have the same or similar psychometric properties as the original MMSE.

Similarly, Ganguli et al. (1995) developed the Hindi version of the MMSE known as the HMSE which involved the adaption of most items based on cultural relevance, translatability, and adaptability. Therefore, the cross-cultural adaption of tests like the MMSE often leads to the development of a test which is significantly different from the original version.

Tabassum and Jawed (2010) conducted a piece of research to explore the exposure of psychiatrists from the West Midlands region of the UK to South Asian patients and determine their level of awareness and usage of translated versions of the MMSE. They found that many of the psychiatrists in their sample were unaware of the availability of translated and adapted versions of assessments like the MMSE and these were not routinely used. This suggested that although translated and adapted versions of the MMSE are available, these may not be widely used in clinical settings.

Further to the above, with regards to translations of the MMSE, there is an item which requires participants to repeat the phrase 'no ifs, ands or buts'.

However, translating this phrase word by word is not possible because none of the South Asian languages have the equivalent to this phrase which also maintains the context of what it intends to measure (Waheed et al., 2020; Noroozian et al., 2014). For example, the closest translation into Hindi and Urdu changes the meaning to “neither this nor that” (Ganguli et al., 1995). This indicates that this is not an easily translated phrase, and when translated, there is potential that its articulation complexity can be lost (Shim et al., 2017). Further to this, the adaption of this phrase into the different languages may also imply that the new phrase assesses a different cognitive domain which consequently questions the validity of the item in adapted versions of the MMSE for South Asian older adults.

Overall, the MMSE was developed with an English-speaking population (Folstein et al., 1975) and it is a quick and easy assessment to deliver. However, many words in the MMSE cannot be directly translated and some concepts (e.g., seasons and dates) may not be relevant to people from other cultural backgrounds. Test scores on the MMSE are also influenced by education, ethnicity, and language (Pinto et al., 2019; Ortega et al., 2019; Zahodne et al., 2015) making it unsuitable for use in populations like the South Asian older adults.

5.1.2. The RUDAS and its use in multicultural cohorts

With the increase in the cultural diversity of the aging population in Europe, and the lack of culturally appropriate brief cognitive screening tools, the RUDAS (see chapter [4] for detailed outline) was developed as an alternative to the MMSE (Nielsen et al., 2019; Storey et al., 2004).

Storey et al. (2004) conducted the preliminary research to pilot the use of the RUDAS in a multicultural sample of 90 participants residing in Australia, and originating from Asia, Central and South America, Africa, and the Middle East. The results revealed that the RUDAS was not affected by education, language, or gender, and that it can be translated into other languages without the need for cultural and linguistic adaptions. This implies that, when compared with the MMSE, it is more reliable as the process of translation does not lead to the loss of the items' contextual meaning when adapted for non-English speakers (Goudsmit et al., 2018; Storey et al., 2004).

Studies comparing the RUDAS with other cognitive assessments including the MMSE and the MoCA have also found comparable diagnostic accuracy for dementia (Cheung et al., 2015; Matias-Guiu et al., 2017).

Naqvi et al. (2015) conducted a systematic review of studies implementing the RUDAS in adult samples (aged over 18 years) and found that it had high sensitivity and specificity as an assessment of cognitive function, and it was less affected by language and education levels when compared to the MMSE. They concluded that the RUDAS is a practical brief screening test which has adequate psychometric properties, and the reduced effect of language, and education makes it more adequate for people from culturally diverse backgrounds (Naqvi et al., 2015).

Nielsen et al. (2013) carried out a research study which aimed to compare the RUDAS with the MMSE as a screening tool to detect early signs of dementia in a culturally diverse sample. Data was collected from 137 patients recruited from three Danish memory clinics. Thirty-four participants originated from the Middle East, Asia, Europe, America, and Africa. In addition to the standard diagnostic procedures at the clinics, all participants completed the MMSE and the RUDAS. The analysis of the data indicated that the diagnostic accuracy of the RUDAS was comparable to the MMSE, and it was significantly less affected by education.

However, an influence of education has been reported in research using samples with fewer years in education (Nielsen et al., 2019; Chaaya et al., 2016; Limpawattana et al., 2012; Iype et al., 2006).

Nielsen et al. (2019) conducted a study which aimed to explore the diagnostic accuracy of the RUDAS in an immigrant sample from across various Western European countries and develop normative data. The study sample was formed by 80 dementia patients and 341 cognitively-healthy controls recruited from memory clinics. All participants completed the RUDAS in their preferred language. The results revealed that the RUDAS had a high diagnostic accuracy. The best optimal cut-off score for cognitive impairment was identified as being 25/30. Moreover, and to the contrary of previously discussed evidence, test scores on the RUDAS were affected by education levels, whereby higher education levels correlated with increased test scores. However, there were no significant effects of ethnic background on test scores. As a result, education adjusted normative data was produced which further improved the diagnostic accuracy of the RUDAS.

Overall, the RUDAS appears to be as accurate as the MMSE in identifying dementia, and the minimal requirement for cultural and language adaptations suggests that it may be more suitable for ethnically diverse populations. However, some studies do report an education bias (Nielsen et al., 2019; Chaaya et al., 2016). Also, a large body of research validating the use of the RUDAS comes from migrant populations residing in other European countries, and to our knowledge, there is no UK based research exploring the use of the RUDAS in the growing South Asian older adults. This gap in the research will be addressed in this chapter by exploring the use of the RUDAS in an underrepresented sample of South Asian older adults to determine its feasibility comparatively to the more established MMSE.

5.1.3. Summary

The MMSE remains as one of the most widely implemented assessments of general cognitive function (Nielsen et al., 2019). However, despite its diagnostic qualities, the MMSE is known to be affected by education, language, and culture (Pinto et al., 2019). In view of these limitations, the RUDAS was developed as a culturally fair assessment for use in multicultural populations but, some evidence indicates that the RUDAS may also be influenced by education (Nielsen et al., 2019; Chaaya et al., 2016). However, both, the MMSE and RUDAS, have not been extensively validated in the increasing aging populations from minority backgrounds in the UK. Further research is required to explore their use in South Asian older adults who represent the largest aging BAME group in the UK (Blakemore et al., 2018).

5.2. The present study: Research aims

This piece of research aims to investigate the use of the MMSE and RUDAS in a sample of South Asian older adults and explore whether the language in which the assessments are administered in (English or Urdu) has any influence on test scores. This chapter will also explore the use of the RUDAS to determine whether this assessment may prove to be more suitable to be used in South Asian older adults when compared to the MMSE.

As a marker of verbal fluency in English and Urdu, the study in this chapter also aimed to implement a selection of pictures from the Snodgrass and Vanderwart's (1980) picture naming test (SVPT) to compare with participants self-reported English language fluency. This was introduced to assess self-reported fluency against a more objective marker of verbal fluency which has not been reported in previous studies.

It is hypothesised that South Asian older adults would score higher, indicating better performance, on both the RUDAS and the MMSE, when the tests are administered in their native/familiar language (Urdu) compared to in English. Participants are also hypothesised to score higher on the RUDAS in both testing languages due to its alleged sensitivity to culture.

5.3. Methods

The research followed the ethical guidelines set by the British Psychological Society and ethical approval was granted by the Chair of the Humanities, Social and Health Sciences Research Ethics Panel at the University of Bradford on 23rd June 2016.

5.3.1. Participants

Forty participants (eight females and 32 males) of South Asian origin (Pakistani, Indian, and Bangladeshi) aged 60 years and over participated in this study. They all confirmed proficiency in the Urdu language.

The exclusion criteria specified that participants must not have any diagnosed neurological disorders, cognitive impairments and/or sensory impairments. Participants were also required to be aged 60 years or over, and fluent in Hindi/Urdu as both languages share commonalities in their spoken format and they are understood and spoken by South Asians of Pakistani, Bangladeshi, and Indian origin (UNICEF, 2019; UNHCR, 2009). This would allow the researcher to test all participants in the same language.

5.3.2. Design

A within subjects/repeated measures experimental design was implemented. The dependent variables consisted of the test scores on the MMSE and RUDAS and the independent variables consisted of the language in which the assessments were administered (English and Urdu).

5.3.3. Materials

Cognitive performance was assessed on the MMSE and the RUDAS. Both tests were discussed in detail in chapter [4]. A summary of the materials used is provided next.

***MMSE* -** the MMSE is a test of general cognitive function assessing a variety of cognitive domains (Folstein et al., 1975). It is scored out of 30.

RUDAS- The RUDAS is also a test of general cognitive performance and it is claimed to be culturally fair (Storey et al., 2004). It is also scored out of 30.

Self-reported scale of English fluency: This assessed participants' verbal, written, and reading skills in English. The scale ranged from 1-10 with lower scores indicating poor fluency and higher scores on the scale representing higher fluency. The questions on the scale were read aloud to participants in Urdu, and the researcher marked the answers on the scale.

SVPNT: This test consists of a set of 260 standardised black and white pictures which were developed by Snodgrass and Vanderwart (1980) to investigate for differences and similarities between the processing of pictures and words. The current research implemented 80 pictures from the original article (Snodgrass and Vanderwart, 1980). When selecting the pictures, it was ensured that these had an equivalent word in Urdu. Participants were shown the selected pictures one by one and asked to verbally name them in English and Urdu. This was implemented to verify the reliability between self-reported fluency in English and actual level of fluency. It was expected that if participants rated their self-reported fluency as high, then they would also identify a larger number of words on the SVPNT in English. Therefore, this was implemented as an objective measure of English fluency to be correlated with self-reported levels of English fluency.

5.3.4. Procedure

All participants were recruited from Girlington Community Centre (Bradford). They were approached during a coffee morning and provided with an information sheet which was read to them in Urdu. The cognitive testing sessions took place in an interview room at the community centre where informed consent was obtained. The information in the consent form was also relayed verbally in Urdu to confirm definite understanding. The testing session then commenced with participants first verbally completing the self-reported English language scale followed by the SVPNT. Next, participants completed the MMSE followed by the RUDAS. Both tests were completed in English first. In both languages, instructions for each item were provided verbally and the responses were recorded by the researcher, except for the responses for items requiring the use of a pen to write or draw figures.

5.4. Results

This piece of research explored the influence of the language cognitive tests were administered in (English and Urdu) on test scores in two assessments of general cognitive function, the MMSE and the RUDAS in a sample of cognitively-healthy South Asian older adults. This chapter also explored the use of the RUDAS to determine whether this assessment may prove to be more feasible to be used in South Asian older adults when compared with the MMSE.

5.4.1. Main participant demographics

The sample's mean age and years in education are presented in table one.

Table one: Mean and SD for age and number of years in education

	Mean	±SD
Age (years)	69.18	±6.74
Education (years)	3.73	±3.19

Participants mean age was 69.18 years and there was a large variance in age range around the mean age values. As expected, participants had a low level of education with a mean of 3.73 years with a moderate variance around the mean values.

5.4.2. Objective and subjective markers of English fluency

The research aimed to explore the effects of the testing language on the test scores obtained on the MMSE and RUDAS. Therefore, the sample's self-reported fluency in spoken English was recorded and this was also objectively assessed using the SVPNT which involved participants being shown pictures and asked to name them in English and Urdu. The results with this regard are presented in table two.

Table two: Mean and SD scores on the SVPNT and participants' self-reported fluency in spoken English

Assessment	Language	Mean	SD (±)
SVPNT (Max. score= 80)	English	18.92	±19.65
SVPNT (Max. score= 80)	Urdu	68.10	±12.64
Self-Reported fluency in spoken English **(One = low fluency; ten = high fluency)**	English	3.55	±2.47

The results in table two illustrate that on average, participants reported their fluency in spoken English as 3.55 which represents poor on a scale from one to ten. On average, participants were also able to name 49.18 more pictures in Urdu compared to in English. The variance of scores around the mean values was larger for the number of pictures identified in English compared to in Urdu.

A Pearson correlation analysis was carried out to determine the association between the scores on the SVPNT (English) and participants' self-reported fluency in spoken English, with $r = 0.81$, $p<0.01$. There was a positive and significant correlation; the higher participants reported their fluency in spoken English, the higher they scored on the SVPNT (English). See figure one for a scatterplot of these results.

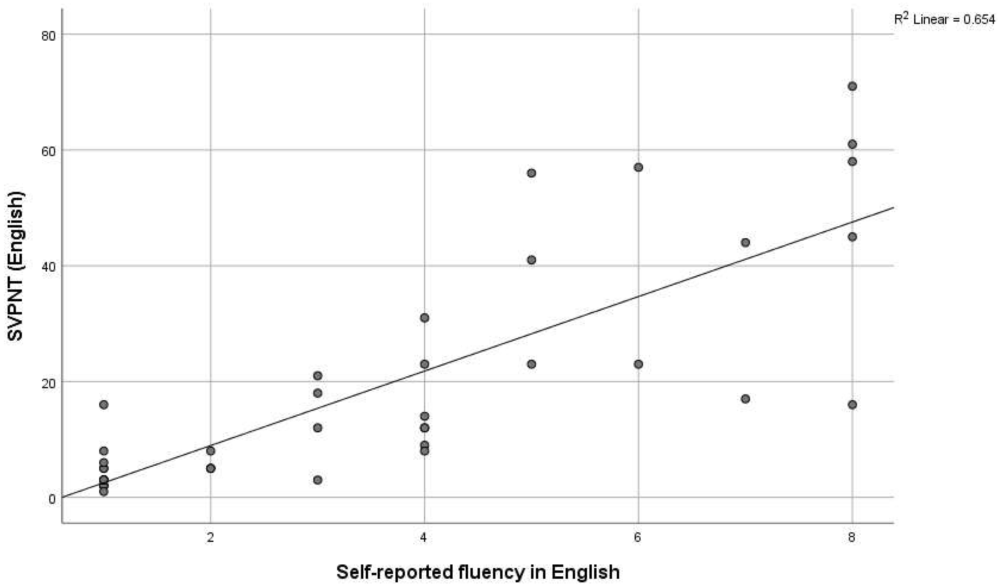


Figure one: Positive and significant correlation indicating that the higher participants subjectively reported their spoken fluency in English, the higher they scored on the SVPNT in English.

5.4.3. Main effects of age and education on test scores

A multivariate analysis was conducted to investigate the main effects of age and education on test scores. The alpha level was set to 0.05 in all analysis. Age and education were entered into the model as covariates and test scores on the MMSE and RUDAS in both testing languages as the dependent variables. Wilks Lambda was significant for the main effect of age on tests scores (Λ = 0.29, $p<0.001$) and for the main effect of education on test scores (Λ = 0.24, $p<0.001$).

The multivariate analysis revealed a significant decline in test scores with increasing age on the **MMSE (English)** ($F(1,38)= 11.93$, $p<0.05$; $B=-0.57$, $p<0.05$); **MMSE (Urdu)** ($F(1,38)= 83.40$, $p<0.05$; $B=-0.62$, $p<0.001$); **RUDAS (English)** ($F(1, 38)= 4.50$, $p<0.05$; $B=-0.41$, $p<0.05$) and **RUDAS (Urdu)** ($F(1,38)= 8.66$, $p<0.05$; $B=-0.36$, $p<0.05$). The parameter estimates indicated that age had the least effect on the RUDAS (Urdu) followed by RUDAS (English); MMSE (English) and MMSE (Urdu).

These main effects of age are represented in the scatterplots in figure two.

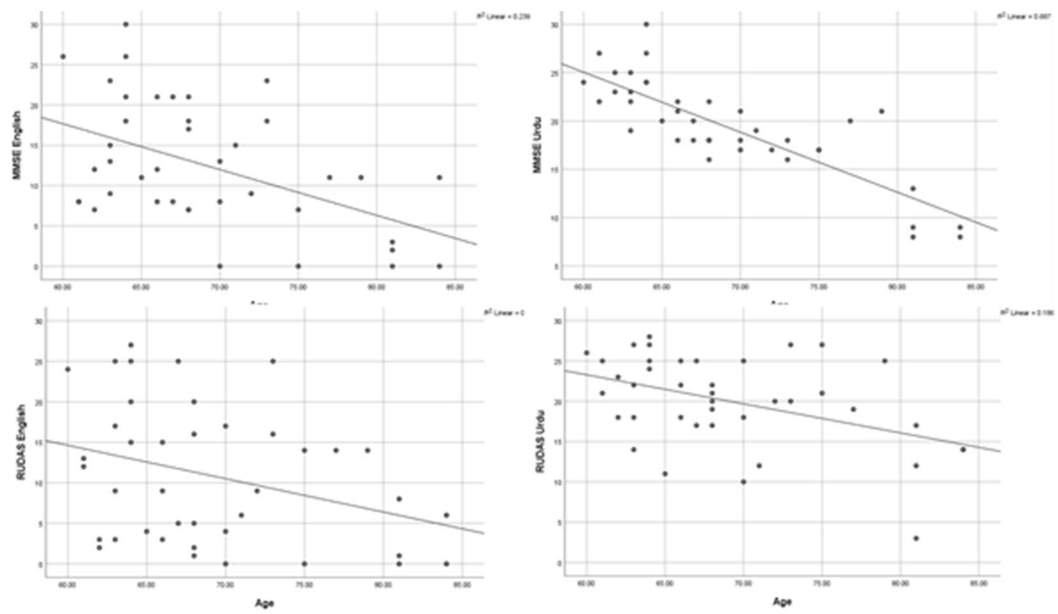


Figure two: Scatterplots of the main effect of age on tests scores on the MMSE (English and Urdu), and RUDAS (English and Urdu) indicating a linear decrease in test scores with increasing age.

The multivariate analysis also revealed a significant effect of education on test scores on the **MMSE (English)** ($F(1,38)=116.41$, $p<0.001$; $B=2.13$, $p<0.05$); **MMSE (Urdu)** ($F(1,38)=9.62$, $p<0.001$; $B=0.71$, $p<0.05$); **RUDAS (English)**

(F(1,38)=34.58, p<0.001; B=1.85, p<0.05) and **RUDAS (Urdu)** (F(1,38)=5.80, p<0.001; B=0.64, p<0.05). Parameter estimate values indicated that education had the least effect on test scores on RUDAS (Urdu) followed by MMSE (Urdu), RUDAS (English) and the largest effect of education was observed in test scores on the MMSE (English). These main effects are depicted in figure three.

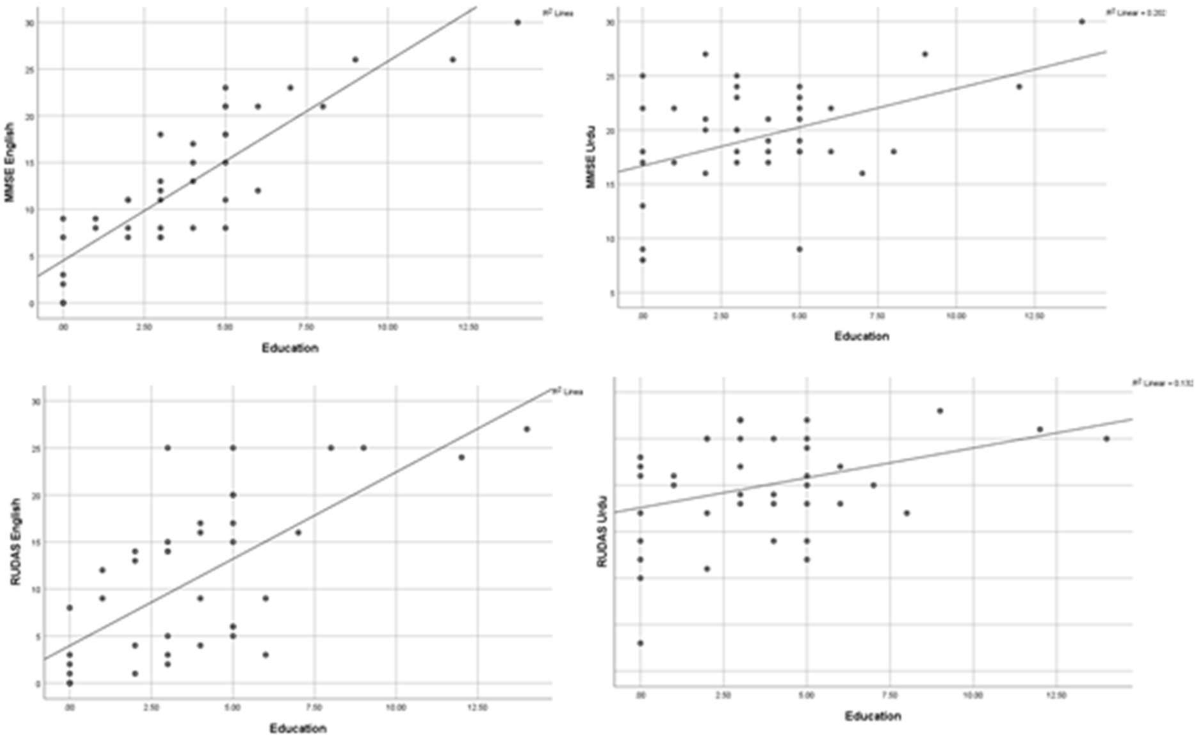


Figure three: Scatterplots depicting the main effect of education on test scores on the MMSE (English and Urdu) and RUDAS (English and Urdu) indicating a linear increase in test scores with increasing number of years in education.

Overall, there was a main effect of age and education on the MMSE and RUDAS in both testing languages. With increasing age, test scores experienced a significant decline, and with increasing number of years in education test scores also experienced a significant increase. Based on parameter estimate data, test scores on the RUDAS (Urdu) were the least affected by age and education.

5.4.4. Performance on the MMSE and RUDAS in English and Urdu

The MMSE and RUDAS were administered to the sample in English and Urdu. Table three presents the mean and SD values for test scores on both assessments and in both testing languages. The level of cognitive impairment is also noted based on currently established normality cut-off scores by Storey et al. (2004) and the NICE (2018) dementia guidelines.

Table three: Mean and SD scores on the MMSE and RUDAS for both testing languages (English and Urdu) and cognitive impairment status

Assessment	Testing language	Mean and SD	Cognitive impairment status
MMSE	English	12.45 (±7.82)	Moderate (NICE, 2018)
MMSE	Urdu	19.38 (±5.03)	Moderate (NICE, 2018)
RUDAS	English	10.85 (±8.52	Probable cognitive impairment (Storey et al., 2004)
RUDAS	Urdu	19.98 (±5.63)	Probable cognitive impairment (Storey et al., 2004)

Average test scores were higher on the MMSE and RUDAS when these were completed in Urdu. When the assessments were completed in Urdu, average test scores were higher on the RUDAS when compared to the MMSE. The variance around the mean scores was higher when the tests were completed in the English language.

The results also revealed that on average, the sample of cognitively-healthy participants scored within the cognitive impairment spectrum range in both assessments in English and Urdu.

Normality checks were carried out using the Shapiro-Wilk test as it is more suitable for small sample sizes (Ghasemi and Zahediasl, 2012). The analysis revealed that only the MMSE (English) data was normally distributed ($p>0.05$). Nonetheless, normality was also checked on QQ plots (see figure four) which revealed that the data was only slightly deviated from the normality line by 1-2 points. Therefore, based on this, normality was assumed, and the data was analysed by implementing parametric tests.

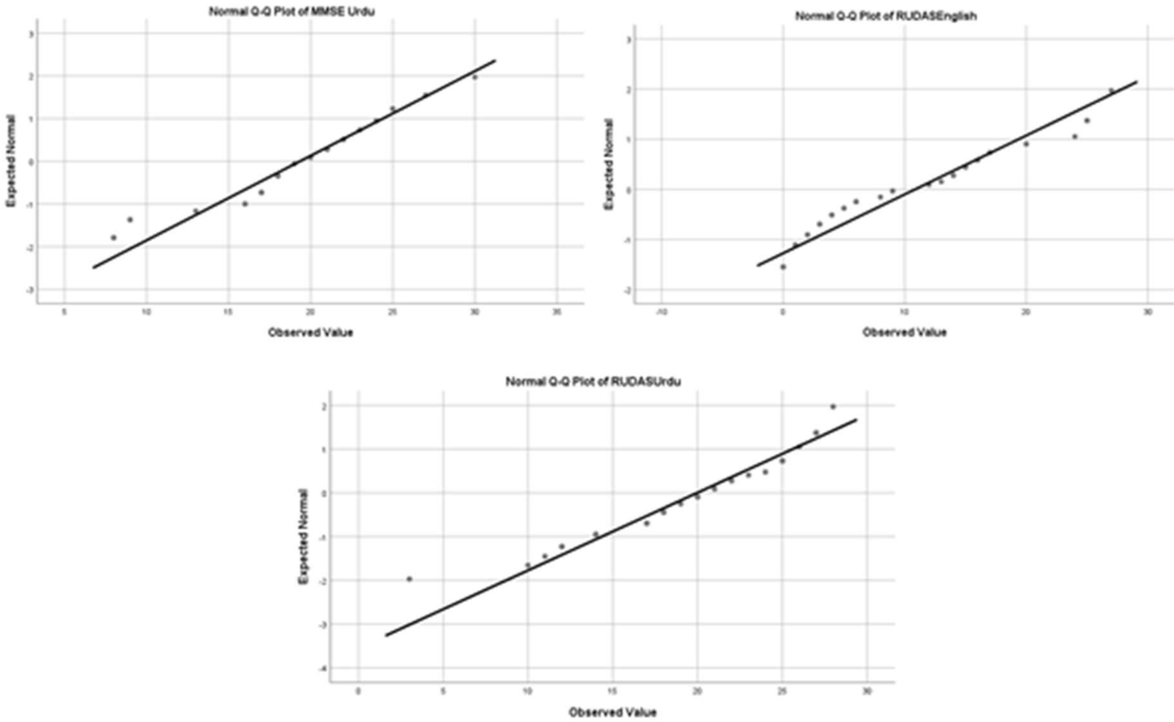


Figure four: Q-Q scatter plots for MMSE (Urdu), RUDAS (English) and RUDAS (Urdu) indicating normal distribution line

Test scores on the MMSE and RUDAS in English and Urdu were submitted to four paired sample t-tests to determine whether the differences in performance between the two tests and in the different testing languages were significant. To account for multiple tests, Bonferroni correction was applied which created a new significance alpha value of $p=0.0125$. The results from this analysis are presented in table four.

Table four: Mean scores and paired t-test analysis between test scores on the MMSE and RUDAS in the different testing languages

Comparison group	Mean Scores	Outcome
MMSE English/ MMSE Urdu	English – 12.45 Urdu – 19.38	t (39) = - 6.85, p<0.0125
RUDAS English/ RUDAS Urdu	English – 10.85 Urdu – 19.98	t (39) = - 8.34, p< 0.0125
MMSE English/ RUDAS English	MMSE – 12.45 RUDAS – 10.85	N.S.
MMSE Urdu/ RUDAS Urdu	MMSE – 19.38 RUDAS – 19.98	N.S.

As expected, the sample performed significantly better on the MMSE and RUDAS when the testing language was Urdu. However, no significant differences were observed between test scores on the MMSE and the RUDAS in either testing language.

5.4.5. Changes in domain specific scores from English to Urdu

The MMSE and RUDAS tax similar cognitive domains and further analysis was carried out to determine which domains experienced the largest improvement in test scores from completion in English to Urdu.

Test scores on the six domains assessed in English and Urdu were submitted to six paired sample t-tests. To account for multiple tests, Bonferroni correction was applied which created a new significance alpha value of p=0.008. The results from this analysis are presented in tables five (MMSE) and six (RUDAS).

Table five: Mean, SD (±) scores and change in scores from English to Urdu in domain specific items as measured by the MMSE

Domain	MMSE English (Mean±)	MMSE Urdu (Mean±)	Change in score	Percentage increase in scores from English to Urdu	T-test outcome
Orientation **Max. score 10**	4.90 ±3.18	7.68 ±1.99	+2.78	+56.73%	t(39) = 6.38, p<0.008
Registration **Max. score 3**	2.45 ±1.11	2.85 ±0.36	+0.4	+16.33%	n.s.
Recall **Max. score 3**	0.93 ±1.07	1.65 ±1.05	+0.72	+77.2%	t(39) = 4.13, p<0.008
Attention, concentration, and calculation **Max. score 5**	0.93 ±1.58	1.33 ±1.46	+0.4	+43.01%	n.s.
Language **Max. score 8**	3.36 ±2.49	5.93 ±1.95	+2.57	+76.49%	t(39) = 7.34, p<0.008
Visuospatial (pentagon copying) **Max. score 1**	0.20 ±0.41	0.25 ±0.43	+0.05	+24.99%	n.s.

On average, participants performed better on each domain when they performed the task in Urdu. These differences were statistically significant for the items measuring orientation, recall and language which were also the domains with the largest change in scores from English to Urdu. SD scores were generally larger when the test was completed in English compared to in Urdu.

The same analysis was repeated for the domains assessed by the RUDAS. Test scores on the six domains assessed in English and Urdu were submitted to six paired-sample t-tests with an alpha value p=0.008. The findings are presented in table six.

Table six: Mean, SD (±) scores and change in score from English to Urdu in domain specific items as measured by the RUDAS

Domain	**RUDAS English (Mean and SD)**	**RUDAS Urdu (Mean and SD)**	**Change in score**	**Percentage increase in scores from English to Urdu**	**t-test outcome**
Visuospatial orientation **Max. score 5**	2.48 ±1.96	4.52 ±0.88	+1.68	+82.26%	t(39) = 7.33, p<0.008
Praxis **Max. score 2**	1.18 ±0.84	1.78 ±0.48	+0.6	+50.85%	t(39) = 4.21, p<0.008
Visuo-constructional drawing (cube copying) **Max. score 3**	0.90 ±0.96	1.23 ±1.00	+0.33	+36.67%	n.s.
Judgment **Max. score 4**	1.48 ±1.54	3.23 ±0.95	+1.75	+118.24%	t(39) = 7.43, p<0.008
Memory recall **Max. score 8**	1.98 ±2.56	4.10 ±2.32	+2.12	+107.07%	t(39) = 5.51, p>0.008

Language **Max. score 8**	2.68 ±2.26	5.10 ±1.95	+2.42	+90.3%	t(39) = 6.58, p<0.008

Table six shows that participants performed better on each domain in the RUDAS when they performed the task in Urdu. The differences were statistically significant, except for scores on the visuo-constructional drawing domain (cube copying). The results also indicated that the largest change in scores from English to Urdu was given in the items measuring judgement, memory recall and language which is similar to the MMSE**.** SD values were larger in all domains when the test was completed in English.

5.5. Discussion

This piece of research aimed to investigate the use of the MMSE and RUDAS in a sample of cognitively-healthy South Asian older adults to explore whether the language in which the assessments were administered in (English or Urdu) had any influence on test scores. This chapter also explored the use of the RUDAS to determine whether this assessment may prove to be more feasible to be used in South Asian older adults when compared to the MMSE.

5.5.1. Main findings

(i) Test scores on the MMSE and RUDAS declined significantly with increasing age when administered in both, English, and Urdu; **(ii)** test scores on the MMSE and RUDAS, administered in both English and Urdu, increased significantly with increasing number of years in education. Education had the least effect on test scores on the RUDAS and MMSE when completed in Urdu; **(iii)** test scores were significantly better on the MMSE and RUDAS when these were completed in Urdu; **(iv)** no significant differences were found between test scores on the MMSE and RUDAS when administered in English and Urdu; **(v)** the sample of cognitively-healthy South Asian older adults, on average, scored within the cognitive impairment spectrum on both assessments and in both testing languages; **(vi)** the largest, and statistically significant, improvement in test scores from English to Urdu was found in the items measuring recall, language and orientation on the MMSE and in the items measuring judgement, memory recall, language and orientation on the RUDAS.

5.5.2. The influence of the testing language on test scores

As expected, participants performed significantly better on the MMSE and the RUDAS when these assessments were administered in Urdu, a language that the sample confirmed fluency in. The significant improvement in test scores in Urdu is important considering that the MMSE has been widely translated into different languages, including Hindi (Ganguli et al., 1995); Urdu (Awan et al., 2015) and Bangla (Kabir and Herlotz, 2000). The RUDAS is also designed to be translated into different languages without the need for linguistic adaptions (Storey et al., 2004). Therefore, the current findings, to an extent, favour the use of translated versions in populations who may not speak English to enhance the accuracy of the scores obtained.

However, it is important to note that currently available translated versions of assessments like the MMSE are non-standardised adaptions (Shim et al., 2017). For example, the Urdu MMSE by Awan et al. (2015) modified two items, the Hindi MMSE developed by Ganguli et al. (1995) required the modification of over half of the items, whilst the Bangla version developed by Kabir and Herlitz (2000) led to changes in all items. As a result, most of the existing translations and adapted versions of the MMSE are practically new assessments which are no longer comparable with the original. Moreover, Tabassum and Javed (2010), as previously discussed, found that despite the availability of adapted and translated versions of the MMSE, these are not commonly used by psychiatrists and clinicians in the UK.

Also, despite a significant improvement in test scores in the Urdu language, the sample of cognitively-healthy older adults, on average, continued to score within the cognitive impairment spectrum on both assessments. Moreover, test scores on items requiring an understanding of numbers (calculation item on MMSE) or copying geometric figures (pentagon in the MMSE and cube on

RUDAS) experienced the least improvement in test scores when the test was administered in Urdu which was also statistically non-significant.

This suggests that although reducing the linguistic barrier has a beneficial effect on improving cognitive test scores, this is not sufficient and the cultural and educational relevance of items may also be important factors to account for when testing minority populations with lower levels of education.

5.5.3. Domain specific performance on the MMSE and RUDAS

The largest and most significant improvement in test scores from English to Urdu was displayed on the items measuring the domains of memory recall, language, and orientation on the MMSE and judgement, recall, language, and orientation on the RUDAS. All these items place high reliance on familiarity and comprehension of the English language which supports the claim that the use of assessments like the MMSE and the RUDAS may disadvantage non-English speaking populations.

For example, poor performance on items measuring recall in English in the present sample may have resulted from a lack of familiarity with the English words used (MMSE - ‘apple, table, penny’; RUDAS - ‘tea, cooking oil, eggs and soup’). The lack of familiarity and understanding of the language may have led participants to face difficulties in visualising the relevant words leading to poor performance (Dodge et al., 2009). On the other hand, the translation of these items into a familiar language may have assisted the process of visualising the relevant words, leading to more enhanced performance. However, direct translations of these assessments were not sufficient to increase their validity because average test scores in Urdu remained below the established normality cut-off scores in this cohort.

Also, the differences in performance on some items from English to Urdu were not statistically significant. This was the case for the items measuring attention and calculation, and visuo-spatial drawing (pentagon) on the MMSE and the item measuring visuo-constructional drawing on the RUDAS (cube copying). This is interesting to note as these items require knowledge with regards to mathematical skills (subtraction) and geometric figures which implies that their successful completion relies on education-based experiences (Goudsmit et al., 2018; Kosmidis, 2018; Ardila et al., 2010). Considering the lower number of years in education in the present cohort, this may have contributed towards the significant effects of education on test scores on both assessments, and in both testing languages.

Education had the least effect on test scores on the RUDAS (Urdu) followed by the MMSE (Urdu). Considering that the effects of education were less pronounced when completed in Urdu, this supports the previous claim that linguistic adaptations are useful. However, they are not sufficient and further adaptions are needed to reduce bias beyond linguistic barriers.

5.5.4. Education bias and adequacy of the MMSE and RUDAS

Main effects of education were observed in both assessments in English and Urdu despite the sample's overall number of years in education being low with a relatively moderate variance around the mean values.

The educational bias is also consistent with previous literature (Goudsmit et al., 2018; Mateos-Alvarez et al., 2017; Young et al., 2017; Naqvi et al., 2015; Ardila et al., 2010). For example, Mateos-Alvarez et al. (2017) explored the use of the MMSE and RUDAS in a sample of native Spanish participants with lower levels of education. Consistent with the present findings, Mateos-Alvarez et al. (2017) found that the MMSE was significantly affected by education levels. However, this was not observed for test scores on the RUDAS which is not consistent with the present findings.

In this study, test scores on the RUDAS were influenced by education, although the Urdu version was affected to a lesser extent when compared to the English version and the MMSE. This may suggest that the influence of education is likely to be more heightened when combined with other cultural factors, such as lack of understanding of the English language and grasp of the concepts measured by assessments like the MMSE and the RUDAS.

The education bias present in the RUDAS has not been widely investigated, and to our knowledge, this study was the first one to explore this in a sample of UK based South Asian older adults. One of the limited pieces of research in this cohort was carried out by Iype et al. (2006) in a native Indian sample. Iype et al. (2006) explored the use of the RUDAS and the MMSE in a Malayalam speaking sample from Kerala (India). The sample was formed by 58 patients diagnosed with dementia, and 58 cognitively-healthy controls. The sample's mean number of years of formal schooling was 5.59 years. The analysis of the data gathered revealed that the RUDAS and the MMSE had similar levels of sensitivity in detecting dementia, but the RUDAS had better specificity. Nonetheless, the RUDAS was found to be significantly influenced by education levels which challenges its use in South Asian older adults.

Notwithstanding, in the present study, the influence of education was less pronounced on the RUDAS when compared to the MMSE. This suggested that the RUDAS is a step closer towards improving the screening of cognition in different populations. However, validation research in more diverse cultural groups is required to reduce the influence of education. This may be achieved by developing education adjusted cut-off scores, particularly when the assessment is used with minority migrant populations, like South Asian older adults.

5.5.5. Implications of the research findings

The results of this study have shown that the MMSE may not be adequate for use in South Asian older adults. Moreover, on average, performance on the RUDAS, which is claimed to be a culturally fair assessment, was also within the cognitive impairment spectrum. Both assessments were also influenced by education, and based on established normality cut-off scores, the sample of cognitively-healthy older adults performed within the cognitive impairment spectrum, both on the MMSE and RUDAS in Urdu and English.

This has implications for researchers and clinicians. The results suggest that simply using interpreters in clinical and research settings may not be sufficient considering that the educational bias present in the MMSE and RUDAS was not corrected by simply translating these assessments.

This calls for a need to reconsider cognitive testing in minority populations and promote research which explores the use of alternative measures in less educated populations. However, until new adequate measures are established, the present findings support the practice of detailed history taking with the aim to identify language and educational barriers to ensure that these are controlled and accounted for when interpreting cognitive test scores.

These findings are also likely to apply to the use of other neuropsychological assessments, and not only the MMSE and RUDAS, considering that many of these tests have been developed with similar constructs and validated in predominately Caucasian samples (Goudsmit et al., 2018; Ardila et al., 2010).

The present findings also highlight the potential for discrimination based on culture/race. Individuals who are less educated and from a non-English background may be disadvantaged by assessments requiring familiarity with English words (delayed recall), and items requiring the presence of skills acquired through education (e.g., subtraction and pentagon or cube copying tasks) (Goudsmit et al., 2018). This potential disadvantage may have detrimental consequences on the ability of minority migrant groups to have equal access to dementia diagnostic pathways. This may also lead to important legal issues for organisations like NICE who recommend the routine use of cognitive assessments in all populations, with limited practical guidance on tackling with the educational and linguistic bias preventing the equality of cognitive screening in diverse populations (NICE, 2018).

5.6. Summary and conclusion

The results of this chapter have demonstrated that the MMSE and RUDAS were not suitable to assess cognitive functioning in the present sample of South Asian older adults. On average, participants performed below the cut-off points for normal cognition, both when the assessments were delivered in English and Urdu. This can bias the interpretation of test scores which has implications for establishing a valid and reliable diagnosis, both in research and clinical settings. This may place minority groups, like South Asian older adults, at a disadvantage and compromise their equality of access to current diagnostic pathways.

In view of these findings, it is important to explore the use of alternative measures which may place lower reliance, both on language and education, to improve cognitive screening in South Asian older adults.

The next chapter will aim to address this issue by exploring the use of a brief domain specific battery of short assessments proposed to have lower reliance on language and education. The assessments which will be explored have not been widely implemented and validated in culturally diverse populations, and it will be novel to explore their use in the underrepresented South Asian population.

5.7. Chapter highlights

- The experiment in this chapter examined the effects of the language in which cognitive tests are presented in (English or Urdu) on test scores in two assessments of general cognitive function, the MMSE and the RUDAS.

- Results revealed that participants performed significantly better on the MMSE and RUDAS when these were completed in Urdu. However, both assessments were affected by education.

- The sample of cognitively-healthy South Asian older adults scored poorly and within the cognitive impairment spectrum on both assessments and in both testing languages.

- The results demonstrated that both, the MMSE and RUDAS, may not be suitable for South Asian older adults with lower levels of education.

Chapter 6: Exploring the use of a battery of brief domain-specific tests

6.1. Introduction

The previous chapter of this thesis found that even when cognitive assessments were administered to participants in their native language (Urdu), they scored significantly lower and within the cognitive impairment spectrum, both on the MMSE and the RUDAS. Moreover, test scores on both assessments in English and Urdu were affected by education. This suggested that simply translating neuropsychological assessments to improve language comprehension may not be sufficient to improve their validity for use in culturally diverse populations. Therefore, indicating that there is a need to explore the use of alternative assessments which place lower reliance on both, language, and education.

To address this issue, the present chapter aims to explore the use of a battery of brief neuropsychological assessments taxing several domains in a sample of South Asian older adults. These have been selected for their proposed lower reliance on language and education with the aim to investigate whether these may be more suitable for use in a migrant population known to have lower levels of education. These tests, to our knowledge, have not been widely used in this population and it is therefore logical to explore their use in South Asian older adults, particularly because these type of assessments are likely to be used in referrals for additional testing in memory clinics.

6.1.1. Clinical pathways to diagnosis and study rational

The process of diagnosing cognitive impairment characteristic of AD was discussed in detail in chapter [2].

In the UK, guidance with regards to the diagnosis and treatment of AD is provided by the NICE dementia guidelines which were last reviewed in 2018 (NICE, 2018). One of the key changes in this updated guidance was that shorter cognitive tests, such as the 10-point cognitive screener (10-CS) and the 6-item cognitive impairment test (6CIT), were recommended to assess cognitive functioning in primary care settings. These replaced the use of longer assessments, like the MMSE, as no evidence was found to suggest that these were more accurate than the shorter versions (NICE, 2018). However, these shorter assessments are broadly similar in their properties and they have adapted items from the MMSE (see chapter [2]). Moreover, in a review of the updated NICE guidance, Pink et al. (2018) highlight that these assessments have limited sensitivity which often implies that normal scores do not always preclude the presence of a clinically significant cognitive impairment. Also, there is very little evidence which validates the use of assessments like the 10-CS. For example, to date, to our knowledge, there is only one publication on the 10-CS (Apolinario et al., 2016) and no validation studies in patient cohorts exist and their recommendation is largely based on opinions of what constitutes good practice (Larner, 2018). This lack of validation is likely to imply that specialist cognitive screening services do not have access to suitable population norms for what is considered “normal” scores on these assessments for the populations being tested.

Nonetheless, the recommendation to use shorter cognitive assessments is reasonable for a society where the demand for these services is increasing. If shorter assessments can be as effective as the longer alternatives in identifying cognitive impairment, then this could offer a more efficient method to screen for cognitive functioning. This can facilitate the assessment of more patients in each day, reducing the overall waiting times for memory clinics, and potentially contributing towards early diagnosis.

The previous chapters of this thesis have already shown that longer assessments, like the MMSE and RUDAS, may not be suitable for the current sample of cognitively-healthy South Asian older adults. Based on the lack of suitability of assessments like the MMSE, and the preference to use shorter assessments in primary care settings (NICE, 2018), the next step is to now explore the use of shorter assessments in the underrepresented South Asian older adults (Blakemore et al., 2018; Hossain et al., 2017). To our knowledge, performance on domain specific assessments has not been widely explored in this population.

However, it may not be plausible to use the assessments recommended by NICE (2018) due to the lack of validation studies and their lack of sensitivity to mild impairment. There are many other validated short assessments available, which although have not been specifically validated in ethnically diverse populations, some evidence does suggest that these assessments tax domains known to be affected early in the development of AD, and they may be less biased by education and culture related knowledge. Therefore, potentially making them more suitable as the choice of short cognitive assessments for less educated, culturally and lingustuially diverse populations. The assessments which will be explored and the reasons for their selection are detailed in the next section of this chapter.

6.2. The present study: Evaluating the battery of assessments used

A neuropsychological battery is formed by a selective set of cognitive assessments taxing different domains which provide a comprehensive overview of a patient’s cognitive functioning, and like with the assessments of general cognitive function, these can be administered and scored fairly quickly (Jakob et a., 2016). This may offer a more enhanced way of assessing cognitive decline as assessments of general cognitive function broadly assess different cognitive domains. However, the use of brief domain specific assessments may offer the opportunity to target domains known to be affected early in the development of AD quickly and in more detail, which may enhance the ability of cognitive testing to identify early decline.

The battery of brief neuropsychological tests administered in this chapter is formed by the assessments of DR, PCS, LCS, the adapted TMT A&B for less educated populations (Kim et al., 2014), SDMT, DSF, DSB and DT (see chapter [4] for detailed outline). These assessments are commonly used in the cognitive literature, and in particular the selection of assessments was guided by previous research by Lesk et al. (2009) and Walters and Lesk (2015, 2016) who implemented these assessments to explore the influence of several external factors on cognitive performance in a sample of older adults. However, these pieces of research did not account for their sample's ethnicity or cultural background in the analysis, and it will therefore be novel to explore their use in a minority underrepresented population.

The battery of cognitive assessments administered in this chapter is outlined in detail in chapter [4] and a summary of the neuropsychological battery, testing domain and skills required to complete the short assessments is provided in table one. All assessments will be delivered to the sample in Urdu.

Table one: Summary of the short battery of neuropsychological tests by cognitive domain measured and skills required to complete the tests used in the present study

Assessment	Testing domain	Skills required	Paper and pencil required
DR	Short-term memory	Verbalised response (spoken language – repeating and recalling words in Urdu)	No
PCS	Processing speed	Verbalised response (spoken language– verbally conveying responses in Urdu stating "same" or "different") Visual scanning Familiarity with abstract shapes.	No

LCS	Processing speed	Verbalised response (spoken language – verbally conveying responses in Urdu stating "same" or "different") Visual scanning Familiarity with Latin alphabet.	No
DSF	Working memory	Verbalised response (spoken language– repeating back sequence of numbers in Urdu) Mathematics/ familiarity with Western numbers	No
DSB	Working memory	Verbalised response (spoken language – repeating back sequence of numbers in Urdu) Mathematics/ familiarity with Western numbers	No

SDMT	Executive function Processing speed	Writing/hand dexterity (substituting geometric figures by Western numbers from a key) Reading (Western numbers) Mathematics/ familiarity with Western numbers	Yes
TMT A	Processing speed	Reading (Western numbers) Writing/hand dexterity (drawing lines to connect circles) Mathematics/ familiarity with Western numbers	Yes
TMT B	Executive function Processing Speed	Reading (Western numbers) Writing/hand dexterity (drawing lines to connect circles) Mathematics/ familiarity with Western numbers	Yes
DT	Executive Function	Verbalised response (spoken language –	Yes

	Working memory	repeating back sequence of digits in Urdu) Mathematics/familiarity with Western numbers Writing/hand dexterity (placing crosses inside empty boxes)	

For most of the assessments listed in table one, in the skills column, it is stated that the tests require the use of verbalised responses (spoken language) when this battery is proposed to have lower reliance on language. The use of language is limited to providing verbal instructions and prompting verbal responses which can take place in the participants native language, minimising the risk of poor performance due to poor linguistic comprehension of a different language.

All the assessments part of the battery of brief domain specific neuropsychological tests have been outlined and discussed in detail in chapter [4]. However, a brief reasoning for the implementation of each assessment in this study is outlined in the next subsections of this chapter.

6.2.1. DR – Short-term memory

Memory impairment is one of the most common symptoms in MCI and it is often reported as one of the first symptoms in AD (Bregman et al., 2020; Brooks and Loewenstein, 2010). Therefore, an assessment measuring DR is incorporated as part of this short cognitive battery. This assessment is suitable as it provides the freedom to select words which are appropriate for the cultural context of the population being tested as opposed to conforming to the unfamiliar or abstract words often used in currently established cognitive assessments (e.g., MMSE, MoCA, RUDAS, 10-CS). Moreover, the words can be read aloud in the participants native language which reduces the impact of language comprehension and reading ability on cognitive performance.

DR is also argued to be more sensitive in detecting MCI and early AD and it has been found to be a good predictor of future cognitive decline (Talamonti et al., 2020; Dubois et al., 2007).

6.2.2. PCS and LCS – Processing Speed

Processing speed is a cognitive skill which slows down with normal ageing, however disproportionate slowing has been found in patients diagnosed with MCI and AD (Daugherty et al., 2020; Haworth et al., 2016). Reaction times in processing speed tasks have been found to be associated with functions involving attention and perception and are a useful indicator of changes in everyday behaviour related to MCI and AD, such as cessation of driving, slowed walking speed and dependence on other ADL, such as cooking, eating, and managing finances (Haworth et al., 2016).

The current study implemented Salthouse and Babcock's (1991) paper version of the PCS and LCS (see chapter [4]). This has been the choice of assessment because the PCS and LCS require participants to visually identify whether a set of patterns, or alphabetical letters are the same or different. Therefore, the task itself does not require familiarity or understanding of the patterns or letters used.

The original version of the PCS and LCS requires participants to use a pen to mark their responses, however, to reduce any language and education bias, in this study participants will be asked to look at the patterns and letters and verbally state their responses (i.e., state "same" or "different") which will then be recorded by the researcher.

6.2.3. Digit Span (DSF and DSB) – Working memory

The digit span assessment is a component of the Wechsler adult intelligence scale revised (WAIS-R) (Wechsler, 1981) (see chapter [4]). The original assessment would require participants to read out digits from a paper and then repeat those back in a forward and backward order. However, this has been adapted for the present research whereby the digits are read aloud to participants in Urdu and repeated back in Urdu. Therefore, verbalising numbers in Urdu is expected to reduce the education bias in this assessment of working memory, potentially making it more suitable for South Asian older adults. However, this has not previously been explored in the present literature.

Further to the administration benefits of the DSF and DSB in minority populations, deficits in working memory have often been associated with MCI and subsequent progression into AD (Garcia-Alvarez et al., 2019; Kessels et al., 2011; Cherry et al., 2002). Assessing these deficits are important because working memory is involved in coordinating cognitive, emotional, and behavioural functions to optimise performance in pursuit of activities of daily living as it involves planning, problem solving, updating information, and simultaneously storing and manipulating information (Garcia-Alvarez et al., 2019).

Garcia-Alvarez et al. (2019) aimed to explore working memory and EF deficits in MCI patients. They recruited a sample of 48 patients with MCI, 124 cognitively-healthy controls and 57 AD patients who were assessed on a range of working memory and EF measures, frontal lobe integrity indexes and functioning. They found that patients with MCI exhibited poor performance on most of the working memory and EF measures which were also associated with compromised frontal cortex activity.

Therefore, implementing the DSF and DSB in this short battery of assessments will provide a basis to assess working memory, known to deteriorate in the early stages of AD, with reduced reliance on education in South Asian older adults.

6.2.4. SDMT – Processing speed and EF

The SDMT was devised by Smith (1968) as an assessment of general neuropsychological dysfunction, and in particular as a measure of EF and processing speed. It requires individuals to substitute abstract symbols for numbers using a key. The SDMT is argued to have good psychometric properties and purported to be appropriate for people with speech disorders, relatively free from cultural bias, and suitable for people for whom English is not their native language (Ryan et al., 2020; Kiely et al., 2014; Smith, 2007).

The SDMT is also gaining recognition as an assessment of choice in multiple medical fields to assess for cognitive decline in conditions such as AD, Huntington's disease, and Parkinson's disease (Pascoe et al., 2018). It has also been found to be minimally affected by education level and language abilities due to the use of symbols and its non-verbal test component (see chapter [4]) (Smith 2007; Lopez et al., 2008).

O'Bryant et al. (2007) carried out a piece of research to assess the use of the SDMT in an ethnically diverse student sample formed by cognitively-healthy Caucasians (n=81); African Americans (n=49); Asian Americans (n=20) and Hispanics (n= 18). They had a further sample formed by 24 patients with Hepatitis C of which 12 were Caucasian and 12 Hispanic. O'Bryant et al. (2007) justify implementing a sample diagnosed with Hepatitis C based on research findings by Hilsabeck et al. (2002, 2003) whereby they found that patients with Hepatitis C demonstrate poor SDMT performance compared to healthy controls. From the data obtained, O'Bryant et al. (2007) found that ethnicity only accounted for a very small percentage of the variance in SDMT scores for the patient (2%) and student group (3%). It was thereby concluded that this offers preliminary support for the use of the SDMT in ethnically diverse samples (O'Bryant et al., 2007).

Although there is no study exploring the use of the SDMT in a South Asian older adults' sample, the available literature does suggest that it may serve as a valuable screening tool to assess cognitive function in less educated populations with poor proficiency in the English language.

6.2.5. TMT A&B – Processing Speed and EF

The adapted TMT A&B (Kim et al., 2014) is an assessment of processing speed and part B also measures the domain of EF. It is a cultural adaption of the original TMT A&B (Reitan and Davison, 1974) (see chapter [4]).

The original TMT A&B is implemented to identity MCI and early stages of AD (Bigler at al., 2002; Pena-Casanova et al., 2014) and it has been widely administered in English speaking populations. However, its use with alternative populations is very limited because it involves familiarity with the Latin alphabet in part B of the assessment (Zhao et al., 2013).

Due to the above limitations, an alternative TMT, known as the trail making black and white was developed by Kim et al. (2014) and piloted in a lower educated Korean sample. The adapted version requires participants to switch between black and white numbers, as opposed to between numbers and letters in ascending order.

This is a relatively new assessment compared to the original TMT A&B, and it has not been widely validated. However, some studies have suggested that the adaption of the TMT is more reliable, and it is not affected by education (Kim et al., 2014; Han et al., 2019). The attempt to make the assessment more relevant for those who lack familiarity with the English alphabet implies that it may be more suitable for individuals from culturally diverse backgrounds. This is because despite the adaption, it has retained many of its psychometric properties allowing to measure higher end functions, such as processing speed and EF (Han et al., 2019). The adapted TMT A&B has not been validated in a South Asian older adults' sample. Thus, it will be novel to explore its use in this population which shares similarities with the Korean population that the assessment was developed with (e.g., lower education levels).

6.2.6. DT – EF and working memory

DT is a paper and pen assessment of EF and working memory (Della Sala, 2010; Baddeley et al., 1991). It consists of an A4 paper representing a string of connected empty boxes. The first part of the assessment involves participants being timed for one minute during which they are required to place a cross in each box following the direction of the string (Baddeley et al., 1997). During the second part, participants are required to repeat the first task, however they are required to simultaneously remember and repeat the strings of numbers based on their digit span score (Jaroslawska et al., 2018).

Therefore, DT does not appear to require education related knowledge to complete as the digits can be verbally relayed in the sample's native language. However, there is no data to draw conclusions with this regard as the DT assessment is not widely used in the screening of cognitive performance in research or clinical settings, and there is a lack of normative data for this assessment (Della Sala, 2010). Particularly, there is no research exploring its use in minority and less educated populations.

Through early investigations by Baddeley et al., (1986; 1991), it was claimed that patients with AD experience a decline in their ability to perform two tasks simultaneously which is not seen in the process of normal ageing (Della Sala and Logie, 2001). This is argued to be caused because of a deficit in the central executive component of working memory (Baddeley et al., 1991) which leads to poor performance on DT in patients with AD and MCI (Lonie et al., 2009). This indicates that it may be suitable to facilitate an early diagnosis.

Although the DT assessment is not commonly used in the present literature on cognitive testing, based on its reduced reliance on language and education and potential to tax on domains affected early in the development of MCI and AD, it may prove to be a suitable assessment to be used in a sample of South Asian older adults.

6.2.7. Implementation of the MoCA as a comparison

The current chapter also aims to implement the MoCA in conjunction with the short battery of cognitive assessments outlined earlier in this chapter. The properties of the MoCA were discussed in detail in chapter [4].

The MoCA is being used in this study to explore whether global cognitive functioning can be better assessed by one single assessment of general cognitive function, in this case the MoCA, or by the battery of several short domain specific assessments outlined earlier.

The rationale for implementing a test of general cognitive function in this battery of domain specific tests is to allow for a comparison to be established between the proposed short battery of neuropsychological assessments claimed to have lower reliance on language and education, and an assessment of general cognitive function known to be influenced by education and culture related variables (Hicks et al., 2020). The previous chapter of this research has already explored the use of the MMSE. Also, unlike the MMSE, the MoCA assesses EF, and it has been shown to identify MCI and AD more accurately (Zhou et al., 2014; Pereiro et al., 2017). Therefore, considering that the current battery of assessments aims to cover cognitive domains which are not addressed by the MMSE (e.g., EF), the MoCA is a more appropriate assessment of general cognitive function to compare with the global scores on the battery of domain specific neuropsychological assessments being used in this chapter.

6.2.8. Population norms used and calculation of z-scores

Despite the importance of population norms in neuropsychological testing, the present literature review failed to find any established population norms developed with a minority, less educated sample with similar characteristics as the South Asian older adults. Where norms were available for culturally diverse samples, these had been developed with adapted versions of the assessments which could not be used in the present study (e.g., Hayek et al., 2020 (MoCA – Lebanese sample); Gozalez et al., 2007 (SDMT – African American, and Hispanic sample).

Whilst it was not possible to find culture specific population norms which were entirely representative of the South Asian older adults' sample, age, gender, and education adjusted norms were to some extent more available. Having said this, no normative data was available in the current literature for the assessments of DR and DT. The lack of published normative data for the assessment of DT was also noted in an earlier paper by Della Sala (2010). As a result, the mean and SD scores for these assessments were derived from research by Walters and Lesk (2015) and Lesk et al. (2009) to develop the norms used in this study.

The normative data which was available was used to calculate z-score transformed means with the aim to compare performance differences between the MoCA (a test of general cognitive function) and the assessments forming the battery of domain specific cognitive tests. Calculating z-scores is a common method to compare performance on assessments using different scoring systems and measuring different domains (Mielke et al., 2017). Z-scores are calculated by subtracting the raw score from a population-based mean and dividing it by the population SD (Li et al., 2012). The transformation of raw mean scores into z-scores allows to then compare the scores on different cognitive assessments with different scoring systems. Z-scores generate a positive or negative score. A positive score indicates that the sample is performing above (better) the established population norms, whereby a negative score is indicative of performance which is below the published population norms.

Overall, cognitive performance was determined in this chapter by comparing normative data from the following sources: MoCA (Pereiro et al., 2017); DR (Walters and Lesk, 2015); PCS and LCS (Salthouse, 1994); DSF and DSB (Choi et al., 2014); SDMT (Kiely et al., 2014); TMT A&B (Tombaugh, 2004); DT (Lesk et al., 2009). This is outlined further in the results section of this chapter.

6.2.9. Summary

The present chapter has proposed to develop a battery of brief domain specific neuropsychological assessments to explore whether the accuracy of cognitive screening in South Asian older adults can be improved by implementing shorter assessments with lower reliance on language and education. This was guided by the recommendations from NICE (2018) to use shorter assessments in primary care settings. Performance on the battery of brief assessments will also be compared with performance on a single and longer measure of general cognitive function, the MoCA.

The assessments being used have not been tested or validated in South Asian older adults and there is limited to no evidence of use in other minority populations. This is a novel battery of neuropsychological assessments which may prove to be more suitable for less educated populations whose first language is not English. If this transpired to be the case, it could potentially provide some preliminary data to address the issues with the present NICE (2018) guidelines which do not offer clinicians with a choice of alternative brief cognitive assessments for less educated individuals who may or may not speak English.

6.3. The Present Study: Research aims

This chapter aims to explore **(i)** the performance of South Asian older adults on a battery of brief domain specific assessments proposed to have lower reliance on language and education, **(ii)** the influence of the different types of skills required to complete the assessments on cognitive test scores and **(iii)** whether cognitive performance can be better assessed in this cohort by implementing one single assessment of general cognitive function, the MoCA, or when using the battery of several domain specific assessments.

The use of these assessments, to our knowledge, has not been assessed by any previous literature in this participant cohort.

6.4. Methods

Ethics approval for this research was granted by the Chair of the Humanities, Social and Health Sciences Research Ethics Panel at the University of Bradford on 23/03/17.

6.4.1. Participants

Forty-five participants (21 females; 24 males) from a South Asian background took part in this study. They were aged 60 years and over and were residents of the UK.

The inclusion criteria specified that participants must be aged 60 years or over, be from a British South Asian background (defined in this study as Pakistani, Bangladeshi, or Indian) and fluent in Urdu/Hindi. To minimise interference with cognitive performance, as part of the exclusion criteria, participants were required to not possess any sensory impairments, have an existing diagnosed neurological condition, or suffer from any severe physical disability.

Although the inclusion criteria specified for participants to be from Pakistan, India or Bangladesh, the final sample was predominantly formed by Muslim Pakistani older adults.

6.4.2. Design

A repeated measures experimental design was implemented. All participants completed the full battery of cognitive assessment tests. The dependent variables consisted of the test scores on the MoCA and the scores on the battery of brief domain specific cognitive assessments. The independent variables consisted of the type of cognitive domains and skills assessed by the tests administered.

6.4.3. Materials

Participants completed a battery of cognitive assessments which included DR, MoCA, PCS, LCS, DSF, DSB, SDMT, TMT and DT. A detailed description of the battery of neuropsychological assessments administered can be found in chapter [4]. Participants also completed a demographics questionnaire which collected participants demographic data and the time of the day the research commenced.

6.4.4. Procedure

Participants were recruited form Girlington Community Centre and through snowball sampling in the areas of Bradford and London. They were provided with an information sheet, which was read to them in Urdu, and contacted 48 hours later to confirm whether they wished to participate. The research took place in participants' home in the presence of a carer or relative. Electronic devices which emit noises (e.g., TVs, radios) were turned off to minimise the number of distractions present at the time of testing. Participants signed a consent form, the contents of which were read to them in Urdu. Next, the demographics questionnaire was verbally completed in Urdu. Following this, participants completed the battery of cognitive assessments in a randomised order. Instructions for all assessments were conveyed verbally in Urdu, and the responses for items not requiring the use of a pen to draw or copy were conveyed by participants verbally and noted down by the researcher.

6.5. Results

This chapter aimed to explore **(i)** the performance of South Asian older adults on a battery of brief domain specific assessments proposed to have lower reliance on language and education, **(ii)** the influence of the types of skills required to complete the assessments on cognitive test scores and **(iii)** whether cognitive performance would be better assessed in this cohort by implementing one single assessment of general cognitive function, the MoCA, or when using the battery of several domain specific assessments.

6.5.1. Main participant demographics

Table two next shows the demographic characteristics of participants.

Table two: Mean and SD for demographic characteristics (age, education, and gender)

	Mean	**SD**
Age (years)	69.69	±6.40
Education (years)	4.24	±4.41
Gender (males: females)	24:21	

To assess whether any of the above characteristics influenced any of the cognitive test scores from the battery of neuropsychological tests administered, a multivariate analysis of covariance (MANCOVA) was conducted with test scores submitted as dependent variables, gender as a fixed factor, age, and education as covariates. No significant main effects of gender and age were found on any of the tests administered.

Significant main effects of number of years in education ($\lambda = 0.33$, $p<0.05$) were found on the assessment of general cognitive function, the MoCA ($F(1,45) = 54.69$, $p<0.05$); on assessments of processing speed, specifically the PCS ($F(1,45) = 8.07$, $p<0.05$); LCS ($F(1,45) = 4.57$, $p<0.05$) and TMT A ($F(1,45) = 9.44$, $p<0.05$); and on assessments taxing the domains of processing speed and EF, namely the TMT B ($F(1,45) = 12.99$, $p<0.05$) and the SDMT ($F(1,45) = 16.64$, $p<0.05$). The direction of these significant main effects is depicted in figure one which indicates that test performance on these assessments increased significantly with increasing number of years in education.

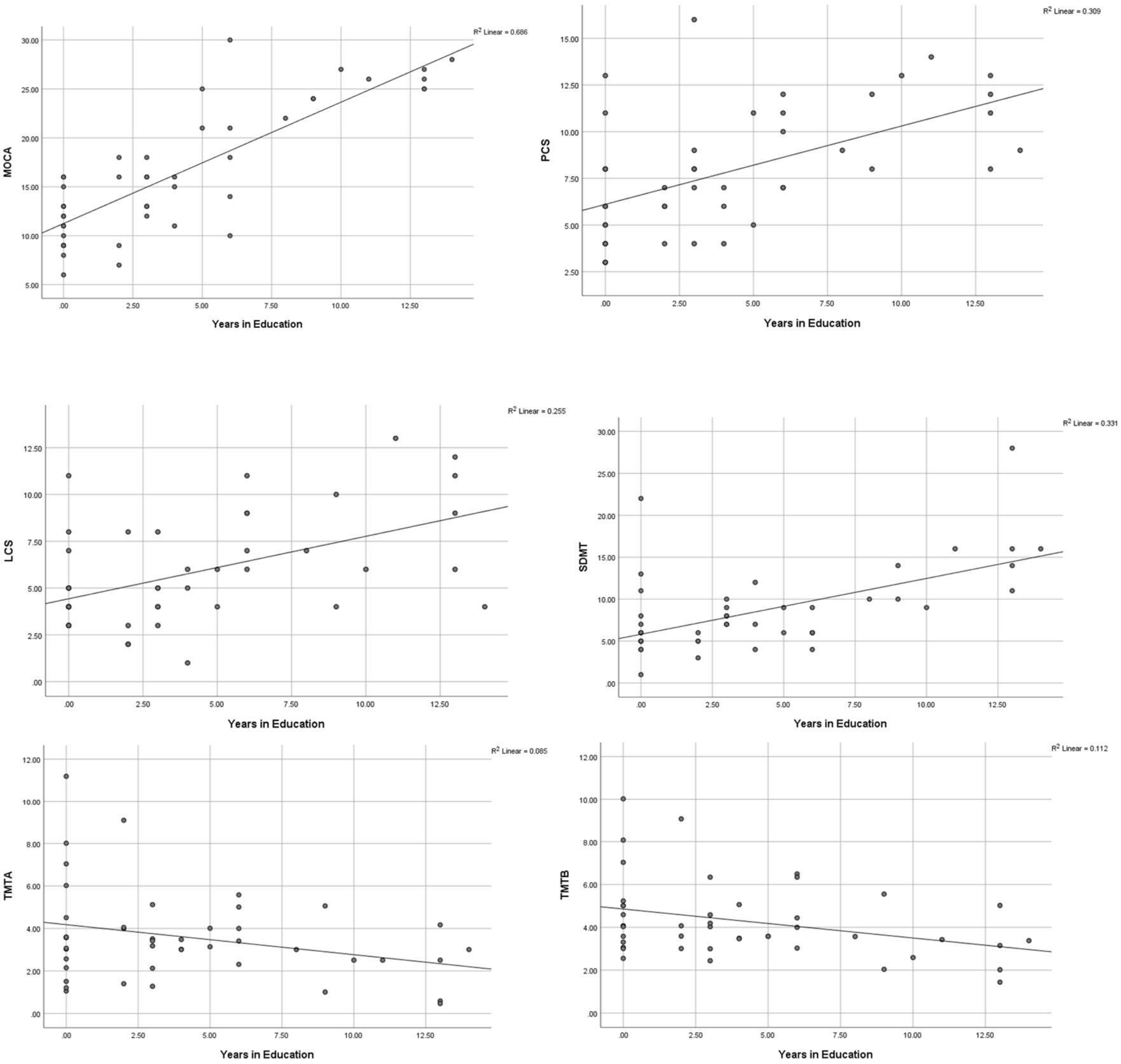


Figure one – Scatterplots showing a significant linear increase in test scores on the MoCA, PCS, LCS and SDMT with increasing number of years in education and a linear decrease in time taken to complete the TMT A&B with increasing number of years in education.

6.5.2. Performance on domain-specific assessments and z-scores

The sample of South Asian older adults completed a battery of brief neuropsychological assessments which included nine short domain specific assessments measuring short term memory (DR), processing speed (PCS, LCS, TMT A&B), EF (SDMT, DT and TMT B) and working memory (DSF, DSB and DT). The mean test scores obtained on each assessment are presented in table three. However, due to the differences in the maximum test scores and scoring systems between the different assessments, the mean scores obtained are not comparable. To compare performance on the different tests administered, for each individual test, a z-score was calculated using the respective population mean and SD scores which are also presented in table three.

Standardised z-scores were calculated by subtracting individual test scores from the normative mean scores and divided by the population SD. The mean z-scores and SDs obtained for each test are also presented in table three. Negative z-score values indicate performance which is below the published population norms (therefore indicating poor performance) and positive values are indicative of performance above the published norms, therefore indicating improved performance.

Table three: Mean and SD for cognitive test scores, population norms used, and z-score transformed means on the battery of brief neuropsychological assessments administered.

Assessment	Mean and SD score	Population Mean and SD score	Mean and SD z-scores
DR	2.82(±2.03)	5.21[1] (±1.65)	-1.25 (±1.00)
PCS	7.89 (±3.33)	9.40[2] (±3.4)	-2.25 (±0.99)
LCS	5.84 (±2.92)	5.40 (±1.56)	-1.22 (±1.00)
DSF	3.53 (±0.76)	5.52[3] (±2.48)	-3.79 (±1.00)

[1] DR population norms taken from Walters and Lesk (2015)
[2] PCS and LCS population norms taken from Salthouse (1994)
[3] DSF and DSB population norms taken from Choi et al. (2014)

DSB	2.69 (±1.36)	4.47 (±1.56)	-1.42 (±1.00)
SDMT	8.64 (±5.10)	31.10[4] (±10.51)	-5.17 (±1.00)
TMT A	3.58 (±2.14)	0.71[5] (±15.15)	1.49 (±1.01)
TMT B	4.28 (±1.78)	1.83 (±35.15)	1.61 (±1.01)
DT Ratio	0.64 (± 0.14)	1.50[6] (±1.7)	-3.19 (±1.00)

The results in table three indicate that on average, participants performed below the population norms on seven out of nine assessments (specifically on DR, PCS, LCS, DSF, DSB, SDMT and DT ratio). Test performance was above the population norms, and therefore better, only in the adapted assessments of TMT A&B (Kim et al., 2014) which have been specifically developed for less educated populations by replacing the alphabetical component in the original TMT A&B.

The data in table three also shows that participants performed the furthest away from the population norms on the SDMT, a measure of processing speed and EF.

The variance around the mean z-score values on all assessments, which has been rounded to two decimal points, was small indicating that on average participants performed close to the mean z-score values.

[4] SDMT population norms taken from Kiely et al. (2014)
[5] TMT A&B population norms taken from Tombaugh (2004)
[6] DT population norms taken from Lesk et al. (2009)

6.5.3. Cognitive performance by domains assessed

Test performance was only above (therefore better) the mean population norms on the adapted assessments of TMT A&B which tax the domains of processing speed and EF. Based on these findings, z-score transformed means were also used to calculate a computed mean z-score for each cognitive domain assessed by the battery of brief domain specific assessments. This was calculated to explore whether there were any significant differences in test scores between the different cognitive domains assessed. This was calculated by summing the mean z-scores for tests in each domain divided by the total number of assessments (e.g., for working memory z-scores on DSF, DSB and DT were summed and divided by three to obtain the mean z-score for the domain of working memory).

The results are presented in table five. Some assessments are included in more than one category as these assess more than one cognitive domain as illustrated in table one in the introduction of this chapter.

Table four: Mean and SD z-scores for domain specific cognitive performance on the battery of brief domain specific assessments

Testing Domain	Mean	SD
Short term memory (DR)	-1.25	±1.00
Working memory (DSF, DSB, DT)	-2.80	±0.60
Executive Functioning (TMT B, DT, SDMT)	-2.25	±0.54
Processing Speed (PCS, LCS, SDMT and TMT A&B)	-1.11	±0.55

The data in table four indicates that participants performed the closest to the population norms in assessments measuring processing speed followed by short term memory, EF and working memory. SD values were small for all domains indicating a small variance of scores around the mean z-score values.

Three paired sample t-tests were conducted to compare performance on the domain of processing speed with the domains of short-term memory, working memory and EF to explore whether performance on assessments of processing speed was significantly better. This was particularly important to explore as the average z-scores in table three suggested that performance was above the population norms (therefore better) only on the adapted assessments of TMT A&B which tax on the domain of processing speed. Therefore, if performance on the domain of processing speed transpired to be significantly closer to the population norms compared to the other domains assessed, this may indicate that the adapted TMT A&B may be suitable for South Asian older adults.

Bonferroni correction was applied generating an alpha value of $p=0.016$ and the paired-sample t-test analysis revealed that test scores on assessments of processing speed were significantly better when compared with assessments testing the domains of EF ($t(44)= 17.50$, $p<0.016$) and working memory ($t(44)=17.93$, $p<0.016$).

6.5.4. Cognitive performance by skills assessed

The analysis was expanded further to explore whether the different types of skills required to complete the battery of domain specific assessments had any influence on the scores obtained.

To explore this, an average z-score was calculated for the assessments part of each skills category by summing the mean z-scores of each assessment and dividing these by the total number of tests part of the particular skills category (e.g., for the skills category of non-verbalised response component the test scores on TMT A, TMT B and SDMT were added together and divided by three to obtain the mean z-score for the non-verbalised skills category). These are presented in table six. As with the domains table (four), some assessments involve the use of more than one skill, and therefore some assessments are featured within more than one category. Please refer to table one in the introduction of this chapter for the development of the skills category presented in table five.

Table five: Mean and SD z-scores on the battery of brief neuropsychological assessments by skills required to complete.

Skill type	Mean	SD
Non- verbalised response (TMT A, TMT B, SDMT)	-0.70	±0.57
Verbalised response (DR, PCS, LCS, DSF, DSB, DT)	-2.19	±0.64
Written component/hand dexterity (SDMT, TMT A, TMT B, DT)	-1.32	±0.54
Mathematics/Numbers (DSF, DSB, SDMT, TMT A, TMT B)	-1.46	±0.45
Reading (TMT A, TMT B, SDMT)	-0.70	±0.57

The data in table five indicates that on average, participants scored the closest to the population mean values in tests with a non-verbalised response component and a reading component followed by assessments with a written component, mathematics/numbers and they performed the furthest away from the population means in tests involving a verbalised response component.

Because the assessments with a non-verbalised response were the closest to the population norms, four paired sample t-tests were carried out to investigate whether the differences in scores between the assessments with a non-verbalised response component were significantly different when compared with the other skills assessed.

Bonferroni correction was applied providing a new significance alpha value of $p=0.0125$. The analysis revealed that participants performed significantly better and closer to the population norms in assessments with a non-verbalised response component when compared with assessments with a verbalised response component ($t(44)=12.30$, $p<0.001$); writing/hand dexterity ($t(44)=16.15$, $p<0.001$) and mathematics/numbers component ($t(44)=11.82$, $p<0.001$). However, the differences between mean z-scores on assessments with a non-verbalised response component and reading were non-significant which was given as the assessments in these category are the same.

6.5.5. Summary of performance on domain-specific tests

It has transpired that the sample of cognitively-healthy South Asian older adults scored below the population norms on all cognitive tests administered, except for test scores on the adapted TMT A&B. Domain specific performance on the battery of brief assessments was also explored which indicated that participants performed significantly closer to the population norms on the assessments with a processing speed component when compared with the assessment taxing working memory and EF.

T-test analysis also indicated that participants performed significantly closer (therefore better) to the population norms on assessments which did not have a verbalised component and performance was the furthest away from the population norms in assessments with a verbalised response component.

6.5.6. Comparisons between the MoCA and the domain specific battery

The present research also aimed to explore whether cognitive performance would be better when using a single assessment of general cognitive function, the MoCA, or when using a battery of several brief domain specific assessments. To achieve this, in addition to the calculation of z-scores for each individual test score, a global cognitive test z-score was also created by summing the z-scores of the nine assessments part of the short domain specific battery of tests (DR, PCS, LCS, DSF, DSB, SDMT, TMT A, TMT B and DT) and dividing these by nine. This provided a score of global or general cognitive functioning on the battery of domain specific assessments which was compared with the mean z-scores obtained on the MoCA. This is presented in table six.

Table six: Mean and SD z-scores for the global cognitive test scores on the battery of domain specific neuropsychological assessments and the single assessment of general cognitive function, the MoCA.

Test Category	Total mean z-score	SD
General Cognitive Function (MoCA)	-0.84	±0.90
Global cognitive scores on domain specific battery (sum of z-scores of the nine assessments in the domain specific battery divided by nine)	-1.69	±0.50

The results in table six indicate that on average, South Asian older adults scored the closest to the population means on the single assessment of general cognitive function, the MoCA, when compared with the global z-score mean values for scores on the battery of domain specific neuropsychological assessments. However, the variance around the mean values was larger for scores on the MoCA.

To confirm whether performance was closer to the population means on the assessment of general cognitive function, the mean z-scores on the MoCA and the global cognitive z-scores from the domain specific battery were submitted to a paired-sample t-test. An alpha level of 0.05 was used. Participants scored significantly closer to the population norms on the single assessment of general cognitive function, compared to performance on the battery of domain specific assessments ($t(44)=6.66$, $p<0.01$).

This confirmed that cognitive performance in the present sample was better (but not above the population norms) on the MoCA when compared with performance on the battery of domain specific assessments as measured by the global cognitive z-scores.

6.6. Discussion

This chapter aimed to explore **(i)** the performance of South Asian older adults on a battery of brief domain specific assessments proposed to have lower reliance on language and education, **(ii)** the influence of the types of skills required to complete the assessments on cognitive test scores and **(iii)** whether cognitive performance would be better assessed in this cohort by implementing one single assessment of general cognitive function, the MoCA, or when using the battery of several domain specific assessments.

This was novel to explore as cognitive performance on these assessments, to our knowledge, had not previously been assessed in this cohort.

6.6.1. Main findings

(i) Test scores on the MoCA, PCS, LCS, TMT A&B and SDMT were affected by education. Performance on these assessments increased significantly with increasing number of years in education; **(ii)** participants performed below the population norms on all assessments administered except for test scores on TMT A&B, which is an assessment of processing speed and EF adapted for less educated populations (Kim et al., 2014); **(iii)** test scores on assessments of processing speed were significantly closer to the population norms when compared with scores on the assessments measuring working memory and EF; **(iv)** test scores were also significantly closer to the population norms in assessments requiring a non-verbalised response when compared with assessments with a verbalised response, writing/hand dexterity and use of numbers/mathematics; **(v)** test scores on the assessment of general cognitive function (MoCA) were significantly closer to the population norms when compared with the global cognitive z-scores on the battery of brief domain specific neuropsychological assessments.

6.6.2. Education related skills and cognitive performance

The sample of South Asian older adults performed below the published population norms on all assessments, except TMT A&B. Also, they performed significantly closer to the population norms in the assessment of general cognitive function when compared with the computed global z-scores on the battery of domain specific brief cognitive assessments with proposed lower reliance on language and education.

Several factors may have potentially contributed towards these findings. The normative data used for the MoCA was derived from norms adjusted by education level and in addition to this, the scoring of the MoCA also allows for an additional point to be awarded to participants with 12 or less years in education. On the other hand, the scoring of tests part of the battery of short assessments did not allow for any additional points to be awarded to lesser educated participants. Therefore, considering that the current sample had an average of four years in education, the lack of an education adjusted scoring system for the battery of brief cognitive assessments may have potentially contributed to cognitive performance being closer to the population norms on the MoCA.

Nonetheless, it is important to note that despite the double adjustment for education, test scores on the MoCA continued to be affected by education and except for test scores on TMT A&B, South Asian older adults scored below the population norms in all cognitive tests administered. This was the case despite the battery of domain specific assessments having been developed based on data suggesting that these may place lower reliance on language and education, arguably making them more suitable for less educated migrant populations like South Asian older adults.

However, this was not the case, and it is important to note that participants performed the furthest away from the population means in assessments requiring a verbalised response followed by those with a mathematical component. The assessments requiring a verbalised response included DR, PCS, LCS, DSF, DSB and DT. With this regard it is important to note that except for DR, the rest of the assessments involve the use of numbers (DSF, DSB and DT) or Latin alphabetical letters (LCS). Therefore, considering that the verbal responses were conveyed by participants in their own native language, the results are more indicative of the poor performance being attributed to the presence of numbers and letters, which South Asian older adults may not have been familiar with based on their lower levels of education. This may have led to poorer performance on these tests, despite the fact that an actual understanding of numbers and letters was not necessary to complete, which was initially proposed to lower the education bias in testing.

These findings are important as they indicate that attempting to reduce the education bias in cognitive testing by reducing the verbal component of assessments may not be sufficient to improve the accuracy of cognitive testing in culturally diverse and less educated populations. This may be because many existing neuropsychological assessments have been developed in Western populations to assess skills which are more enhanced in those who have attained higher levels of education (Franzen et al., 2020; Fujii, 2018; Ostrosky-Solis et al., 2010). Education not only transmits knowledge and skills, but it also improves information-processing efficiency and test taking skills in general (Goudsmit et al., 2018; Kosmidis, 2018; Ardila et al., 2010). The "test-witness" effect is relevant here as it refers to an individual's knowledge about how assessments are designed, the expectations and strategies for taking the tests independent of the actual content that the assessment is designed to measure (Ardila et al., 2010; Fujii, 2018).

This suggests that the differences in cognitive performance on tests between educated and less educated or illiterate individuals may not entirely be due to their cognitive abilities per se. Cognitive performance may be more largely affected by experience related to test taking abilities and familiarity with the testing situation (Goudsmit et al., 2018). Education provides a means to acquire information by different means (books, journals) and the process of learning to read and write may contribute towards the training of additional skills such as spatial perception and hand dexterity/motor skills (Kosmidis, 2018; Ardila et al., 2010).

This may explain the education bias found in the present study in the assessments of TMT A&B, SDMT and MoCA, as these assessments, amongst other school related skills, require participants to copy or draw figures which are dexterity related skills that less educated populations may not have had the opportunity to develop (Ardila et al., 2010; Parker and Philp, 2004). Also, the SDMT asks participants to copy and match numbers to corresponding abstract symbols from a key. To complete successfully, participants do not require to understand numbers, they just require copying these which appears to be a simple enough task that was initially thought to reduce its education bias. Nonetheless, contrary to what was initially proposed, it appears that even when an assessment does not require a direct understanding of numbers and figures, the task may not be as simple as it appears to someone who has limited experience in using a pen and paper and has potentially never seen these figures before or is unfamiliar with the numbers used. This may also explain the South Asian older adults' performance being the furthest away from the population means on the assessment of SDMT.

The present findings suggest that when attempting to reduce educational bias in neuropsychological testing, the method in which cognitive assessments are administered has important implications for performance (Kosmidis, 2018; Ardila et al., 2010). It has transpired that abilities such as copying figures or simply taking part in assessments may have significantly influenced cognitive test scores in this sample of less educated South Asian older adults. This may indicate that even when tests do not appear to have an obvious requirement for education related knowledge, such as in the case of the battery of domain specific assessments used in this chapter, the way these assessments are conducted and required to be solved may still be affected by academic and cultural related experiences and attitudes. This is likely to be caused because less educated or illiterate individuals are not likely to be used to testing procedures (Kosmidis, 2018).

For example, disparities in cultural attitudes towards time have been found to influence neuropsychological performance (Agranovich et al., 2011; Agranovich and Puente, 2007). This argument is based on the distinction between clock-time versus event-time orientation which determines the level of importance paid on timeliness and punctuality. Clock-time is more prevalent in individualistic Western societies where there is an emphasis on scheduled appointments, ensuring that clocks and watches are precise and completing tasks and activities within a specific time limit (Agranovich et al., 2011; Agranovich and Puente, 2007). In contrast, event-time attitudes have been found to be characteristic of developing countries where more emphasis is placed on people and events, rather than on schedules, and time is more flexible and something to be enjoyed, rather than saved (Puente & Agranovich, 2004).

Agranovich et al., (2011) argue that the Russian society is an example of an event-time orientation whilst the American society is more clock-time orientated. Based on this, they carried out a piece of research with the aim to explore the cultural differences in attitudes towards time and their influence on timed neuropsychological assessments. They recruited a non-clinical sample of 100 participants who were part of two equal groups based on their cultural background (Russians and Americans). Cognition was assessed on the Colour Trial Test (Mitrushina et al., 2005), Ruff Figural Fluency Test (Ruff, 1996), SDMT (Smith, 1982) and the Tower of London-Drexel Edition (Culbertson and Zilmer, 1998). Attitudes towards time were assessed on the Culture of Time Inventory developed by Agranovich et al. (2011). The analysis of the data indicated that the American sample performed significantly better on all cognitive assessments when compared with the Russian sample. Significant differences in attitudes towards time between the Russian and the American group were also observed. The American sample had a greater agreement with time related rules associated with schedules. Also, the American sample reported being more familiar with timed testing procedures compared to the Russian sample and this lack of familiarity with timed testing procedures in the Russian sample negatively correlated with cognitive performance. This shows that culturally specific attitudes towards time and familiarity with timed procedures may influence test scores on timed cognitive assessments. This has implications for the battery of test used in this chapter, as assessments like the PCS, LCS, SDMT and DT are all timed. Therefore, differences in attitudes towards time may also have potentially contributed to the poorer performance on these assessments in the sample of South Asian older adults.

This suggests that to improve the interpretation of cognitive test scores in less educated populations, there is a need to develop new measures which account for the effects of education beyond the ability to read, familiarity with geometric figures and carrying out calculations.

The present findings highlight the need to develop cognitive assessments for less educated minorities which are more appropriate for the living contexts of illiterate or less educated individuals. This is particularly important considering that existing measures to reduce bias, such as the use of education-based cut-off norms, do not appear to be suitable to improve the validity and reliability of cognitive testing in South Asian older adults. Even when education-based adjustments are made, such as in the case of the MoCA, some items cannot be scored for what they intend to measure. For example, less educated or illiterate individuals cannot reasonably be scored on items which require the ability to read (e.g., MMSE “Ask the patient to read and obey a written command”), write or copy figures (e.g., pentagon copying task on MMSE, numbers on SDMT and clock drawing task on the MoCA). Therefore, if an individual is not familiar with geometric figures, does not have the ability to read and/or write and tell the time, then it is fair to argue that poor performance on such assessments is not necessarily an indication of pathologically significant cognitive impairments. Subsequently, this increases the chances of minority less educated samples, like South Asian older adults, being misdiagnosed in clinical settings.

The lack of relevance and educational bias present in assessments like the MMSE, MoCA and the SDMT may also increase the risk of deterring less educated individuals from seeking help, which as discussed in chapter [3] is already a challenge preventing early diagnosis in South Asian older adults.

6.6.3. Lack of culture specific population norms

The South Asian sample performed below the mean population norms on all assessments except TMT A&B, which was the only assessment developed with a less educated sample from Korea (Kim et al., 2014). Considering that the normative data sources used were not culture specific, highlights that the poor cognitive performance of the present cohort may also be reflective of the lack of suitable normative data for culturally diverse populations.

As previously discussed, there is a significant lack of adequate normative data reflecting the characteristics of minority populations (Ryan et al., 2020), and the present study failed to find any population-based norms developed with a minority sample with similar characteristics to South Asian older adults. Where populations norms were developed for minority populations, these were based on adapted assessments (Gonzalez et al., 2007; Hayek et al., 2020).

Therefore, the population norms used were not developed with ethnically diverse populations, and although these did account for education, the level and quality of education across different countries is also unlikely to be the same (Black et al., 2019; Ardila et al., 2010).

These findings highlight the importance of developing more accurate normative data in older and ethnically diverse populations which considers, not only age and education related factors, but also cultural and ethnic differences, such as attitudes towards time and familiarity with the testing situation.

The lack of normative data is also an important issue in clinical settings, because as discussed earlier, the current shorter cognitive assessments recommended by the updated NICE (2018) dementia guidelines do not have any corresponding norms for less educated and culturally diverse populations. This challenges their use in clinical settings due to the increased risk of misdiagnosis in the absence of appropriate norms to determine true levels of cognitive impairment in different groups.

6.6.4. Suitability of the adapted TMT A&B

Participants performed above the published norms only on the adapted TMT A&B, which is a measure of processing speed, with part B also taxing EF (Kim et al., 2014). The adapted version of the TMT A&B was developed for a Korean sample with lower education levels by removing the alphabetical component. It is also important to highlight that performance on this assessment was above the published population norms despite the norms used being from the original TMT A&B (Tombaugh, 2004), as there were no available norms for the adapted TMT A&B potentially due to it being a relatively new assessment which has not been widely validated.

Also, performance was significantly closer to the norms on assessments measuring processing speed which is the principal component assessed by TMT A&B when compared with performance on the domains of working memory and EF. In addition to this, performance was also significantly better on assessments with a non-verbalised response component and the TMT A&B was also part of this category. This supports Kim et al.'s (2014) findings that the adapted TMT A&B may have potentially minimised the education bias present in the original version. These findings also support the inclusion of non-verbal assessments of processing speed when testing for cognitive performance in populations like South Asian older adults.

Despite these positive findings, the present research did report that test scores on the adapted TMT A&B were influenced by education. This may have resulted due to the use of Western numbers which lesser educated populations may not be entirely familiar with, particularly if they have not been to school in a Western country. This suggests that the adapted TMT A&B could potentially be modified to remove the numerical component and further enhance its suitability. This will be addressed in the next chapter of this thesis.

6.6.5. Implications of the research findings

The present research, to our knowledge, was the first piece of research to explore the use of a comprehensive battery of brief domain specific cognitive assessments with proposed lower reliance on language and education in a sample of South Asian older adults.

This study has highlighted that cognitive testing of lower educated populations should place emphasis on detailed history taking to understand their cognitive functioning as a reflection of their cultural and social context. Less educated populations may perform below the published population norms on currently established assessments of cognitive function as these often measure constructs and skills commonly learnt through the process of education in Westernised societies (Ardila et al., 2010).

The findings also indicate that the education bias in commonly used cognitive assessments cannot be rectified by just using education adjusted population norms in culturally and ethnically diverse populations. It is challenging to account for, and isolate the effects of education from culture, particularly when interpreting test scores on items which require reading, writing, or carrying out calculations as these skills may not be present in less educated samples (Fuji, 2017; Ardila et al., 2010). This highlights the need to develop new assessments for minority migrant populations with lower education levels by developing items which place increased emphasis on the living contexts of less educated individuals. This will be explored in the next chapter of this thesis.

The present findings also highlight the importance for researchers to develop cultural appropriate normative data to improve the interpretation of cognitive test scores and make neuropsychological testing more reliable for ethnically diverse populations. Consequently, enhancing cross cultural comparisons of cognitive performance which may improve the quality of cognitive research in this field.

The present study also found that South Asian older adults performed significantly better on assessments of processing speed when compared with performance on the domains of working memory and EF. This is an important finding, because as previously highlighted, processing speed deficits are observed in MCI patients (Daugherty et al., 2020; Lu et al., 2017), indicating that it may be an important domain to assess to identify early cognitive impairments in underrepresented minority populations. However, this domain is not assessed by the commonly used assessments of general cognitive function, and more importantly it is not acknowledged by the current NICE (2018) dementia guidelines as a domain of interest in the diagnosis of different types of dementias. Therefore, these preliminary findings may have important policy implications for NICE, particularly if future studies yield consistent findings.

6.7. Summary and conclusion

In this chapter, a comprehensive battery of brief domain specific neuropsychological assessments was developed which was proposed to have lower reliance on language and education. However, to our knowledge, none of the assessments forming part of this battery had previously been tested in South Asian older adults.

To compare and interpret test scores on the different assessments used, z-scores were calculated based on available population norms. Contrary to the expected, test scores on all assessments, except for the adapted TMT A&B, were below the population norms.

The results highlighted that the cognitive performance of South Asian older adults with lower levels of education may be more reflective of their limited experience and familiarity with the testing situation which is likely to be higher in those who have attained an education.

The results also showed that South Asian older adults performed significantly closer to the population norms on assessments of processing speed, which is a domain known to be sensitive to early decline (Daugherty et al., 2020; Lu et al., 2017), however it is currently not assessed by the commonly recommended brief assessments of general cognitive function by the NICE (2018) dementia guidelines.

The results indicate that for optimal clinical and research practice when carrying out cognitive testing, the consideration of cultural factors is necessary to improve the accuracy of neuropsychological assessment in culturally diverse populations. Although performance was below the population norms on most assessments, the present findings have provided an indication as to which domains and types of assessments may be more suitable for South Asian older adults. In particular, the enhanced performance on assessments of processing speed, such as the adapted TMT A&B, suggests that this may be a suitable domain that can be incorporated into an assessment of general cognitive function to make it more adequate for South Asian older adults.

The next chapter of this thesis aims to address some of the issues identified in this chapter (e.g., lower education, differing cultural attitudes towards time, lack of test taking experience) and develop an assessment of general cognitive function with the purpose to minimise the educational, linguistic, and cultural bias present in existing and commonly used assessments of cognitive function.

6.8. Chapter highlights

- This chapter explored **(i)** the performance of South Asian older adults on a battery of brief domain specific assessments proposed to have lower reliance on language and education, **(ii)** the influence of the type of skills required to complete the assessments on cognitive test scores and **(iii)** whether cognitive performance could be better assessed in this cohort by implementing one single assessment of general cognitive function, the MoCA, or when using the battery of several domain specific assessments.

- The results revealed that the sample of cognitively-healthy South Asian older adults scored below the published population norms on all assessments, except for TMT A&B.

- Test scores were also closer to the population norms on assessments with a processing speed component (PCS, LCS, TMT, SDMT) and on assessments with a non-verbalised/non-spoken language response component (TMT, SDMT).

- Test scores were significantly closer to the population norms (but not above) on the single assessment of general cognitive function, the MoCA, when compared with the global z-scores on the battery of several brief domain specific assessments.

- The results highlighted that the cognitive performance of this sample may have been more reflective of their limited experience and familiarity with the testing situation which often resembles school-based tasks.

Chapter 7: Development of the Universal Neuropsychological Assessment Scale and the Spatial Associative Learning Test

7.1. Introduction

As discussed in chapters [4-5], conventional neuropsychological assessments have not been widely validated for use in ethnic minorities in the UK, and their implementation with these groups is often inadequate and misleading due to influence from external factors (Kenning et al., 2017; Nielsen et al., 2018, 2019; Pedraza and Mungas, 2008). This is particularly the case for migrant populations with limited education and proficiency in the language of the receiving country (Magklare et al., 2018; Nielsen et al., 2012).

This is of concern because based on the changing cultural and linguistic compositions of the older adults in the UK, the availability and accessibility of accurate neuropsychological methods which account for the needs of people from culturally diverse backgrounds becomes increasingly important. However, as reported in the previous chapters of this thesis, existing assessments are not suitable for the present cohort of South Asian older adults which calls for a need to develop culturally appropriate assessments.

7.1.1. Context: Developing an assessment of general cognition

Previous studies forming part of this thesis have yielded alarming findings with regards to the use of established assessments of cognitive functioning in South Asian older adults. A significant number of cognitively-healthy participants were scoring within the cognitive impairment spectrum on the MMSE (chapter [5]) and the MoCA (chapter [6]). More importantly, this was also the case for scores on the RUDAS which was developed as a culture-free cognitive assessment (Storey et al., 2004). However, despite the assessments being administered in the participants' native language (Urdu), the sample of cognitively-healthy older adults scored within the impairment spectrum. In clinical settings, they may have potentially been referred to specialist services for a more in-depth assessment with a probable diagnosis of AD.

The next piece of research within this thesis (chapter [6]) focused on assessing cognitive performance on a brief battery of domain specific neuropsychological assessments proposed to have lower reliance on language and education (DR, PCS, LCS, DSF, DSB, TMT A&B, SDMT and DT) comparatively to an assessment of general cognitive function, the MoCA, with high reliance on language comprehension (both written and spoken).

However, it transpired that participants were performing closer to the population norms in the single assessment of general cognitive function when compared with the global z-scores on the battery of brief assessments. Performance on all assessments, except for the adapted TMT A&B, was below the population norms. This suggested that even when assessments may not have an obvious education effect, familiarity with the testing situation, which is often better in those who have higher levels of education (Goudsmit et al., 2018), is an important factor to be considered when administering cognitive assessments to less educated minority populations.

Notwithstanding, some interesting findings emerged which indicated that the sample of South Asian older adults performed significantly closer to the population norms in assessments measuring the domain of processing speed. This is an aspect of cognition not assessed in commonly used general cognitive assessments like the MMSE, RUDAS and MoCA. This is despite research demonstrating that individuals with phosphorylated tau pathologies, which are biomarkers in the early stages of AD (chapter [2)], experience a significant decline in processing speed ability (Ho and Nation, 2018; Haworth et al., 2016).

Based on this, the current chapter aimed to apply the knowledge gained from the studies in this thesis so far to develop and pilot a new assessment of general cognitive function, and a novel assessment of spatial associative memory which are discussed in more detail later in this chapter. These tests are being developed to address the current lack of validated cognitive tests conceptualised and developed with an ethnic minority population.

7.1.2. Why an assessment of general cognitive function?

Cognitive decline characteristic of conditions like AD is progressive in nature and it cannot be explained by impairment of a single domain (Duong et al., 2017). Therefore, assessments of general cognitive function are more appropriate as these allow researchers to assess a wide range of cognitive domains within one single test. Also, chapter [6] of this thesis revealed that performance on the MoCA, a single assessment of general cognitive function, was closer to the population norms when compared with performance on brief domain specific assessments.

NICE (2018) also recommend the routine use of assessments measuring more than one aspect of cognition in primary care settings. This provides an overview into the patient's cognitive functioning and allows clinicians to determine the severity of symptoms and need for further referral and treatment.

Therefore, the present chapter aimed to develop and evaluate the preliminary use of a newly developed assessment of general cognitive function in a sample of South Asian older adults. This assessment was conceptualised by building on the limitations of established assessments like the MMSE, MoCA and RUDAS. The reason these assessments were used as a guide is because despite their flaws in detecting early cognitive impairment in minority samples, their sensitivity in accurately identifying cognitive impairment has been established in Caucasian samples which is also reflected in their continued widespread use in the present research literature (Blakemore et al., 2018).

7.2. The Universal Neuropsychological Assessment Scale (UNAS)

When developing the items on the UNAS, the aims were to **(i)** identify cognitive domains associated with early cognitive impairment; **(ii)** formulate potential items which allow to measure the cognitive domains identified; **(iii)** optimise the formulation of items to ensure that cultural and linguistic adaptions allow to maintain their psychometric properties **(iv)** and pilot the assessment in a sample of cognitively-healthy South Asian older adults.

The next section describes and evaluates the items assessed by the UNAS. A copy of the UNAS can be found in the materials section of this chapter.

7.2.1. Item 1: Orientation to time

Research has suggested that orientation to time is a good predictor of cognitive decline overtime in older adults, and not being able to identify the time or month correctly is argued to be a sensitive indicator to warrant a more detailed assessment into an individual's cognitive abilities (Guerrero-Berroa et al., 2009). This is further supported by O'Keeffe et al. (2011) who assessed orientation to time in an older adults' sample formed by 262 participants of which 62 were diagnosed with dementia (type not specified). Their research findings suggested that the inability to correctly identify the year was the most salient sign of dementia and the severity of this inability was also strongly associated with the severity of dementia.

Moreover, Yew et al. (2013) investigated whether orientation (spatial and temporal) was a better diagnostic marker for AD compared to memory, and whether it could be attributed to other neurodegenerative conditions, such as frontotemporal dementia. They studied this in a sample of 190 participants (73 = AD patients; 54 = patients with frontotemporal dementia; 63 = cognitively-healthy controls). Participants were assessed using voxel-based morphometry analysis and MRI scanning. Memory and orientation were assessed on the Addenbrooke's Cognitive Examination which is a measure developed with the aim to identify dementia and differentiate between AD and frontotemporal dementia (Bruno and Vignaga, 2019). The findings from Yew et al.'s (2013) research indicated that patients with AD had memory and orientation impairments, whilst patients with frontotemporal dementia performed at control level (below the cognitive impairment spectrum) for orientation but scored poorly on memory. They also conducted voxel-based morphometry analysis which showed that the neural correlates for orientation and memory were disassociated, with orientation being associated with the posterior hippocampal cortex and memory with the anterior hippocampus, both in patients with AD and frontotemporal dementia. Yew et al. (2013) concluded that orientation deficits caused by atrophy in the posterior hippocampus are specific to AD which should allow clinicians to discriminate AD patients from those suffering from memory deficits characteristic of other conditions.

Therefore, with evidence suggesting that orientation is an important early predictive factor for cognitive decline in AD, and objective evidence confirming its physiological basis (Yew et al., 2013) makes it imperative to include this item in the new assessment.

This has been incorporated into the new assessment by asking participants the year, month, and day of the week on the day of the assessment. Also, the item in the MMSE which prompts participants to state the time has been modified. As opposed to asking the time, participants are asked to state whether it is the morning or the afternoon. This aims to minimise the chance of participants losing a point due to not being able to tell the time due to lower literacy levels, which are common in South Asian older adults residing in the UK (Blakemore et al., 2018).

7.2.2. Item 2: Registration

As discussed, memory is an integral part of any neuropsychological assessment (Kuo, 2017) and therefore it was important to incorporate an item assessing registration for the purposes of assessing delayed word recall. Registration plays an important role in the formation of memories by allowing to encode the information received which is then processed and stored for later retrieval (Kuo, 2017). Therefore, in the absence of an item adequately measuring registration, there is a potential for the test scores on the delayed word recall item to be misleading.

De Simone et al. (2019) assessed whether free immediate recall and recognition might be a key factor in predicting amnesia in MCI cases and subsequent progression to AD. To investigate this, they assessed immediate and delayed recall in 80 patients diagnosed with MCI on a 15-word list. They implemented a longitudinal research design whereby participants were re-assessed after a period of three years from the first assessment. The results indicated that patients who developed aMCI forgot significantly more words from immediate to DR when compared with the healthy controls. De Simone et al. (2019) concluded that this could prove to be a useful diagnostic tool in predicting the progression from MCI into more severe stages. Therefore, considering that the UNAS also incorporates an item of DR, it makes it imperative to incorporate an item of registration.

In the UNAS, the registration task requires participants to repeat ‘money’ ‘chair’ and ‘biscuit’ which have been chosen due to their cultural irrelevance and availability of corresponding words in the Urdu language (“paisa”, “kursi” and “biskit”). For example, in the MMSE the word ‘penny’ is used, however some South Asian older adults may not deal with money in the UK due to reliance and dependability on carers which is common in this group of people (Blakemore et al., 2018) making this word potentially inappropriate in the current sample. The generic word “money” has been used as opposed to the more particular word “penny”. Also, the current assessment aims to develop a standardised test which can be accessible and utilised by other populations with similar characteristics, and not just in the UK. Therefore, it is important that words such as, “penny”, are replaced as these refer to the currency in the UK which would not be culturally appropriate for use in other countries with similar populations, but different currencies. Penny is also the informal version of “one pence”, and therefore individuals from diverse backgrounds may not be aware of this also.

7.2.3. Item 3: Attention and Calculation

Attention and calculation deficits have been identified as the first non-memory domain affected in AD and they are reported to be a good predictor for the presence of MCI (Bracco et al.,2014; McGuinness et al., 2010; Ivanchak et al., 2012). McGuinness et al. (2010) investigated information processing and attention in patients with mild AD and vascular dementia. They investigated this in a sample of 75 patients diagnosed with AD, 46 patients with vascular dementia and a healthy control of 28 participants. They assessed attention and information processing on the original TMT A&B and the Stroop test. Participants also had a CT scan to measure white matter changes. The findings revealed that attention was affected both in patients with AD and vascular dementia, with vascular dementia patients exhibiting more impaired reaction times as opposed to attention deficits. From their findings, McGuinness et al. (2010) concluded that attention networks are affected in mild stages of AD and proposed that attention should be routinely measured in clinical settings as an early biomarker for AD.

Further to the above, Niccolai et al. (2017) investigated decline in financial capacity in individuals with MCI. Their sample was formed by 66 cognitively-healthy participants (mean age = 66.3 years; mean years in education = 15.1 years) and 48 participants diagnosed with MCI (mean age = 71.4 years; mean years in education= 14.7years). The Financial Capacity Instrument (FCI) was administered which assesses financial abilities through seven core domains including basic monetary skills, financial conceptual knowledge, cash transactions, chequebook management, bank statement management, financial judgement, and bill payment skills (Marson et al., 2000). Niccolai et al. (2017) assessed their sample on the FCI at baseline and after a follow-up period of two years. The findings demonstrated that the MCI group experienced a significant decline on FCI scores while the control group's performance remained stable. In particular, the MCI group experienced a significant decline in the items measuring written arithmetic (e.g., tasks involving the manipulation of numbers – subtractions, multiplications, and divisions). Moreover, and to a lesser degree, a significant decline was also observed in items measuring attention. It was thereby concluded that clinicians should consider arithmetic abilities when assessing patients with MCI. A previous study by Martin et al. (2003) also found that decline in calculation abilities is a cognitive hallmark of AD.

Notwithstanding, research in this thesis has suggested that cognitively-healthy South Asian older adults tend to experience a decline in their test scores in assessments involving the completion of mathematical tasks. This is potentially attributed to the lower literacy and education levels characteristic of this group (Blakemore et al., 2018) (chapter [3]). Based on this, the UNAS will replace the serial subtraction tasks present in the MMSE and MoCA by requesting participants to name the days of the week in reverse order in a familiar language to screen for attention.

As a measure of calculation, participants will be required to perform a subtraction task. However, to make it appropriate for a sample known to have lower literacy levels, the use of written numbers has been limited by providing a context which gradually requires the participant to verbally tell the researcher how many books remain following a chain of events.

7.2.4. Item 4: Language

Speech and language difficulties are also a salient aspect in the development of AD, and patients often demonstrate difficulties in word finding, sentence comprehension and a lack of cohesion in discourse (Banovic et al., 2018; Tsantali et al., 2013; Kempler and Goral, 2008).

For example, Tsantali et al. (2013) investigated language deficits in a sample of 28 patients with aMCI, 53 with mild AD (mAD) and a cognitively-healthy control of 38 participants. Language was assessed on the Boston Diagnostic Aphasia Examination. The results indicated that verbal fluency, reading comprehension and narrative ability were the main language domains affected in AD and were almost intact in normal controls. This is also consistent with research by Schecker et al. (2014) who investigated the association between cognitive slowing and speech in patients with AD. They assessed processing speed and language performance on a computerised Stroop paradigm in a sample of 72 healthy controls and 52 patients with mild AD. The results of the data obtained indicated that the AD group scored significantly worse in all language related items and had longer reaction times.

Therefore, the above literature supports the inclusion of an item assessing language in the new assessment. Language will be measured by requiring participants to verbally form a sentence in the correct grammatical order as opposed to requiring them to read or write a sentence. The reading and writing items, which are present in the MMSE, RUDAS and MoCA, will be avoided in this new assessment due to the requirement of literacy skills to complete these items, which again are likely to be lacking in some participants if not all in this cohort as discussed in chapter [3].

7.2.5. Item 5: Processing Speed

An item assessing processing speed is implemented because this is a cognitive domain not assessed by the MMSE, RUDAS or the MoCA. This is despite research suggesting that processing speed deficits are common in MCI and early stages of AD (Lu et al., 2017).

Lu et al. (2017) investigated the characteristics of processing speed and their diagnostic value in NCD patients, which is a term for MCI. They assessed a sample of 31 adults with NCD caused by vascular disease (mean age = 73.46 years), 36 patients with NCD due to AD (mean age = 73.35) and a healthy control of 137 participants (mean age = 71.45 years). Amongst other domains, Lu et al. (2017) assessed processing speed on the flanker test which involves the presentation of a conflict between an intended correct response and an irrelevant/misleading alternative and reaction times in identifying the correct target are recorded. Lu et al. (2017) found that the NCD-AD group of patients experienced a significant decline in reaction times compared to the healthy controls, as well as the NCD-vascular group. Therefore, supporting the presence of processing speed deficits in patients with early stages of AD.

Processing speed has also been associated with tau pathologies which are reported to be present in the earliest stages of AD (Ho and Nation, 2018; Haworth et al., 2016; Jack et al., 2013). Research shows that tau is one of the earliest pathological biomarkers to develop in AD (Aksman et al., 2020) and ongoing treatment trials call for reliable and quantifiable tau biomarkers to improve treatment effectiveness (Cumming et al., 2018). Moreover, the National Institute on Ageing and Alzheimer’s Association claims that there is a direct association between tau and early stages of AD, and they have subsequently incorporated the presence of tau biomarkers in their research criteria for the diagnosis of AD in its earlier stages (Jack et al., 2018).

This evidence supports the claim that the absence of processing speed items in existing assessments can lead to a failure in detecting early pathologies and cognitive changes in a timely manner. This is particularly concerning due to the long prodromal stage of AD (Beason-Held et al., 2015**).** Moreover, the findings from the current thesis suggested that South Asian older adults performed the closest to the population norms in assessments of processing speed. This offers potential to further explore the use of assessments taxing processing speed as part of the process to improve neuropsychological testing in this population.

The processing speed item in the UNAS has been adapted from the PCS and LCS (Salthouse and Babcock, 1991). To assess for processing speed, participants will be presented with five pairs of pictures and asked to confirm whether the two items are the same or different. They will have ten seconds to complete this task and points will be awarded for the number of correct responses within the period of ten seconds. This assessment is being timed because it is a processing speed task and the original PCS and LCS are also timed tasks. The timing of ten seconds has been determined to allow 2 seconds per pair, however the adequacy of this time limit requires to be explored in this study and future continuations which may lead to potential alterations.

This assessment has removed the geometric and alphabetical element used by the PCS and LCS. The task only requires visualising photographs of objects which is proposed to reduce the chances of distraction due to being presented with an unfamiliar stimulus (e.g., English letters or abstract symbols). Moreover, a previous study discussed in chapter [4] by Lusting et al. (2006) found that their sample of cognitively-healthy adults failed to perform well on the PCS and LCS and proposed that this was given due to the paper and pen version presenting a large number of letters and patterns on a single piece of paper which acts as a distraction, slowing down overall reaction times in healthy cohorts. To limit the chances of distraction, the current assessment has limited the number of objects to five, which has required for the overall time to complete the task to be reduced to ten seconds. The pictures used can be seen in figure one.

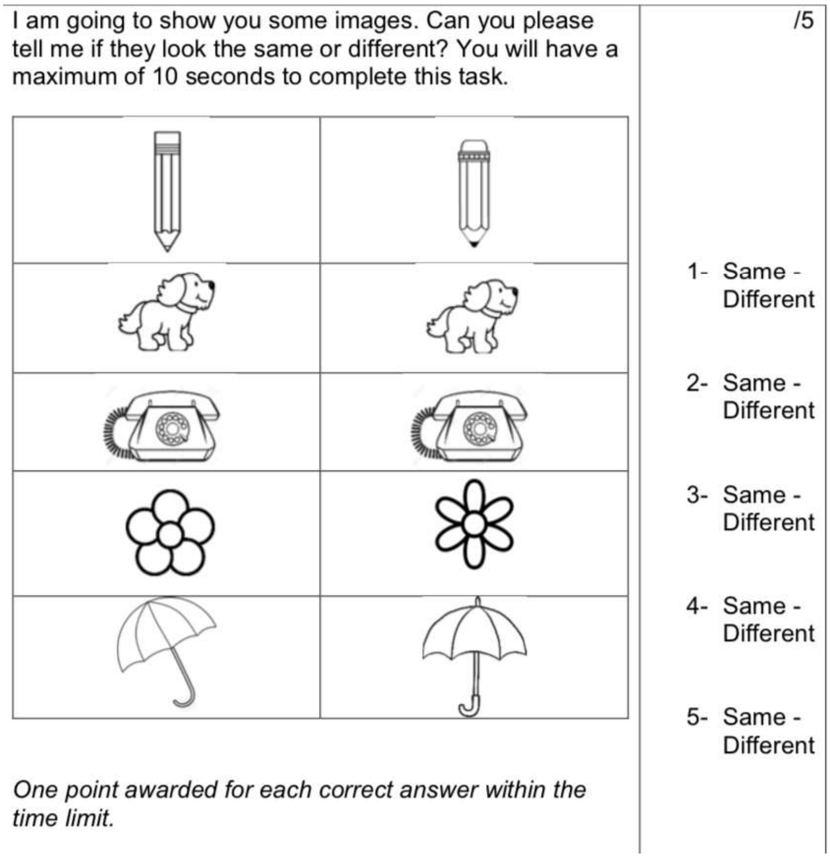


Figure one: Item 5 of the UNAS, test of processing speed.

7.2.6. Item 6: Executive Function

The current knowledge base on AD suggests that deficits in frontal lobe activity, which modulate EF, are an important hallmark of the disease in its early stages (Bellaj et al., 2017). However, assessments like the MMSE fail to adequately measure this cognitive domain.

Garcia-Alvarez et al. (2019) investigated working memory and EF impairments in MCI. They assessed a sample of 48 MCI patients, 57 AD patients and 124 cognitively-healthy controls on a range of assessments measuring working memory and EF. MRI and brain morphometry measures were also taken to assess frontal lobe integrity indexes and functioning. The results demonstrated that patients with MCI exhibited the worse performance on almost all assessments of working memory and EF. Garcia-Alvarez et al. (2019) found that EF impairments were associated with reduced prefrontal cortical thickness which accounted for over 50% of the variance in functional competence on EF tasks. It was thereby concluded that EF impairments are characteristic of MCI, and even in this prodromal stage they have the potential to cause deleterious consequences due to compromised activity in the frontal cortex (Garcia-Alvarez et al., 2019).

Based on the above, a new version of the TMT A&B has been developed for use in the UNAS (see figure two below). In this task, participants will be asked to join circles in ascending order by counting the number of lines inside each circle and alternating between white and black circles. This has been adapted from Kim et al.'s (2014) adapted version of the original TMT A&B which reduced the education bias by removing the alphabetical component in the original test. The current version further adapts this assessment by removing the western numerical values (i.e., 1,2,3, etc) and replacing them with lines representing the quantity of the numbers (e.g., I = 1; II = 2; III = 3) which is aimed to further reduce the educational bias in this assessment.

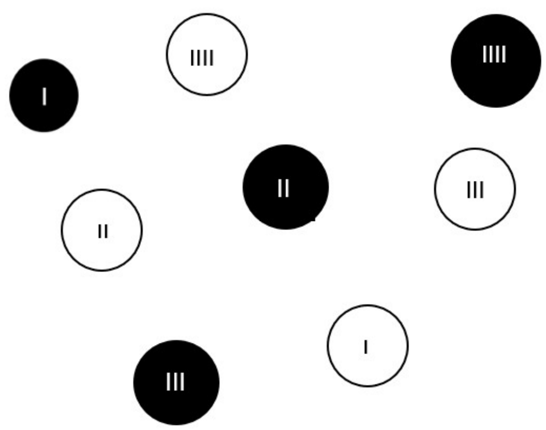


Figure two: Item 6 of the UNAS, the adapted TMT A & B.

7.2.7. Item 7: Delayed Recall (DR)

A DR item will also be incorporated as a measure of short-term memory whereby participants will be required to recall the three words in the registration task (money, chair, and biscuit). Items measuring DR are being retained in the development of a new assessment as DR is argued to be more sensitive to MCI and early AD and has been found to be a good predictor of future cognitive decline (Gustavson et al., 2020; Talamonti et al., 2019; Champan et al., 2011; Dubois et al., 2007). Moreover, research by Lu et al. (2017) (discussed in section 7.2.5.) further found that their sample of patients with early AD performed significantly worse on the DR assessment measuring short-term memory when compared to the healthy controls. The involvement of memory in the early stages of AD is also discussed in section [7.2.2.] above.

7.2.8. Deletion of the copying task

The pentagon (MMSE) or cube copying tasks (RUDAS, MoCA), which assess visuospatial abilities, are characteristic of all the commonly used general cognitive tests. However, the UNAS will not incorporate copying tasks because these place a high reliance on literacy skills to complete successfully (Goudsmit et al., 2018; Ardila et al., 2010), which was also observed in chapter [6] of this thesis. This may be explained by the lower levels of education in this group of individuals implying that they may not have had the opportunity to develop dexterity skills to a higher level through frequent writing and drawing as well as a lack of familiarity with geometric shapes (Ardila et al., 2010; Parker and Philp, 2004).

7.2.9. Scoring and normality cut-offs

The UNAS is a quantitative measure which, in its preliminary form will be scored out of 30 to allow for direct comparability between the MoCA which also assess EF and is thought to be a better measure of MCI (Pinto et al., 2019). However, the scoring may need adjustments in future continuations of this research. The current chapter will also apply the same cut-off scores as the MoCA, however true cut-off scores cannot be determined at this stage until further work has been carried out in clinical samples.

To assess the psychometric properties of the new assessment and its usefulness, reliability will be assessed by using a Cronbach Alpha analysis. Test re-test reliability will be checked by re-assessing participants following one week from the initial session. The re-test period was determined based on research by Storey et al. (2004) who developed and piloted the use of the RUDAS and re-tested their sample following one week from the initial testing session for the purposes of the test re-test reliability analysis.

7.2.10. Proposed advantages of the UNAS

The UNAS is hoped to be relatively easy to administer taking no longer than 15 minutes to complete and it can be administered by skilled and un-skilled health workers without the need for any additional training. Unlike other established tests, such as the MMSE, the new assessment incorporates items measuring EF as well as processing speed which have been associated with decline in the early stages of AD (Lu et al., 2017; Bellaj et al., 2017). The assessment of domains which are more sensitive to decline in the earlier stages of the disease may contribute towards early diagnosis increasing the potential for treatment interventions to be more effective in delaying the progression of the disease (Liew et al., 2019). Moreover, early identification offers an opportunity to participate in clinical trials aimed at contributing towards the development of disease modifying drugs (Kriebel-Gasparro, 2020; Liew et al., 2019).

The items on the new assessment have also been developed to allow for direct translations without the items losing their meaning or conceptualisation. This is important to achieve because it is aimed that with future testing, the UNAS will be suitable for use in people from across different backgrounds with similar characteristics. Therefore, the potential for direct linguistic translations without losing contextual meaning will be highly imperative and beneficial in ensuring a reliable use of the UNAS in different populations.

The items in the UNAS have significantly limited the use of a pen and paper to complete the test, which is particularly important when working with a population that is known to have lower levels of education and literacy skills (Blakemore et al., 2018). Assessing and interpreting an individual's poor drawing abilities and reading is unlikely to be valid when someone has potentially never, or very rarely used a pen or attained any education. Also, reducing the use of items requiring the use of a pen and paper removes potential issues in completing neuropsychological assessments by people with motor diseases, such as Parkinson's disease or arthritis, which tend to be common in older adults (Willis, 2013), for whom this assessment has been developed for.

7.3. Development of the Spatial Associative Learning Test (SALT)

This chapter further aimed to develop and evaluate a newly created assessment of visual associative memory, the Spatial Associative Learning Test (SALT) which was administered to the sample in conjunction with the UNAS.

The rationale behind developing and implementing the SALT comes from current literature which suggests that a particular type of memory which has been shown to be sensitive in the earliest stages of AD is spatial/episodic memory which forms part of associative memory (Parra et al, 2010; Della Sala et al., 2012; Rubino and Andres, 2018).

Associative memory is defined as the ability to learn and remember the association between unrelated items (e.g., the name of a person with a particular aroma) (Suzuki, 2005) and it is argued to be mediated by the activity of the medial temporal lobe which is shown to experience atrophy in the early stages of AD (Spaan, 2016; Shen et al., 2011). This area has also been found to play a crucial role in memory function (Feczko et al., 2009), navigation (Laczo et al., 2009) and has been implicated in MCI and early AD (Chen and Chang, 2016; Della Sala et al., 2012; Amariglio et al., 2012).

There are a range of tests available which assess associative learning, these include the Face-Name Associative Memory Exam which includes 16 face-name pairs and 16 face-occupation pairs for participants to remember and it has been found to be a useful measure to assess subtle changes in the preclinical phase of AD (Rentz et al., 2011; Parra et al., 2010).

A further assessment of associative memory is found in the Cambridge Neuropsychological Test Automated Battery (CANTAB) which is a computerised tool dedicated to assessing detailed cognitive functioning and it includes an item measuring paired-associative learning (PAL) (Cacciamani et al., 2017). The PAL is an assessment of visuo-spatial associative memory and requires the participant to learn the association between a visual stimulus and a spatial location (Egerhazi et al., 2007). Participants are presented with a computer screen with six white boxes which open in a random order. Participants are required to remember the box in which a pattern appeared, and their responses are recorded by pressing the relevant box on a touch screen. The task progressively increases in difficulty by requiring participants to remember two different patterns and their location, which subsequently increases to a maximum of six patterns across six locations. The scoring involves calculating the number of errors made on the six-pattern stage which has been shown to be sensitive to MCI and early AD (Blackwell et al., 2004; De Rover et al., 2011).

Early research in associative learning and the implementation of the PAL comes from research by Blackwell et al. (2004). They investigated performance on the PAL, amongst other cognitive assessments, as a potential marker for pre-clinical AD in a sample of 43 participants with a mean age of 64.83 years. Following a period of 32 months, 11/43 participants met the criteria for probable AD diagnosis (converters) and 29 remained free from AD (non-converters). This was assessed by the means of 20 neuropsychological assessments implemented at four intervals (baseline, after eight, 16 and 24 months). The results indicated that based on the scores on the battery of neuropsychological assessments, the two assessments of memory which had the highest accuracy in identifying probable AD were the CANTAB-PAL and the Graded Naming Test, which the authors concluded to be highly accurate assessments in the detection of cognitive impairment in preclinical AD.

The above findings are linked with neuroimaging studies which demonstrate that spatial associative memory has its basis in the entorhinal cortex, which is the first point to degenerate in the hippocampus in cases of early AD (Howett et al., 2019; Blackwell et al., 2004). In particular, NFTs and tau pathologies (see chapter [2]) are often first visualised in the entorhinal cortex in MCI cases (Soldan et al., 2016; Guillozet et al., 2003)

For example, Soldan et al., (2016) assessed cognitive performance on the CANTAB-PAL with the aim to establish an association with biomarkers of amyloid, tau, and phosphorylated tau (p-tau) which had been obtained approximately ten years earlier through CSF. The results indicated that poor performance on the CANTAB-PAL was strongly associated with higher levels of CSF p-tau. Based on this, Soldan et al. (2016) concluded that performance on the CANTB-PAL was associated with CSF p-tau pathologies which, as previously stated, cause atrophy in the entorhinal cortex early in the development of AD (Howett et al., 2019).

In line with the above findings, research has also found that one of the early symptoms in AD is that people struggle to learn new routes and they tend to get lost in 40% of AD cases which increases to 70% in more severe cases often leading to institutionalisation (Yatawara et al., 2017). It is stipulated in the literature that these navigational deficits are associated with changes in visuo-associative spatial memory which has implications for successful navigation through the environment and it has its basis in the hippocampus as discussed above (Laczo et al., 2019; Burgess et al., 2002; Lithfous et al., 2013). Issues in navigating and orientating in the environment are referred to as "topographical disorientation" (TD) which subsequently causes difficulties in navigating through locations and recalling known routes as well as learning new routes (Barrash et al., 2000)

TD has been found to be one of the earliest symptoms of AD and it is an aspect of associative memory (Lithfous et al., 2013; Serino and Riva, 2013). It is estimated that 25% of AD patients present with TD and this increases to 50% within the first three years following diagnosis (Pengas et al., 2010). It is further important to acknowledge that these figures are likely to be an underrepresentation as often patients hide their TD by implementing new strategies and avoiding new routes or places (Serino and Riva, 2013). Consequently, this leads carers only becoming aware of patients' spatial difficulties when they are away from home and must remember new places and routes (Pengas et al., 2010).

Navigational deficits have also been found in patients with MCI (Cushman et al., 2008). Moreover, patients with MCI who experience navigational deficits have been found to be at a greater risk of rapid conversion to AD (Laczo et al., 2011).

Therefore, widespread evidence supports the importance of spatial associative memory abilities as a salient factor in the early stages of AD and MCI and this is also supported through neuroimaging studies (Lithfous et al., 2013; Laczo et al., 2011).

However, to the best of our knowledge, there is little to no mention of any papers in the literature investigating this cognitive domain in South Asian older adults in the UK. Moreover, measures of general neuropsychological assessment do not incorporate assessments of associative learning as a standard procedure. Therefore, based on the lack of implementation of assessments of associative learning as a standard measure of cognitive decline, the current chapter aimed to develop and pilot the use of the SALT as a novel test of spatial associative memory in the underrepresented South Asian older adults.

Commonly available assessments of associative learning, such as the CANTAB-PAL, involve the use of electronic devices. However, this is unlikely to be adequate for individuals who have poor literacy and education levels as they may not be familiar with using electronic devices, which often require participants to follow written instructions on the screen.

Based on the needs of the current sample, a visuospatial associative task has been developed which is discussed in detail in the materials section of this chapter.

It is important to acknowledge that although in this study the UNAS and SALT are being administered together, it is not being suggested that this should be the standard practice. Moreover, assessments of associative learning discussed offer a potential to be adapted in a way that the involvement of cultural related knowledge and experience in completing the assessment is limited. Existing assessments of associative learning do not have a language or numerical component and they simply rely on visual cues and presentation of patterns. It should be easy to adapt these by creating a paper version, and instructions can be verbally relayed by the researcher in a language that the participant is familiar with.

To summarise, the UNAS and SALT have been developed to target cognitive domains known to decline in the early stages of impairment. Moreover, the items have been conceptualised and developed to reduce the educational and cultural bias associated with established assessments like the MMSE and MoCA. This is aimed to improve the adequacy of cognitive screening in the underrepresented South Asian community in the UK.

7.4. The present study: Research aims

The current research aimed to **(i)** pilot the use of the UNAS and SALT as novel measures of cognitive performance in a South Asian older adults sample; **(ii)** compare cognitive performance on the UNAS with test scores on the established assessment of general cognitive function, the MoCA, which has similar psychometric properties to the UNAS; **(iii)** assess the effect of education on test scores on the UNAS, MoCA and the SALT **(iv)** and assess the internal and test re-test reliability of the UNAS, MoCA and SALT.

Based on the literature discussed, it is hypothesised that **(i)** participants will perform better on the UNAS compared to the MoCA; **(ii)** the UNAS and SALT will not be affected by education levels, however education effects will be present in the MoCA and **(iii)** the UNAS and SALT will have high test re-test and internal reliability as assessed by a Cronbach Alpha and Pearson correlation analysis.

7.5. Methods

Ethics approval for this research was granted by the Chair of the Humanities, Social and Health Sciences Research Ethics panel at the University of Bradford on 18 April 2019.

7.5.1. Participants

The sample was formed by 49 participants (28 males, 21 females) from a South Asian background (Pakistani, Bengali, and Indian).

The inclusion criteria for the present study specified that participants were required to be aged 60 years or over, residing in the UK, from a South Asian background (Pakistani, Bengali, or Indian), fluent in Urdu/Hindi, must not poses a medical condition affecting their cognitive abilities or the ability to provide informed consent to understand the procedures of the study and that they must have adequate motor and sensory capabilities to perform neuropsychological assessments.

7.5.2. Design

A within subjects/repeated measures experimental design was implemented as all participants completed the UNAS, the MoCA and the SALT at baseline and they were re-tested following one week.

7.5.3. Materials

Participants were administered two assessments of general cognitive function (UNAS and MoCA) and a novel assessment of associative memory (SALT).

UNAS: The UNAS is a seven-item questionnaire assessing the domains of short-term memory, working memory, orientation, EF, processing speed, language, attention, and calculation. In its preliminary form, it is scored out of

30 to allow for direct comparisons between the UNAS and the MoCA. However, unlike with the MoCA, in its current form no education related adjustments will be made as it is proposed that the UNAS will not be affected by education levels.

The assessment was administered verbally in Urdu and the responses were recorded by the researcher. A pen and paper were only required for participants to complete the EF and processing speed task of TMT A&B whereby participants were required to connect circles using a line. A copy of the UNAS can be found in figure three below.

Universal Neuropsychological Assessment Scale (UNAS)

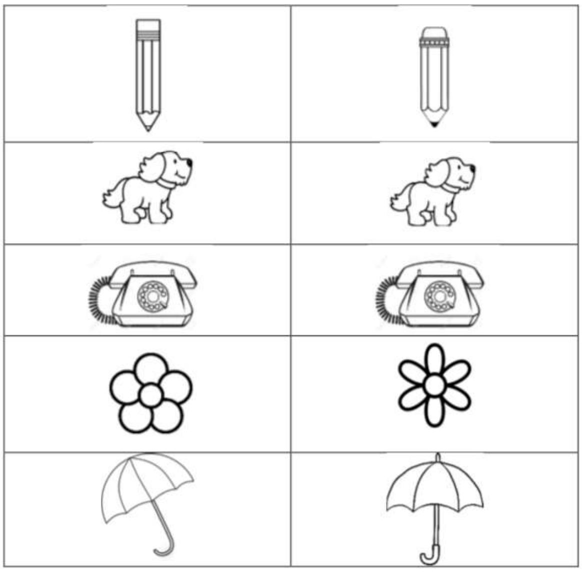
Participant Number:

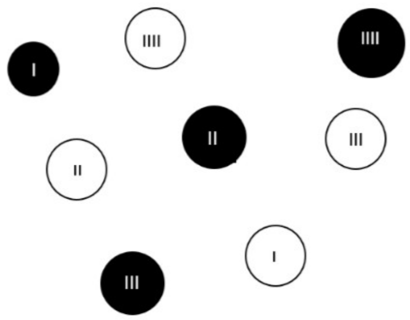
Researcher:

Date:

Time:

Domain	Item	Score
Item 1. Orientation	Could you please tell me the following? What year is it? What month is it? What day of the week is it? Is it the morning, or the afternoon? *One point per correct answer.*	/4
Item 2. Registration	Can you please repeat the following words after me? Money Chair Biscuit *One point per correctly repeated word (these will only be repeated once).*	/3
Item 3. Attention	Could you please tell me the days of the week from Monday-Friday in reverse order? Friday Thursday Wednesday Tuesday Monday *One point per correct day stated.*	/5
Calculation	You buy eight books. You arrive home and realise that the bag you were carrying these in has a big hole and two books have fallen out. How many books do you have left? You then decide to gift two of the books to your nephew, how many do you have left now? Later, your friend comes over, and he borrows two books. How many do you have left now? *One point per correct calculation.*	/3

Item 4. Language	Could you please form a complete sentence about anything you wish? *The sentence must include a noun and a verb in correct order.* Following a command: Can you please pick-up the piece of paper on the table and fold it in half? *Point for each command followed correctly.*	/1 /2
Item 5. Processing Speed	I am going to show you some images. Can you please tell me if they look the same or different? You will have a maximum of 10 seconds to complete this task.  *One point awarded for each correct answer within the time limit.*	/5 1- Same - Different 2- Same - Different 3- Same - Different 4- Same - Different 5- Same - Different
Item 6. Executive Functioning	Could you please join the circles in ascending order based on the number of lines inside them by alternating between white and black circles?	/4

	 *Points awarded for correctly completing the full task.*	
Item 7. Recall At end	Could you please tell me the three words I asked you to repeat earlier? *One point per correct word recalled.*	/3

Total Score: /30

Figure three: Copy of the Universal Neuropsychological Assessment Scale (UNAS)

MoCA (Nasreddine et al., 2005): This is an established assessment of general cognitive function which has similar psychometric properties to the UNAS (see chapter [4] for detailed outline of the MoCA). The MoCA is scored out of 30 and scores of 26 or above represent normal cognition (Nasreddine et al., 2005). As part of the standard scoring system for the MoCA, an additional point is awarded to participants with 12 or less years in education. The use of a paper and pen was required to complete the items in this assessment. However, all instructions were provided verbally in Urdu.

SALT: This is a measure of visuospatial associative memory. It involves participants being presented with six different A4 sized papers representing six trials. Each sheet contains six rectangular boxes and a circle in the middle. In the first trial, five of the boxes were black and the sixth box contained a neutral image and participants were required to remember and recall the location of the image. There is a total of six trials and with each increasing trial the number of boxes containing a picture also increases.

Participants were presented with the first sheet (trial) for three seconds and the time increased in intervals of additional two seconds per additional trial. They were then asked to remember the location of each picture and requested to identity the box they saw this picture in a blank sheet with all six boxes covered. In the first trial, only one picture is to be shown and this increases with the number of trials. Therefore, the second trial displayed two pictures to be remembered, the third three pictures and so on. Therefore, task difficulty progressively increases with each trial.

Participants were only provided with one chance to correctly identify the box and the total number of correctly identified boxes was scored. Therefore, the assessment carries a maximum score of 21. The higher the score, the better the performance.

It is also important to note that unlike other assessments of associative memory, the SALT is administrated in the traditional paper format because of the nature of the current sample. Namely, due to the sample having lower literacy levels they may not be familiar with the workings of a touch screen computer which may bias performance for reasons other than actual cognitive deficits. However, future continuations of the research may evaluate the development of a more simplified electronic version which does not involve the engagement of participants in following instructions on a screen. This would allow to reduce administration time.

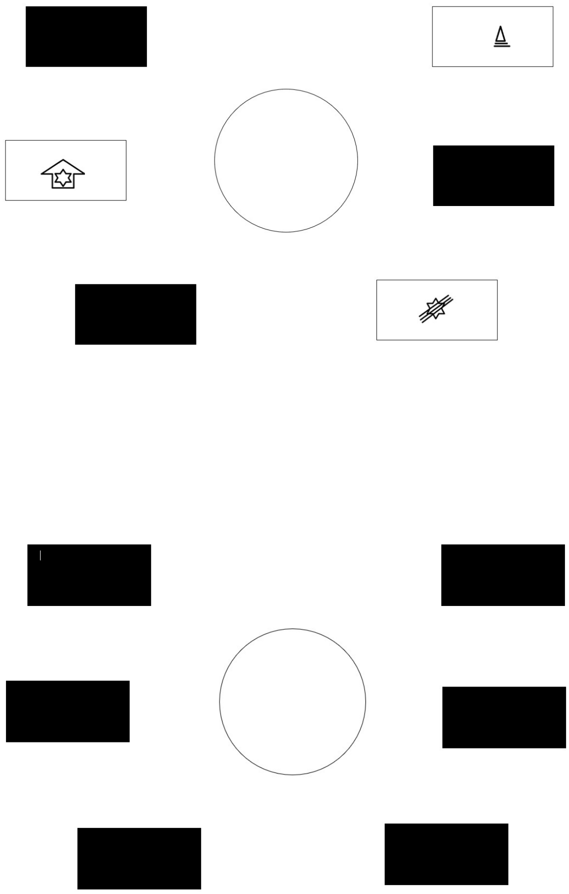


Figure four: Example of a trial in the SALT

Note: In the stage where participants were required to identify the location of the images, the relevant images were not all presented in the circle in the middle. However, single images were displayed one at a time to avoid distraction from displaying all the target stimuli inside one box.

7.5.4. Procedure

All potential participants were provided with an information sheet and read aloud the information in Urdu to ensure understanding. Participants were then contacted after 48 hours to ask them whether they wished to participate in the research. The research took place in participants' home in the presence of a carer or relative. Electronic devices which emit noises (e.g., TVs, radios) were turned off to minimise the number of distractions present at the time of testing. Participants signed a consent form, the contents of which were read to them in Urdu. Next, participants were asked to complete the UNAS followed by the MoCA and then the SALT in Urdu. Following this, participants were informed that this was the end of the first session and a further appointment was arranged to meet with them again after one week. In the second session, participants were required to complete all assessments again in the same order for the purposes of measuring for reliability.

7.6. Results

The current research piloted and evaluated the use of the newly developed assessment of general cognitive function, the UNAS and the novel test of associative memory, the SALT in a sample of South Asian older adults. It also aimed to compare performance on the UNAS with the MoCA to explore the adequacy of the UNAS in comparison to an established assessment. Lastly, the reliability of all three assessments was also measured.

7.6.1. Main participant demographics

Data with regards to the sample's age, years in education and gender is presented in table one.

Table one: Mean and SD for main participant demographics

	Mean	**±SD**
Age (years)	69.37	±7.57
Education (years)	4.88	±4.97
Gender (Males: Females)	28:21	

To explore whether any of the above demographic variables had an influence on cognitive test scores on any of the assessments administered, age, gender and education were submitted to a MANCOVA analysis. Test scores were entered into the model as dependent variables, gender as a fixed factor and education and age as covariates.

7.6.2. Main effects of age, gender, and education on test scores

No significant effects of gender were found ($p>0.05$). Wilk's Lambda was significant for age ($\Lambda = 0.41$, $p<0.01$) which revealed a significant decline in test scores with increasing age on all test scores both at baseline and re-test.

[**MoCA baseline** ($F(1,45)= 25.90$, $p<0.01$); **MoCA re-test** ($F(1,45)= 30.11$, $p<0.01$); **UNAS baseline** ($F(1,45)= 33.38$; $p<0.01$); **UNAS re-test** ($F(1,45)= 12.33$, $p<0.01$); **SALT baseline** ($F(1,45) = 18.39$, $p<0.01$) and **SALT re-test** ($F(1,45) = 13.32$, $p<0.01$)]

A regression analysis revealed a significant linear decline in test scores with increasing age on all assessments at both time points [**MoCA baseline** $\beta= -0.69$, $F(1,47)= 89.75$, $p<0.001$, Y axis intercept = 88.11 with regression correlation coefficient $r= 0.81$, $p<0.001$]; [**MoCA re-test** $\beta= -0.69$, $F(1,47) = 97.75$, $p<0.001$, Y axis intercept = 68.56 with regression correlation coefficient $r= 0.82$, $p<0.01$]; **UNAS baseline** $\beta=-.025$, $F(1,47)= 46.78$, $p<0.001$, Y axis intercept = 1.25 with regression correlation coefficient $r=0.71$, $p>0.001$]; **UNAS re-test** [$\beta= -0.16$, $F(1,47) = 35.24$, $p<0.001$, y axis intercept = 39 with regression correlation coefficient $r= 0.66$, $p<0.001$]; **SALT baseline** [$\beta= -0.27$, $F(1,47)$ 83.88, $p<0.001$, y axis intercept = 35.43 with regression correlation coefficient $r= 0.80$, $p<0.001$] and **SALT re-test** [$\beta= -0.27$, $F(1,47)= 44.10$, $p<0.001$, y axis intercept= 35.31 with regression correlation coefficient $r=0.70$, $p<0.001$].

Performance on neuropsychological assessments is also widely affected by education levels as observed throughout this thesis. Therefore, it was important to assess whether test scores on the UNAS, SALT and MoCA were affected by education levels.

Wilk's Lambda was significant for education ($\Lambda = 0.66$, $p<0.001$) which revealed that there was no significant main effect of education on the UNAS and SALT, both at baseline and re-test. However, a significant main effect of education was found on the MoCA at baseline ($F(1,45)= 17.79$, $p<0.01$) and re-test ($F(1,45) = 11.91$, $p<0.01$). A regression analysis revealed a positive linear increase in tests scores on the MoCA at both time points as the number of years in education increased [**MoCA baseline** β=1.01, F(1,47)= 76.45, p<0.001), y axis intercept = 7.06 with regression correlation coefficient r= 0.79, p<0.001]; [**MoCA re-test** β=0.97, F(1,47) = 63.99, p<0.001, Y axis intercept = 7.35 with regression correlation coefficient r= 0.76, p<0.001]. This is also depicted in figure two.

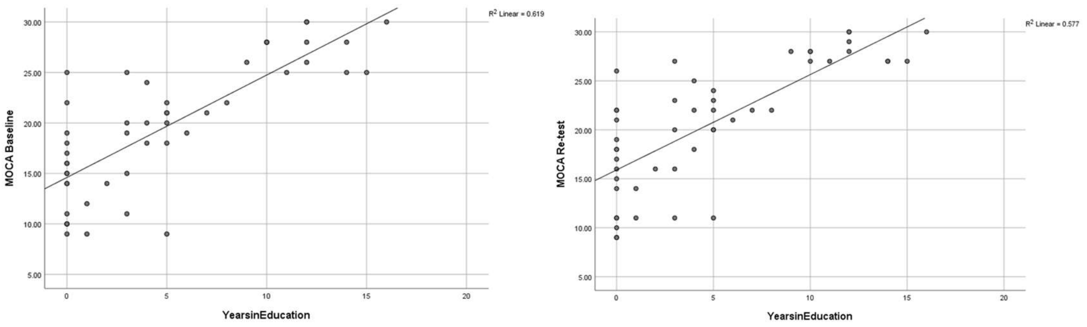


Figure one: Test scores on the MoCA at baseline and re-test indicating a significant linear increase in test scores with increasing number of years in education.

7.6.3. Cognitive performance on the UNAS, SALT and MoCA

Table two provides the mean and SD values for test scores on the neuropsychological assessments administered at baseline and during re-test (following one week from baseline test scores). The cognitive status on the UNAS and MoCA is also noted based on the cut-off scores for the MoCA.

Table two: Mean and SD for scores on the MoCA, UNAS and SALT at baseline and re-test

Assessment	**Baseline scores**	**Re-test scores**	**Cognitive status**
MoCA	19.55 (±6.40)	20.65 (±6.37)	Impaired (<26)
UNAS	27.80 (±2.68)	28.51 (±1.88)	Normal Cognition (>26)
SALT	16.83 (±2.54)	16.76 (±2.91)	N/A

The data in table two shows that scores were higher on the UNAS, and therefore better, both at baseline and re-test, when compared with test scores on the MoCA. The data was normally distributed as assessed by q-q- plots and test scores on the UNAS and MoCA at baseline and re-test were submitted to two paired sample t-tests with a new alpha value $p=0.025$. The analysis found a significant difference between test scores on the MoCA and UNAS at baseline ($t(48) = -12.14$, $p<0.01$) and re-test ($t(48) = -10.52$, $p<0.001$). This confirmed that cognitive performance was better on the UNAS when compared to the established MoCA, both at baseline and re-test.

No comparisons were established with test scores on the SALT as it is not comparable with the MoCA or the UNAS due to having a different scoring system and assessing a different cognitive domain (associative memory).

7.6.4. Reliability analysis of the UNAS, SALT and MoCA

The reliability of the assessments administered (MoCA, UNAS and SALT) was assessed on a Cronbach Alpha and through a Pearson correlation. The results of this analysis are presented in the next subsections.

7.6.4.1. Internal reliability: Cronbach alpha

Cronbach Alpha analysis was carried out as this is argued to be the most valid way to carry out an internal reliability analysis (Tavakol and Dennick, 2011). A coefficient of 0.7 or higher is considered acceptable as representing high internal consistency (Taber, 2017) with some even suggesting a value between 0.6 and 0.7 as reaching an acceptable level of internal reliability (Griethuijsen et al., 2014).

Cronbach's alpha showed that the MoCA (both at baseline and re-test) achieved an acceptable level of internal consistency [**MoCA baseline** $\alpha = 0.81$ (high); **MoCA re-test** $\alpha = 0.83$ (high)] implying that the test items measure the same construct consistently. According to the analysis, most of the items in the MoCA were worthy of retention because if deleted, the alpha value decreased.

The UNAS yielded a Cronbach alpha value of $\alpha = 0.7$ at baseline which is considered high. However, the Cronbach alpha value at re-test was $\alpha = 0.5$ which is considered to be moderate. All the items in the UNAS were worthy of retention because if deleted, the alpha value decreased reducing the overall internal reliability.

With regards to the SALT, a Cronbach alpha value of $\alpha = 0.6$ was achieved at both baseline and re-test which represents high/moderate level of internal consistency.

7.6.4.2. Test re-test reliability – Pearson correlation

Test re-test analysis was carried out on SPSS through a Pearson correlation. To assume consistency in test scores over time, the Pearson correlation must be $p<0.05$ with a correlation coefficient above 0.75. This is the recommended way of carrying out test re-test reliability (Coolican, 2019)**.**

The test scores on the MoCA at baseline and re-test reached high consistency over time with a correlation coefficient $r= 0.91$, $p<0.01$. Similarly, the UNAS achieved a correlation coefficient $r= 0.89$, $p<0.01$, and the SALT achieved a correlation coefficient of $r= 0.85$, $p<0.01$. Therefore, all three assessments had high levels of test re-test reliability implying that scores remained stable over a period of one week.

7.7. Discussion

The current research piloted and evaluated the use of the newly developed assessment of general cognitive function, the UNAS and the novel test of associative memory, the SALT in a sample of South Asian older adults. It also aimed to compare performance on the UNAS with the MoCA to explore the adequacy of the UNAS in comparison to an established assessment. Lastly, the reliability of all three assessments was also explored.

7.7.1. Main findings

(i) Test scores on the UNAS, SALT and MoCA decreased significantly with increasing age; **(ii)** test scores on the UNAS and SALT were not affected by the number of years in education, however test scores on the MoCA, both at baseline and re-test, increased significantly with increasing number of years in education; **(iii)** the sample of South Asian older adults scored significantly higher, and therefore better, on the UNAS when compared with test scores on the MoCA; **(iv)** based on the average test scores data, participants scored within the cognitive impairment spectrum on the MoCA (<26/30), however mean scores on the UNAS were significantly higher than those on the MoCA and if the same normality cut-off scores are used, participants would be classified as cognitively normal on the UNAS (>26/30); **(v)** Test scores on the SALT were above chance level; **(vi)** all assessments achieved an acceptable level of internal and test re-test reliability.

7.7.2. UNAS – Education and cognitive performance

The results demonstrated that test scores on the UNAS were not affected by education in this sample of South Asian older adults. This represents a major advantage over several earlier assessments, like the MoCA, in which education has been found to exert a substantial influence on test scores which was also observed in the present study (Larouche et al., 2016; Malek-Ahmadi et al., 2015; Gagnon et al., 2013; Nasreddine et al., 2005). It is further important to note that an effect of education was observed in the MoCA despite an adjustment in test scores accounting for lower education levels, which was not applied to the test scores on the UNAS.

Therefore, considering that the current assessment was not affected by education without the requirement to develop education-based adjustments, suggests that it has the potential to be a useful measure to assess cognitive functioning without compromising the sensitivity of the assessment in measuring the mildest stages of cognitive impairment in less educated populations. This is argued based on previously discussed research by Gagnon et al. (2013) which found that the MoCA had high sensitivity and specificity in identifying MCI when scores were unadjusted for education. However, when scores were adjusted for education, this reduced the ability of the MoCA in identifying MCI cases.

The above is of particular concern when we consider that South Asian older adults residing in the UK tend to have lower proficiency in English and very minimal years of formal schooling (see chapter [3]) (Blakemore et al., 2018; Hossain et al., 2017). Therefore, implying that when using currently available assessments, they are highly likely to require education-based score adjustments, which the above literature suggests may be counterproductive in detecting MCI. Considering that on average individuals were scoring higher on the UNAS and potentially within the normal cognitive spectrum in the absence of an education-based adjustment, implies that it may have the ability to better preserve its psychometric properties in targeting MCI in less educated populations. However, this would need further study with specific recruitment of MCI participants and longitudinal follow-up.

Further to the above, although the MoCA is widely accepted as a better measure than the MMSE in detecting MCI (Pinto et al., 2019; Nasreddine et al., 2005; Damian et al., 2011), some research suggests that the cut-off scores of 26 leads to a high number of cognitively-healthy individuals being identified as cognitively impaired (Carson et al., 2018; Luis et al., 2009) and this is particularly the case for ethnic minority samples. Sink et al. (2015) investigated the adequacy of published cut-off scores on the MoCA in 530 African Americans in a cross-sectional study of cognition and structural brain imaging. They found that 90% of the sample screened as positive for cognitive impairment using the cut-off of 26 on the MoCA. Moreover, Rossetti et al. (2017) also found that around 80% of their sample formed by African Americans scored below the normality cut-off on the MoCA. This was also observed in the present research whereby over 80% of the sample scored below the normality cut-off scores on the MoCA. On the other hand, the sample of cognitively-healthy South Asian older adults obtained a mean score of 27.80 at baseline on the UNAS which is much closer to the maximum score (30), and when cut-offs for this test are determined with further study the sample would be likely to be classified as cognitively normal. This further supports the claim that the items on the UNAS may have potentially reduced the education related cultural bias present in assessments like the MoCA and MMSE. However, this will require further study and piloting before it can be confirmed.

Also, chapter [5] of this thesis explored the use of the RUDAS which was developed as a culturally sensitive screening tool, however despite this claim, research has found that test scores on the RUDAS are often influenced by literacy and education levels (Rowlands et al., 2006; Basic et al., 2009; Storey et al., 2004; Nielsen et al., 2012) which was also found in the present thesis. Therefore, considering that lower education levels are strongly associated with the ageing population from minority backgrounds (Blakemore et al., 2018), an assessment which fails to address this external factor, cannot be considered as being culturally sensitive. However, this is something which appears to have been achieved in this preliminary assessment of the UNAS.

Further to the above, in chapter [6] it was proposed that the effect of culture and education on test scores has the potential to be reduced by limiting and controlling for the use of verbal and mathematical items. Based on this, a short battery of cognitive assessments with lower reliance on language and education was developed and tested in South Asian older adults. It was assumed that performance on non-verbal tasks such as those requiring to copy figures or repeating back digits involves universal skills present in most older adults, regardless of their education level. However, this assumption was proved to be wrong in this particular sample, as participants were performing below the population norms on these assessments implying that both, verbal and non-verbal assessments can potentially be biased by culture. Through the various studies in this thesis, and research findings in the literature, it transpired that abilities such as copying figures and taking part in assessments are often absent in many cultures because these abilities are highly reliant upon school related skills (Kosmidis, 2018; Ardila et al., 2010).

When individuals are presented with tests like the MMSE, RUDAS and MoCA and given a paper and pen to complete by themselves it mirrors the way in which exams and other academic tests are taken. Naturally, people who have more years in education will be more comfortable and experienced with this situation. On the other hand, this may be a novel situation for less educated individuals who may fail to have a grasp of the procedures due to lack of familiarity with the method of administration. Therefore, suggesting that partly, these assessments are unintentionally measuring test-taking abilities and not just cognitive functioning, which may bias test scores leading to an education effect as observed on the MoCA. An unfamiliar situation also has the potential to increase anxiety which can be a further factor contributing to the lower test scores in less educated samples (Ardila et al., 2010).

This issue may have been rectified somewhat by the UNAS as it does not require participants to be left with a pen and paper and asked to complete a series of questions. The administration of the UNAS actively engaged participants in an almost natural conversation where they were prompted to provide verbal responses in their own language minimising the potential for education related experience of test taking skills to affect performance. This is particularly important when considering that due to high illiteracy levels, South Asian older adults are also less likely to have any non-education related form filling experience for which they are likely to rely on younger relatives. This may further reduce the potential of having had any experience which mirrors the process of completing a neuropsychological assessment. Therefore, it is likely that when South Asian older adults present at a clinic for a cognitive assessment, this may be their first time being exposed to a task requiring them to independently respond to questions in a methodical manner.

Overall, based on the current findings, it is fair to argue that existing assessments of general cognitive function tend to assess abilities which educated individuals have been training in, as opposed to cognitive skills systematically related to everyday problem solving associated with impairments in patients with AD and other cognitive conditions. It would therefore be inaccurate to assume that lower test scores on assessments like the MMSE and MoCA are because the less educated groups are somehow cognitively deprived, when they may simply have developed different types of learning. Cognitive tests for ethnic minority populations must target the skills and knowledge developed by individuals from lower educational backgrounds, which the UNAS appears to have achieved in this preliminary study.

7.7.3. Suitability of the UNAS in South Asian older adults

The preliminary results obtained confirm with the hypothesis that the new assessment, the UNAS, seems to be a better measure of cognitive functioning for South Asian older adults as participants performed significantly better on this test compared to the MoCA. Moreover, the sample of healthy older adults, on average, were performing within the impairment spectrum (<26) on the MoCA at baseline and re-test while on the other hand, scores on the UNAS, based on the MoCA cut-off, were within the normal range (however we acknowledge that at this time we cannot determine an actual cut-off for this test without further work). In addition to this, not only did participants perform closer to the maximum scores on the UNAS, but the assessment itself yielded a high level of internal consistency in the items being measured as well as high test re-test reliability suggesting good psychometric properties.

Therefore, this initial data appears to suggest that the UNAS may be an appropriate measure of general cognitive function for South Asian older adults when compared to the MoCA. This supports further testing of the UNAS with the aim to validate its use in clinical settings with the viewpoint to enhance diagnosis in ethnic minorities like the ageing South Asian population in the UK.

7.7.4. Normative Data

Cognitive decline is unquestionably the first and most valid indicator of AD progression, but accurately capturing the earliest stages of cognitive decline is dependent on many external factors such as, culture, psychometric properties and the quality of the normative data used to interpret test scores (Walters and Lesk, 2015; Lesk et al., 2009). Current population norms are largely based on Caucasian samples, or samples where ethnicity has not been specified, implying that there is limited normative data for minority populations (Milani et al., 2018; Nielsen et al., 2019). To the best of our knowledge, currently there are no normative studies conducted with a sample of South Asian older adults.

Considering that the UNAS was not affected by education and the sample of South Asian older adults performed significantly better on this assessment compared to the MoCA, it provides an opportunity to develop universal population norms which can be drawn upon when assessing cognitive performance in South Asian older adults and other minority populations with similar characteristics. This is particularly important because detecting cognitive decline is highly reliant on normative samples being available for comparisons to be established between "normal" and impaired cognitive functioning (Hassenstab et al., 2016; Walters and Lesk, 2016; Lesk et al., 2009).

From previous findings reported in this thesis, it has transpired that when using current norms, populations like South Asian older adults perform within the impairment spectrum in the absence of any diagnosed cognitive impairment. However, this was not the case in the new assessment which implies that the current norms may not be reflective of the performance of minority populations. This significantly increases the risk of false positives when assuming that normative data obtained from ethnocentric measures in Caucasian samples will also apply to populations like South Asian older adults.

Therefore, the development of an assessment which accounts for the characteristics of South Asian older adults provides with the opportunity to develop new norms which can be applied to this group and other groups with similar characteristics. This would allow to minimise the risk of overestimations based on norms developed with other populations, who were also the intended target audience when assessments like the MMSE and MoCA were initially developed. Achieving more culturally sensitive norms would also facilitate cross cultural comparisons between different groups and further enhance the knowledge base of under researched groups who are increasingly requiring access to cognitive screening services due to an increased incidence of AD and other cognitive decline related conditions in BAME communities (Blakemore et al., 2018; Mukadam et al, 2011).

7.7.5. Incorporation of the SALT

The SALT was implemented as a novel assessment of spatial associative memory as literature increasingly suggests that spatial associative memory is sensitive to decline in the early stages of AD (Parra et al, 2010; Della Sala et al., 2012; Rubino and Andres, 2018; Blackwell et al., 2004) and vast amounts of empirical evidence supports this view through biological biomarkers (Laczo et al.,2019; Soldan et al., 2016, Velayudhan et al., 2012; Blackwell et al., 2004). Therefore, cognitive tests which assess this domain are likely to identify early impairment. However, to our knowledge, none of the assessments widely used in clinical settings routinely implement the use of assessments measuring visual associative memory.

Therefore, the current chapter aimed to evaluate the use of the SALT as a possible novel test to detect cognitive function in a culture-free manner in a sample of South Asian older adults.

In this current study, participants scored relatively high with average scores of 16.83/21 (80.14%), implying an average of 4.17 errors in a six-stage trial. Therefore, this indicates that the sample of cognitively-healthy South Asian older adults scored above chance level which offers some support to the use of the SALT in this population. This is particularly important when considering the importance of associative learning deficits in the early stages of AD, which are also corroborated through physiological biomarkers (Spaan, 2016). At this stage, it is not possible to make any inferences with regards to the effectiveness of the newly developed SALT in detecting MCI as this is a novel tool and there are no comparable norms to which this can be directly compared to. However, it is also important to note that despite the lack of comparable data, the preliminary data also indicates that the SALT has good psychometric properties in that it achieved an acceptable level of internal reliability and test re-test reliability.

This was a preliminary test of performance to determine whether South Asian older adults had the capability to complete this task and perform well on this assessment in light of their lower levels of education. To a good extent, this has been achieved as on average the error rate was low, and performance was above chance level (>50%). However, to determine the effectiveness of the SALT as a culture-free assessment targeting early impairment, it is important to monitor its use in minority populations with MCI and AD and establish comparisons with cognitively-healthy controls.

The SALT was also found to be free from an education bias in this sample which further supports its potential as a culture-free assessment designed to detect earlier stages of deterioration in cognitive functioning.

Unlike existing tests of associative learning, the SALT was administered using a traditional paper copy to minimise the chances of performance bias due to lack of experience with computer systems, which is common in people with lower literacy levels (Olney et al., 2017). Moreover, the SALT implemented the use of neutral symbols and it is a visual task whereby instructions were provided verbally in a language that participants were fluent in. Therefore, the assessment can be administered and completed with minimal linguistic and cultural inferences reducing the overall potential for bias in underrepresented ethnic minority populations.

The use of a paper and pen does create practical issues, particularly in that it is more time consuming. However, this was only a preliminary study to determine whether cognitive assessment in South Asian older adults may benefit from an assessment of associative memory. The initial findings are promising as the South Asian older adults performed well on the SALT. Therefore, it is proposed that future continuation studies should aim to explore the potential to develop an electronic version whereby instructions are provided verbally in a selection of languages and the task merely requires participants to make touch selections to identify the location of the relevant stimuli. A test trial should also be incorporated into the electronic version to ensure that participants understand how the task will work and reduce the chances of participants becoming overwhelmed by being requested to use an electronic device, which they may not have previous experience with.

Considering that spatial associative memory has been found to be one of the most common cognitive impairments in AD at the earlier stages (Albert et al., 2011), it supports the use of the SALT which may also offer benefits in the evaluation of new treatment interventions to explore longitudinal improvements or deterioration. Also, initial data supporting its use also provides potential for the UNAS to be developed further to incorporate an item measuring spatial/episodic memory as part of one assessment which would make it more practical to implement, as well as potentially further increase its sensitivity in measuring early cognitive decline. However, this was not developed and piloted at this stage as we required to establish comparisons between the UNAS and MoCA which would have not been possible by the incorporation of an additional item as this would have led to differences in the maximum scores between the UNAS and the MoCA.

7.7.6. Limitations and future continuations

The initial findings are positive in supporting the cultural effectiveness of both assessments as participants performed closer to maximum scores on the UNAS (mean score 27.80/30) compared to the MoCA (mean score 19.55/30) and performance on the SALT was on average above chance level. However, to further determine the culture-effectiveness of these assessments, future research is required in culturally heterogenous populations in research and clinical settings to allow to infer more conclusive evaluations.

Also, the current sample was formed by healthy older adults with no diagnosed cognitive impairments. Consequently, no attempts were made to diagnose AD and therefore the diagnostic accuracy was not determined at this stage. To further explore the sensitivity and specificity of the new assessments, future research is required in patients with MCI and AD. Also, the present sample was formed by predominately Pakistani older adults. Future research requires piloting the use of both assessments in larger and more diverse samples of South Asian older adults to confirm whether these assessments would be suitable for all the different groups of individuals part of the South Asian community in the UK.

It is also important to acknowledge that the current sample was tested only after one week from the initial screening which may not be considered long enough to prevent carry-over effects or learning (Vaz et al., 2013). Due to time constraints, implementing a larger re-assessment period was not possible, also the re-testing period of a week was adopted based on Storey et al.'s (2004) research validating the use of their newly developed (at the time) RUDAS. However, based on these preliminary findings, future continuations of this research should assess whether the UNAS and the SALT can predict cognitive decline overtime by implementing longitudinal designs particularly when evaluating the diagnostic accuracy of these measures in detecting MCI and AD.

This was not possible in the current research as it is beyond the scope of the thesis due to the limitations in the type of samples that can be recruited as part of this PhD thesis. However, the purpose of developing the UNAS is to allow for it to eventually become an established assessment of cognitive function which can be universally implemented with culturally and linguistically diverse populations. Therefore, it is imperative that future continuations of this study expand its focus on what the test aims to do, i.e., diagnose AD in a timely manner by incorporating items which are free from cultural bias and sensitive enough to detect the earliest stages of cognitive impairment. Consequently, leading to improved overall diagnostic and treatment outcomes in underrepresented populations like South Asian older adults.

7.7.7. Implications of the research findings

Previous research findings in this thesis have facilitated the development of the UNAS and SALT which aimed to build on the limitations of current neuropsychological screening measures in assessing cognitive decline in the ageing ethnic minority populations in the UK.

The UNAS and SALT have demonstrated good psychometric properties and in conjunction, both measures cover well-known domains affected in the early stages of cognitive impairment. This, with further validation studies, may facilitate the detection of symptoms in a timely manner when treatment interventions have increased potential to ameliorate symptoms and slow down the progression of further decline (Insel et al., 2018).

The above findings also offer important information for policymakers as they highlight the importance of acknowledging that tests developed in the West cannot be universally implemented. In particular, the recommendations by NICE (2018) to implement measures which do not account for the effects of external cultural, educational, and linguistic factors may reflect a discriminatory practice against certain groups. It is thereby important that organisations like NICE recognise the salience of diversity in understanding cognitive performance in local populations and develop services accordingly, such as by implementing culturally fair assessments. The UNAS and SALT in their preliminary form may offer a better alternative compared to assessments like the MMSE and MoCA. Nonetheless, future continuations of this study are required to first establish the sensitivity and specificity of these tests and validate their use with a larger sample of healthy and cognitively impaired individuals from potentially multiple ethnicities and cultural backgrounds.

The UNAS and SALT were also relatively quick and easy to administer implying that they can be used in a range of clinical and research settings without the need to obtain specialised training. More importantly, they do not appear to be influenced by education or gender, which is something that previous assessments have failed to achieve. The combined administration of the UNAS and SALT may also allow to test for several cognitive domains known to be affected in the early stages of AD in timed constrained primary care settings.

7.8. Summary and conclusion

Existing neuropsychological assessments measure abilities and constructs which may not be present in minority groups like the South Asian older adults with lower levels of education. This can challenge the accuracy of cognitive screening in this group.

Considering these challenges and the lack of literature investigating this topic in the growing South Asian older adults residing in the UK, the researcher developed and piloted the use of an assessment of general cognitive function, the UNAS, and a novel assessment of visual spatial associative memory, the SALT.

The results from the preliminary implementation of the UNAS and the SALT indicated that both assessments achieved an acceptable level of internal and test re-test reliability. Moreover, test scores on the UNAS and SALT were not affected by education, however a significant effect of education was found on test scores on the MoCA. Therefore, this preliminary data supports the use of the UNAS and the SALT as assessments which may be culturally more adequate for diverse populations known to have lower literacy levels, such as the South Asian older adults (Blakemore et al., 2018). However, in this preliminary study, only cognitively-healthy participants were recruited, and therefore the diagnostic accuracy of the UNAS and the SALT was not established at this stage. Nonetheless, the important preliminary findings support further validation of both measures in more diverse and clinical samples, potentially following some modifications.

7.9. Chapter highlights

- Based on the findings in chapters [5-6], this chapter developed an assessment of general cognitive function (UNAS) and an assessment of visual spatial associative learning memory (SALT) with the aim to improve the accuracy of cognitive screening in South Asian older adults.

- Both tests were piloted in a sample of cognitively-healthy South Asian older adults.

- The results revealed that test scores on the UNAS and SALT were not affected by education and both assessments achieved an acceptable level of internal and test re-test reliability.

- These important findings encourage further research validating the use of the UNAS and SALT in more diverse and clinical samples.

Chapter 8: The effect of time of day on neuropsychological test scores

8.1. Introduction

As previously discussed in the introductory chapters of this thesis, brief neuropsychological assessments are often used by healthcare professionals to identify cognitive impairment and diagnose conditions such as MCI and AD (NICE, 2018, Singh et al., 2016). However, performance on these assessments can often be affected by external factors, such as language, education, and culture (Cid et al., 2019; Paddick et al., 2017). If these factors are not identified, noted, or controlled for, they may complicate the clinical inferences derivable from neuropsychological test scores (Lesk et al., 2009; Walters and Lesk, 2016).

Previous chapters of this thesis have so far investigated external factors which relate to issues directly associated with the way currently established assessments have been conceptualised and administered (e.g., language, education, cultural relevance of items). However, there remain many other external factors present at the time testing beyond the context of the assessment itself which may also impact performance.

In particular, cognitive performance is known to vary with circadian cycles, which are a series of physical, cognitive, and behavioural changes that the human body goes through during the typical 24-hour daily cycle (Newman et al., 2020). This may lead to fluctuations in cognitive performance throughout the day (Singh et al., 2016). It is generally accepted that older adults reach their peak cognitive arousal time in the morning (Walters and Lesk, 2015), and assessing their cognitive functioning during this time is considered optimal to obtain valid scores (Walters and Lesk, 2015, 2016; Blatter and Cajochen, 2007). This is known as the time-of-day effect (TOD) (Singh et al., 2016).

If the time at which an assessment is delivered and completed has the potential to affect the scores obtained, then this also has subsequent implications for the interpretation of the data obtained, and more importantly on the ultimate accuracy of the diagnosis established. However, at present and to our knowledge, there is a lack of research exploring the TOD effect in minority populations. The present chapter aims to address this gap in research by exploring the TOD effect in a sample of South Asian older adults. The findings from this chapter may provide important insight with regards to whether all older adults, regardless of ethnicity, should be consistently tested in the morning, which is currently accepted as their optimal time for cognitive performance (Walters and Lesk, 2015). This may have important implications for clinics and researchers when determining appointment schedules for cognitive testing sessions for patients from diverse cultural backgrounds.

8.1.1. Circadian rhythms and peak cognitive arousal

Circadian rhythms (or the internal biological clock) are controlled by the suprachiasmatic nucleus (SCN) which is situated in the anterior hypothalamus and acts as a master circadian clock (Uddin et al., 2020; Facer-Childs et al., 2018). Circadian rhythms determine an individual's peak and off-peak hours for cognitive performance over the course of the day (Schmidt et al., 2015; Froy, 2011; Fabbri et al., 2012). They operate through variations in body temperature, hormone levels, heart rate and blood pressure which modulate the times at which cognitive resources are at their highest level, based on factors, such as the quality of sleep and food intake (Buhr et al., 2010).

Peak arousal, which is the optimal time for cognitive performance, linked with circadian rhythms, varies with age and this is also associated with the sleep-wake cycle (Jun et al., 2019; Hasher et al., 2005). With increasing age, individuals begin to experience a decline in the number of hours of sleep per night as well as a decline in overall sleep quality and depth (Schmidt et al., 2012) leading them to report increased napping during the day (Blatter and Cajochen, 2007). Subsequently, many older individuals state that they consider themselves as morning types, i.e., that their peak cognitive arousal time is in the morning, whilst a significantly lower number of younger people consider themselves to be morning types (Evans et al., 2017; Yoon et al., 1999).

Young adults tend to show improved test performance during the afternoon/evening while the opposite occurs in older people who experience their peak arousal in the morning due to which they show a significant decline in performance the later they are tested into the day (Walters and Lesk, 2015; May and Hasher, 1998; Schmidt et al., 2007; Yang et al., 2007). However, these TOD effects on cognitive performance can be reduced and/or minimised by testing individuals during their peak cognitive arousal time based on their chronotype.

For example, West et al. (2002) conducted a piece of research on the TOD effect in a sample of 20 young participants (mean age = 25.10 years) and 20 older adults (mean age = 72.60 years). Ten participants from each group were tested in the morning and the remaining ten in the evening on a working memory task (four box task) which incorporated an inhibitory component. The four-box task involves the presentation of a target (smiling face icon) which initially appears in one of the four boxes on a computer screen and participants are prompted to press a key to indicate the location of the target. In the second part, an inhibitory component is introduced (a star like-icon) whereby participants must continue to press the box in which the target stimuli appear, but they must simultaneously ignore the box which contains the distractor shape. The study also implemented the Morningness-Eveningness Questionnaire (MEQ) (Horne and Ostberg, 1976) with the aim to assess participants' TOD preference (morning, neutral or evening type) through a 19-item questionnaire and gathered objective measures including body temperature at varying intervals. Subjective alertness levels were also noted. The analysis of the data obtained agreed with previous findings as older adults reported a preference for the morning on the MEQ and this was also matched with higher subjective ratings of alertness in the morning as opposed to the evening. Also, as expected, performance on the inhibitory part of the task was worse in the older group and the age-related differences in performance were greater when participants were tested during their non-optimal time which was the morning for the younger participants and afternoon for the older group of participants (West et al., 2002).

Despite these interesting findings supporting the TOD effect, it is also important to note that most of the research exploring the TOD effect has focused on inhibitory cognitive mechanisms (Hasher et al., 2007), and not all studies addressing this effect report reliable effects. For example, early research by Li et al. (1998) failed to yield a significant influence of TOD. Li et al. (1998) explored the synchrony effect between peak circadian arousal and TOD in older and younger adults. Participants were required to read and comprehend text which included distracting words that were thematically related or unrelated to the target text. However, the time of testing did not have any effect on participants ability to ignore the distraction. Similarly, Hasher et al. (2002) failed to report a reliable TOD effect in older adults in an interference task.

Therefore, many of the studies exploring the TOD effect on cognitive performance have focused on inhibitory/distraction tasks which have generated inconsistent findings. To address this, Borella et al. (2011) conducted a piece of research which aimed to explore the TOD effect on resistance interference, working memory, processing speed and vocabulary in a sample of 40 young (20-27 years) participants and 40 older (60-78 years) participants who were tested in the morning or in the afternoon. The results showed that older adults tested in their non-optimal time (afternoon) were more vulnerable to interference in tasks compared to the younger adults tested during the same time and older adults tested during the morning (optimal time). However, no TOD effects were observed for working memory, processing speed and vocabulary tasks. Therefore, Borella et al. (2011) concluded that the variations of age-related cognitive performance as a function of the time of testing is only specific to tasks requiring resistance to interference.

Contrary to the above, research by Walters and Lesk (2015) supports the presence of a TOD effect in sample of 36 older adults in assessments of processing speed. Walters and Lesk (2015) carried out a piece of research with the aim to explore TOD effects across a range of different cognitive domains including general cognitive function (MoCA, MMSE), EF (SDMT, DT), processing speed (PCS, LCS, TMT A, Stroop test), working memory (DSF, DSB), short-term memory (DR), visuo-spatial associative memory (CANTAB-PAL) and semantic memory (Graded naming test (GNT)). Significant main effects of TOD were observed in assessments of processing speed which included the PCS, LCS and TMT A which indicated a linear decrease in performance as TOD progressed into the afternoon. The same pattern was also observed for test scores on the MMSE and GNT. It was thereby concluded that the presence of a TOD effect highlights a need for the time of testing to be noted and controlled for when scoring and interpreting cognitive test scores in older adults (Walters and Lesk, 2015).

Therefore, based on the evidence discussed, the TOD effect does not appear to affect all domains equally. Moreover, the TOD effect has the potential to be influenced by substances which can alter alertness and tiredness levels. Such substances may include caffeine, which exerts influence over the sleep-wake cycle, and like the TOD effect is also modulated by circadian rhythms (Walters and Lesk, 2016).

Moreover, changes in sleep patterns and sleep disturbances can also affect cognitive performance as these are likely to lead to changes in the circadian cycle (Singh et a., 2016). Therefore, optimal time of the day for cognitive testing could differ from the “normal” expectation in some individuals and cultural practices may play a role in creating these differences. The role of culture in terms of the TOD effect has not been studied previously and this is discussed in the next section of this chapter.

8.1.2. TOD and varying cultural practices

The current literature on the effects of TOD on cognitive performance has been conducted with little to no accountability with regards to the effects of cultural practices on the TOD effect. Moreover, many of the studies exploring the TOD effect fail to state the ethnicity of their sample.

As discussed earlier, the TOD effect is mediated by the sleep-wake cycle (Jun et al., 2019), therefore different cultural practices may shift peak arousal times in individuals from diverse backgrounds. However, this has not been widely investigated and the literature review for the purposes of this thesis only found one piece of non-contemporaneous research by Rana et al. (1996) exploring the effects of TOD on cognitive performance in a sample of Indian children.

Rana et al. (1996) aimed to investigate vigilance performance (alertness) in a sample of 30 children in India aged between ten and 16 years at three different times during the day (9:00 am, 2:00 pm and 6:00 pm). The results revealed that participants performed better in the morning when compared to the afternoon and evening. Moreover, a higher frequency of errors was found in the afternoon. These findings are not consistent with the more recent evidence discussed in this chapter suggesting that younger individuals experience their peak arousal in the afternoon (Evans et al., 2017; Sherman et al., 2016; Borella et al., 2011). Considering that the target population of Rana et al.'s (1996) study was formed by Indian children may imply that the findings could be reflective of potential cultural differences that lead to circadian rhythm patterns which differ from those observed in Western cultures. However, little is known with regards to the effects of culture on TOD due to a lack of research implementing minority populations.

Furthermore, religious practices across different cultures may also have an impact in the regulation of circadian rhythms. In particular, a large proportion of the UK's Pakistani and Bengali population identify as Muslims (ONS, 2011). Muslims engage in five daily compulsory prayers at specified times which vary throughout the year based on the timings of sunrise and sunset (Williamson, 2018). The first prayer of the day begins early in the morning before sunrise with the last one being performed after sunset (Williamson, 2018). The prayers involve the recitation of Quranic verses which are retrieved and recalled from memory (Williamson, 2018). Therefore, this suggests that there is a likelihood that South Asians who identify as Muslim, like the present sample, may be cognitively active throughout the day with varying sleep patterns around prayer times. This subsequently implies that the Muslim population may have variations to their sleep-wake cycle which may alter their peak performance time. Considering that the Islamic prayer requires individuals to remain cognitively active throughout the day, may also imply a lack of a TOD effect in this population. Nonetheless, to date there is no research, as far as the researcher is aware, which explores the influence of the TOD effect across different cultural groups who may engage in cognitively stimulating praying practices.

Therefore, it will be interesting to explore whether the TOD effect would remain consistent despite the diverse cultural practices within the South Asian community.

8.2. The present study: Research aims

The present chapter aims to investigate the effect of TOD on a battery of neuropsychological assessments administered to a sample of South Asian older adults.

8.3. Methods

Ethics approval for this research was granted by the Chair of the Humanities, Social and Health Sciences Research Ethics Panel at the University of Bradford on 23/03/17.

8.3.1. Participants

Forty-five participants from a South Asian background took part in this study. They were aged 60 years and over and were residents of the UK. This sample size was determined based on research by Walters and Lesk (2015) who explored the TOD effect in a sample of 40 older adults (ethnicity not recorded) by implementing a battery of 13 cognitive assessments. The present study used fewer assessments or dependent variables (ten), but it still aimed to achieve a similar sample size.

The inclusion criteria specified that participants must be aged 60 years or over, be from a British South Asian background (defined in this study as Pakistani, Bangladeshi, or Indian) and be fluent in Urdu/Hindi. To minimise interference with cognitive performance, as part of the exclusion criteria, participants were required to not possess any sensory impairments, have an existing diagnosed neurological condition, or suffer from any severe physical disability.

Although the inclusion criteria specified for participants to be from Pakistan, India or Bangladesh, the final sample was predominantly formed by Pakistani older adults. Also, all participants reported their religion as being Islam.

8.3.2. Design

An independent samples experimental design was implemented. All participants completed the full battery of cognitive assessments. The dependent variables being measured consisted of the test scores on the battery of neuropsychological assessments and the independent variable consisted of the time the assessments were administered.

8.3.3. Materials

All participants completed a battery of cognitive assessments including DR, MoCA, PCS, LCS, DSF, DSB, SDMT, TMT A&B and DT. A detailed description of the battery of neuropsychological assessments administered can be found in chapter [4].

Participants also completed the MEQ (Horne and Östberg, 1976) to determine their chronotype preference for the morning, evening or neither (neutral). The MEQ is an assessment developed to assign people to three main categories relating to morning types, neutral types or evening types which are assigned according to the time preference to engage in different tasks. The MEQ is formed by 19 items and it is scored out of 86. Chronotypes are determined by the following scoring: 16-30 (definitely evening), 31-41 (moderately evening), 42-58 (neutral), 59-69 (moderately morning), and 70-86 (definitely morning type).

A demographics questionnaire was also completed which noted the time the cognitive assessment session commenced.

8.3.4. Procedure

Participants were recruited form Girlington Community Centre and through snowball sampling in the areas of Bradford and London. They were provided with an information sheet, which was read to them in Urdu, and contacted 48 hours later to confirm whether they wished to participate. The research took place in participants' home in the presence of a carer or relative. Electronic devices which emit noises (e.g., TVs, radios) were turned off to minimise the number of distractions present at the time of testing. Participants signed a consent form, the contents of which were read to them in Urdu. Next, the demographics questionnaire was verbally completed in Urdu. Following this, participants completed the battery of cognitive assessments in a randomised order. Instructions for all assessments were conveyed verbally in Urdu, and the responses for items not requiring the use of a pen to draw or copy were conveyed by participants verbally and noted down by the researcher.

8.4. Results

The present research aimed to explore the effect of TOD on a battery of neuropsychological assessments administered to a sample of Muslim South Asian older adults.

8.4.1. Main participant demographics

Table one shows the demographic characteristics of participants.

Table one - Mean and SD for main participant demographics

Demographic variable	Mean	SD
Age	69.69	±6.40
Education (years)	4.24	±4.41
Gender (males/females)	24:21	

The MEQ was administered to determine participants preference for the morning or afternoon and the results are presented in table two.

Table two - MEQ am/pm chronotype frequency

MEQ Chronotype	Frequency
Morning	31 (68.9%)
Afternoon	14 (31.1%)

The data in table two demonstrates that based on MEQ scores, 68.9% of older adults were identified as morning chronotypes, whilst fewer participants (31.1%) were identified as afternoon types. A Pearson correlation analysis was carried out to determine the association between the scores on the MEQ and age ($r = 0.71$, $p<0.05$) which indicated that there was a significant positive correlation, whereby as age increased, scores on the MEQ also increased indicating a preference for the morning in older adults with increasing age. This is depicted in figure one.

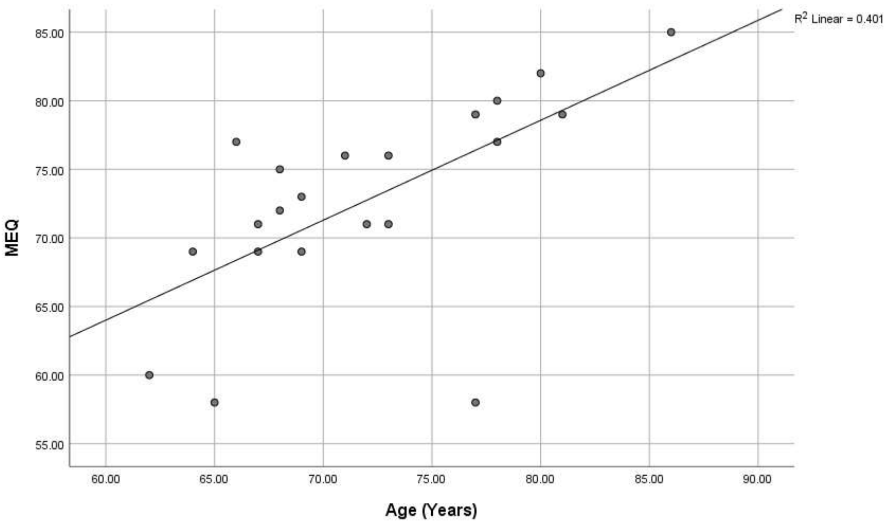


Figure one – Scatterplot depicting a positive linear increase in MEQ test scores with increasing age indicating preference for the morning.

8.4.2. Cognitive performance

The sample's mean test scores on the battery of neuropsychological assessments are shown in table three.

Table three: Mean and SD for scores on the battery of neuropsychological assessments administered

Assessment	Mean (SD±)
DR (max.15)	2.82 (±2.03)
MOCA (max.30)	16.51 (±6.60)
PCS	7.89 (±3.33)
LCS	5.84 (±2.92)
DSF	3.53 (±0.76)
DSB	2.69 (±1.36)
SDMT	8.64 (±5.10)
TMT A (time taken to complete in minutes)	3.58 (±2.14)
TMT B (time taken to complete in minutes)	4.28 (±1.78)
DT Ratio	0.64 (±0.14)

The assessments listed in table three were completed by the sample between the hours of 7:45 am – 7:30 pm. TOD was not formally controlled for to allow participants to participate at a convenient time, but it was noted down. Twenty-seven participants were tested in the morning before 12:00 pm and 18 participants were tested in the afternoon after 12 pm.

8.4.3. Main effects of TOD on cognitive test scores

To formally assess the influence of TOD on tests scores, a MANCOVA analysis was conducted with test scores entered as the dependent variables and TOD as a covariate. Wilks Lambda was non-significant ($p>0.05$), and no further investigation of the output was carried out. Therefore, no main effects of TOD on cognitive test scores were found on any of the cognitive tests administered in this sample of South Asian older adults who identified as being Muslims.

8.5. Discussion

The present research explored the effect of TOD on a battery of neuropsychological assessments in a sample of Muslim South Asian older adults.

8.5.1. Main findings

The analysis of the data revealed that the sample of older adults were predominantly identified on the MEQ as morning chronotypes. However, despite preference for the morning, no main effects of TOD were reported for test scores on any of the neuropsychological assessments administered. Therefore, time of testing did not influence cognitive test scores in this sample of Muslim South Asian older adults.

8.5.2. Lack of a TOD effect in Muslim South Asian older adults

The present research failed to find a TOD effect on cognitive performance in a sample of Muslim South Asian older adults. This is contrary to the existing literature which indicates that for most individuals, cognitive performance fluctuates throughout the day, with older adults experiencing optimal cognitive arousal in the morning (Walters et al., 2015; Rosenberg et al., 2015; West et al., 2002).

To our knowledge, no study has specifically investigated the effect of TOD on cognitive testing in a sample of South Asian older adults, or any other minority BAME group in the UK. Therefore, it is fair to argue that much of the current literature on TOD is of an ethnocentric nature and it fails to account for the potential variations in the TOD effect in individuals from diverse cultures, particularly as many of the previous studies have not provided the ethnicity of their participants.

Previous research by Singh et al. (2016) also failed to report a strong TOD effect in a clinical sample. Singh et al. (2016) explored the TOD effect in patients diagnosed with mild dementia and a cognitively-healthy control. Mild dementia was defined as MMSE scores between 11-27 and the cognitively-healthy control was defined as having MMSE scores between 28-30. The average age of the clinical sample was 85 years and 47.7 years for the cognitively-healthy control. Singh et al. (2016) do not specify the ethnicity of their sample; however, this was recruited from five assisted living facilities and a university in Las Vegas (USA). Cognitive performance was assessed using the MMSE, Mini-cog and semantic verbal fluency using animal names. All tests were administered once in the morning (between 8:30 am-11 am) and once in the afternoon (between 3pm-6pm). There was a two-week period between each testing session to control for practice effects. The findings indicated that scores were significantly better on the MMSE and mini-cog in the afternoon for participants who were tested first in the morning and then in the afternoon. This was not observed in the reverse condition, and the effect was stronger in the mild dementia group. However, this was not attributed to the TOD effect as the analysis indicated that the findings were attributed to test experience. Singh et al. (2016) concluded that in their sample, time of testing was not a significant factor affecting test performance, and other factors such as test experience require to be studied further.

The current findings, and research by Singh et al. (2016), suggest that it cannot be universally accepted that ageing will inevitably lead to people becoming morning types and showing a strong TOD effect. At this stage, it is difficult to explain why this may have occurred, as this was only a first preliminary study in this cohort, and there is a lack of existing data in the current literature for comparisons.

Considering that the present sample was formed by Muslim South Asian older adults, there is a potential that the findings may be attributed to engagement in Islamic praying practices. Individuals who practice Islam, often follow a rigorous prayer routine (Sayeed and Prakash, 2013). This involves engagement in five compulsory prayers spread across the day and there is also a tendency to engage in voluntary prayers throughout the day and night (Sayeed and Prakash, 2013; Williamson, 2018).

Engagement in these types of religious practices involves the constant use of cognitive functions, such as language, attention, and memory, to retrieve and recite the prayers from memory which may contribute towards enhanced or altered cognitive performance (Luhrmann et al.,2013; McLean et al., 2010).

Inzelberg et al. (2013) found that engagement in the Muslim prayer in a group of Arab women (aged ≥65) significantly reduced the chances of developing cognitive impairment based on MMSE test scores. Further to this, praying during the early morning and night-time hours may also require individuals to stay awake until late and wake up early which would consequently influence and modulate the workings of their biological clock differently.

Therefore, differences in sleeping patterns and engagement in the Islamic prayer, which is a cognitively stimulating activity, (Sayeed and Prakash, 2013) may have potentially contributed to the lack of a TOD effect in this cohort of Muslim South Asian older adults. However, this cannot be asserted at this stage because this was a novel investigation in an underrepresented cohort, and further research is required to understand these findings. This thesis will aim to address this in the next chapter by exploring engagement in the daily five Islamic prayer as a potential factor contributing towards the lack of a TOD day effect in this sample of Muslim South Asian older adults.

8.5.3. Implications of the research findings

The present piece of research failed to report an effect of TOD on cognitive test scores in Muslim South Asian older adults. Therefore, and in the absence of previous research in this group of participants suggesting otherwise, there does not appear to be an advantage for testing Muslim South Asian older adults in the morning.

This, despite being a preliminary finding, is increasingly important. As cognitive screening becomes more and more utilised due to the increase in the number of people developing dementia and AD (Silva et al., 2019), the lack of a TOD effect in this group of individuals suggests that the time of testing should not be a major concern for clinics trying to meet the increased demands for their services. If memory clinics do not have to be restricted to be conducted in the morning to optimise the performance of their older adult patients, it implies that a higher number of individuals can be tested across the day reducing waiting times. Subsequently, quicker cognitive screening would also increase the likelihood of cognitive impairments being detected earlier when the prospects of reducing the progression of decline are higher (Insel et al., 2018).

This is also relevant to cognitive researchers. For example, based on the most reported findings with regards to the TOD effect, time of testing could influence cognitive test scores (Walters and Lesk, 2015). Based on this, testing older adults in the morning, and then following up sometime later in the afternoon may lead to reporting a decline which has progressed more rapidly than it actually has. Therefore, requiring researchers to maintain consistency in the time of testing during any potential follow-up periods. However, the current findings suggest that maintaining consistency in the time of testing may not be necessary for all research populations as an advantage for morning testing was not observed in the present cohort in this preliminary study.

Overall, the TOD effect may not apply to all populations equally. Further investigating this factor in more diverse and clinical samples will allow to gain a more in-depth insight into this phenomenon to improve the accuracy of the data obtained from cognitive screening measures in research and clinical settings.

8.5.4. Strengths and limitations

To our knowledge, this was the first piece of research exploring the effect of TOD on a battery of short neuropsychological assessments in a sample of Muslim South Asian older adults. This was important as short cognitive assessments are increasingly used in research and recommended by the NICE (2018) dementia guidelines. Moreover, the present study determined the samples chronotype for the morning or evening by implementing the MEQ, which is an established assessment of chronotype preference for the morning or evening.

Most of the previous research in this area has highlighted that the time of testing is an important variable to account for when carrying out brief cognitive screening tests in the older adults (Walters and Lesk, 2015; Borella et al., 2011; West et al., 2002). However, to date no research has focused on exploring the TOD effect and its relevance in minority populations like the increasing number of Muslim South Asian older adults residing in the UK (Blakemore et al., 2018). The present study, although only a pilot piece of research in this area, has produced insightful findings. These suggest that as the demand for cognitive screening services is increasing, the time of testing may not be a major external factor to be taken into consideration and controlled for in populations like the Muslim South Asian older adults. This has important clinical and research implications which were discussed in the previous section of this chapter.

It is however important to acknowledge some methodological considerations. The present study did not record for participants' subjective levels of tiredness and sleep patterns which have the potential to modulate circadian rhythms and alter TOD effects (Nowack and Van Der Meer, 2018; Bugg et al., 2006). Therefore, this piece of research did not take into consideration participants' peak arousal time which would be important when considering the effects of the time of testing on cognitive performance. Moreover, factors such as prior caffeine intake are also known to affect circadian rhythms and TOD effects (Walters and Lesk, 2015, 2016) which require to be studied in combination in future studies.

Further studies into the TOD effect in minority underrepresented groups require to be conducted in a more controlled manner and by accounting for other factors which may influence the TOD effect. Nonetheless, this is the first piece of novel research highlighting a potentially important but neglected issue of time of cognitive testing in minority populations with varying cultural and religious practices which have the potential to alter the sleep-wake cycle, and subsequently lead to variations in the TOD effects in some individuals.

8.6. Summary and conclusion

The TOD the testing of cognitive functions takes place is known to influence performance (Walters and Lesk, 2015; West et al., 2002). Interestingly, contrary to the existing literature, no TOD effects were observed in a sample of Muslim South Asian older adults. Therefore, indicating that the time of testing did not influence test scores in this sample. A more comprehensive study will be required to better understand these findings. However, to our knowledge, this was the first piece of research addressing the important issue of time of testing in an underrepresented sample, and this has offered novel and insightful findings which question the generalisability of the TOD effect across people from different backgrounds.

The present findings provide an initial basis to argue that the assumption that all older adults should be tested in the morning (their optimal time), may not hold true for all populations. Non-Western cultural and religious practices may have the potential to modulate the working of circadian rhythms differently (Qasrawi et al., 2017), which may subsequently lead to changes in peak arousal times and vary the effects of TOD on cognitive performance.

This cannot be confirmed at this stage, and it is an issue which will be addressed in the next chapter of this thesis by investigating whether engagement in the daily five Islamic prayers may explain the non-significant findings observed in this chapter. However, it is important to acknowledge that these initial preliminary findings suggest that as cognitive screening become increasingly utilised by minority populations, time of testing may not be a factor of concern when scheduling cognitive screening appointments for Muslim South Asian older adults, both in research and clinical settings.

8.7. Chapter highlights

- To our knowledge, no research has explored the TOD effect specifically in people from different ethnic backgrounds.

- This chapter aimed to fill this gap by exploring the TOD effect as a factor which may influence cognitive performance in a sample of Muslim South Asian older adults.

- Interestingly, no TOD effects were noted in this cohort.

- Based on the characteristics of the present sample, a possible explanation may be the engagement of this cohort in the daily five Islamic prayers which take place across the day and may have influenced the TOD effect in this group. This is investigated in the next chapter.

Chapter 9: The daily five Islamic prayers and TOD interactions

9.1. Introduction

As discussed in chapter [8], standard neuropsychological assessment measures are often administered in research and clinical settings throughout the day to assess cognitive deficits irrespective of the optimal time for cognitive performance based on TOD chronotypes (Evansova et al., 2020). Most of the existing studies exploring the TOD effect on cognitive performance report that older adults reach their peak arousal in the morning, and their cognitive performance should be assessed during this time to increase the accuracy of the scores obtained (Walters and Lesk, 2015; Yoon et al., 1999; Li et al., 2017). Contrary to the findings in the existing literature, chapter [8] failed to report a TOD effect in a sample of Muslim South Asian older adults.

To our knowledge, previous research has not explored the TOD effect specifically in people from different ethnic backgrounds and considering that existing research consistently supports a TOD effect in older adults, it is important to explore what may have influenced the lack of a TOD effect in the present cohort of participants.

One of the salient characteristics of the sample in chapter [8] is that they all identified as being Muslims. Based on this, one possible explanation may be the engagement of this cohort in cognitively demanding Islamic praying practices. In particular, Muslims engage in compulsory daily five prayers which take place at specific times and are spread across the day (Williamson, 2018). This may imply that this group of individuals may make constant use of cognitive functions throughout the day when engaging in prayer which may have the potential to influence the TOD effect in Muslim participants.

The present research will aim to carry out the first piece of novel research which explores the interaction between engagement in the daily five prayers, TOD, and cognitive test scores.

9.1.1. The Islamic prayer

The Islamic prayer takes place across the day and into the night (Williamson, 2018) which is likely to influence the sleep-wake cycle, and subsequently the mechanisms by which circadian rhythms operate to allocate resources for optimal cognitive performance.

The Quran is the Islamic holy book which commands Muslims to pray at least five times a day, a practice also known as “Salah” (Kamal et al., 2013). Muslims, as well as learning their own native languages, must also learn to read the Quranic Arabic to allow them to learn and recite the Quran in its original format from a very young age (Akhtar, 2014).

The Quran is formed by a complex grammatical structure and Muslims are required to recite the Quran with correct pronunciation because even small mistakes can significantly change the meaning of the text (Akhtar, 2014). Familiarity and memorisation of certain parts of the Quran is also required to complete the daily five mandatory prayers or salah (Kamal et al., 2013).

9.1.2. The daily five mandatory prayers

The daily five prayers are performed every day at specified times which vary throughout the year based on the timings for sunrise and sunset (Willamson, 2018). They involve the recitation of Quranic verses which are retrieved and recalled from memory (Williamson, 2018). Therefore, the structure and method of these prayers is likely to have long term implications on the brain, and subsequently on cognitive processes (Newberg et al., 2015).

The Islamic salah is a highly disciplined and cognitively demanding task as it requires to be performed at specific times and involves standard elements which include the performance of ablution to cleanse the body and wear a particular dress code (Sayeed and Prakash, 2013). The prayer itself involves the use of speech to recite the prayers from memory whilst using a range of bodily movements involving standing, bowing, sitting as well as other arm and hand movements (Doufesh et al., 2014) (see figure one). Completion time is usually between ten to 20 minutes depending on the prayer being performed, with the morning prayer being the shortest and the evening prayer being the longest. Also, the five prayers are prayed in the direction of Mecca and in Arabic which may or may not be a language that the person performing speaks or understands (Doufesh et al., 2014).

The actual prayer consists of a repetition of units known as “rakah” which are the sequences of actions involved in the prayer (Umar, 2011). The first prayer is known as “Fajr” (meaning: dawn) and it is prayed in the early hours of the morning before sunrise, and it consists of two compulsory rakahs and two voluntary rakahs. The next prayer is “Zuhr” (meaning: mid-day prayer) and it consists of four mandatory rakahs and a set of four and two voluntary rakahs; Zuhr is followed by “Asr” (meaning: afternoon prayer) which is also formed by four mandatory rakahs and four voluntary rakahs; the fourth daily prayer is Maghrib (meaning: sunset prayer) and it consists of three mandatory rakahs and two voluntary rakahs which must be performed at sunset. The last prayer of the day is “Isha” (meaning night prayer) formed by four compulsory rakahs followed by an additional three rakahs known as “Witr” and an additional set of four and two voluntary rakahs (Umar, 2011).

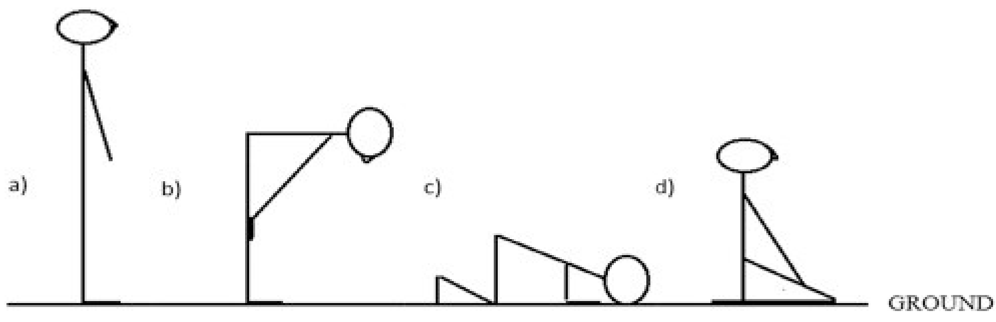


Figure one: Body postures during the performance of the daily five prayers (standing, bowing, prostrating, and sitting) (Doufesh et al., 2016)

9.1.3. Engagement in the Islamic prayer and TOD

Based on the description of the daily five prayers it can be argued that this is a complex cognitive task involving the use of different cognitive abilities and strategies, such as memory, attention, and language and as such it may be associated with changes in neuropsychological performance which have not been investigated in the current literature. Moreover, considering that the Islamic prayer is spread across the day starting early in the morning before sunrise, may also lead to changes in the sleep-wake cycle as individuals are likely to plan their sleeping patterns around prayer times. Also, as the prayers are spread across the day, this may also suggest that individuals who engage in these may be using their cognitive functions more consistently throughout the day. These factors may subsequently have an impact on the modulation of the TOD effect.

Although there is limited literature exploring the specific effects of engagement in the Islamic prayer on circadian rhythms, there is some evidence which indicates that varying sleeping patterns observed during Ramadan fasting have the potential to alter the working of circadian rhythms and the sleep-wake cycle (BaHammam, 2010, 2006) which can subsequently have implications on cognitive performance (Valdez et al., 2012).

During Ramadan, Muslims abstain from food and drink between dawn and sunset and engage in additional prayers at night-time, and this shift in eating and sleeping has been found to alter the sleep-wake cycle delaying circadian rhythms during Ramadan (BaHammam, 2010; Azizi, 2002). Moreover, research by Alfahadi et al. (2020) explored the effect of Ramadan fasting on cognitive functions and fatigue severity in patients with type two diabetes using the CANTAB. Their sample was formed by 82 adult Muslim participants including 43 controls and 39 patients diagnosed with type two diabetes. The analysis of the data gathered revealed that fasting led to changes in cognitive performance, specifically in patients with diabetes who were more likely to show cognitive deficits in working memory capacity and attention compared to the healthy controls due to fatigue and sleep deprivation. However, it is important to note that whereas sleep deprivation negatively correlates with cognitive performance due to delayed circadian rhythms (Alfahadi et al., 2020; Zavecz et al., 2020), engagement in prayer, a cognitively demanding task, is likely to require increased alertness and vigilance throughout the day to perform the prayers. Therefore, increased alertness levels across the day may potentially also lead to more consistent circadian rhythms due to the increased demands of prayer on cognitive processes.

This indicates that there is potential for prayer to influence cognition and the modulation of circadian rhythms differently in people who engage in the daily five prayers. However, to our knowledge, this has not been previously explored which further justifies exploring the lack of a TOD effect as potentially explained by this sample's engagement in the daily five Islamic prayers.

9.1.4. Summary

Overall, the Islamic prayer appears to be a complex cognitive task involving the use of different cognitive abilities and as such, engagement is likely to be associated with changes in neuropsychological performance. Considering that this cognitively demanding activity can take place across the day based on prayer times, there is also a likelihood that this may alter the sleep-wake cycle. Subsequently, suggesting that exploring engagement in the Islamic prayer in conjunction with TOD may offer valuable knowledge with regards to the lack of a TOD effect in this cohort as observed in chapter [8]. To our knowledge, at present, this has not been explored by any previous pieces of research.

9.2. The present study: Research aims

This piece of research will explore the interaction between TOD, engagement in the daily five prayers and cognitive test scores in a sample of Muslim South Asian older adults.

It is hypothesised that participants who engage in the daily five prayers will not experience a TOD effect on test scores. This was hypothesised based on the argument that continuous engagement throughout the day in a cognitively demanding activity, i.e., the daily five prayers, is likely to maintain optimal cognitive arousal consistent throughout the day reducing the likelihood of a TOD effect. This is not expected to be observed in the group of participants who do not engage in the daily five prayers.

9.3. Methods

The data set from chapter [8] was used to investigate the interaction between TOD, engagement in the daily five prayers and test scores on the battery of neuropsychological assessments administered.

9.3.1. Participants

The sample was formed by 45 participants aged 60 years and above from a Muslim South Asian background who confirmed proficiency in the Urdu language.

9.3.2. Design

An independent samples experimental design was implemented. The dependent variable being measured consisted of the test scores on the battery of neuropsychological assessments and the independent variables consisted of the time of testing and whether participants engaged in the daily five prayers.

9.3.3. Materials

Participants were required to complete a battery of cognitive assessments which included an assessment of DR, MoCA, PCS, LCS, TMT A&B, SDMT, DSF, DSB and DT. These assessments are outlined in detail in chapter [4].

Data on engagement in the daily five prayers was collected through a self-report questionnaire which required participants to indicate engagement as "yes" or "no". The time of the day the cognitive assessments were administered was also noted. All questions were asked verbally, and responses were noted down by the researcher.

9.3.4. Procedure

The data set from the study in chapter [8] was used to explore the interaction between TOD, engagement in the daily five prayers and cognitive test scores. All participants completed the full battery of neuropsychological assessments listed in the materials section in Urdu. Responses were recorded by the researcher, with the exception for items requiring participants to use a pen to draw or copy figures. TOD was not controlled for; however, the time of testing was noted down.

9.4. Results

The present chapter aimed to investigate the interaction between TOD, engagement in the daily five prayers and test scores in a sample of Muslim South Asian older adults to determine whether a cognitively demanding activity which takes place across the day, i.e., engagement in the daily five prayers, may explain the lack of a TOD effect observed in this cohort of participants in chapter [8].

9.4.1. Time of testing and engagement in the daily five prayers

The time of cognitive testing was noted before the cognitive tests commenced; however, this was not formally controlled for to allow participants to take part at a suitable time for them. Sixty percent of the sample was tested in the morning before 12 pm and 40% of the sample was tested in the afternoon after 12 pm. Also, 35 participants confirmed engaging in the daily five prayers, and only ten participants did not engage in the daily five prayers.

9.4.2. Interactions: TOD and engagement in the daily five prayers

To explore the aims, two MANCOVA analyses were conducted to explore the interaction between TOD, daily five prayers and test scores in the group of participants who engaged in this prayer type and in the group of participants who did not engage in the daily five prayers. Test scores were entered into the model as dependent variables, TOD as a covariate and the daily five prayers as a fixed factor (“yes”- “no”). An interaction term between TOD and daily five prayers was also entered into the model.

Wilks Lambda was non-significant ($p>0.05$) for both, the group of participants who engaged in prayer, and those who did not engage in prayer. Therefore, no significant interactions between TOD and the daily five prayers were found on any of the tests administered.

9.5. Discussion

The present study aimed to explore the interaction between engagement in the daily five prayers, TOD, and cognitive test scores to determine whether the lack of a TOD effect observed in chapter [8] can be explained by the engagement of this cohort of Muslim South Asian older adults in a cognitively demanding activity which takes place across the day, i.e., the daily five prayers.

9.5.1. Main findings

No significant interactions were observed between TOD, daily five prayers and cognitive test scores on any of the tests administered in those who engaged in the daily five prayers, and neither in those who did not engage in the daily five prayers. Therefore, indicating that the time a cognitive assessment was completed, did not influence test scores in this sample.

9.5.2. TOD and engagement in the daily five prayers

Considering that engagement in the daily five prayers is likely to be a cognitively demanding task which takes place across the day from sunset into the night (Williamson, 2018), it was hypothesised that engagement in this praying practice may explain the lack of a TOD effect observed in chapter [8]. However, although no TOD effects were observed in the group of participants who engaged in the daily five prayers, this was also the case for the group of participants who did not engage in this practice. Based on this, it cannot be concluded at present that engagement in the daily five prayers was a contributing factor explaining the lack of a TOD effect in this cohort of Muslim South Asian older adults.

However, this is only preliminary data and further research in a larger and more diverse sample will be required to understand the nature of the lack of this interaction. In particular, only ten participants in the present sample reported not engaging in the daily five prayers, whilst a much larger number of participants (35/45) reported engaging in the daily five prayers. Considering that the number of participants who did not engage in prayer was relatively small, this may have contributed towards the non-significant findings in this group. Therefore, future research is required in larger non-praying older adults to confirm these findings.

Despite the lack of a TOD effect in both groups of participants, these findings remain important as they further confirm a lack of a TOD effect in this cohort which is not consistent with previous literature (Walters and Lesk, 2015).

This highlights potential inconsistencies in the way the TOD effect may operate in different people. Therefore, emphasising on the importance of future research exploring this in a more controlled manner in people with varying cultural and religious beliefs.

9.5.3. Methodological considerations

The present study, to our knowledge, was a novel piece of research which looked at the interaction between TOD, daily five prayers and cognitive test scores. However, the final sample was formed by a small number of participants reporting that they did not engage in the daily five prayers (10/45) which may have contributed to the lack of significant findings in this group. This will need further testing in future studies by implementing a larger sample with an equal number of participants who engage in prayer and those do not engage in prayer. This will allow to establish more valid and controlled comparisons. Despite the importance of having a larger and equal sample size, it is important to highlight that the current sample was formed by older Muslim adults, and this significantly challenges the recruitment of non-praying older adults. This is because evidence indicates that older adults are more likely to engage in religious practices (Hayward and Krause, 2013; Chaaya et al., 2006).

It important to acknowledge that as the present study only collected self-report data on prayer, there is also potential that prayer engagement may have been overestimated to conform with traditional norms. As discussed in chapter [3], South Asian older adults place high value on their cultural and religious beliefs, and people often hide symptoms of cognitive decline due to fear of being stigmatised as these symptoms are often seen as a punishment from God/s for not fulfilling religious duties (Blakemore et al., 2018; Kenning et al., 2017; Hossain et al., 2018). Therefore, in future continuations of this study it will be important to conduct a more controlled piece of research by confirming prayer engagement with a carer or relative who is familiar with the participant.

The present study only explored engagement in the daily five prayers by simply recording whether participants engaged, or not, in this practice. However, to better understand the interaction between TOD and engagement in the daily five prayers it will be important for future research to also consider the actual number of prayers prayed in the day out of the five prayers, the exact time these are prayed at, the length of each prayer and the length of time the individual has engaged in continuously praying the daily five prayers. Also, previous evidence indicates that fasting in the month of Ramadan leads to changes in circadian rhythms and the sleep-wake cycle (Alfahadi et al., 2020; BaHammam, 2010, 2006). This presents an additional factor associated with the Islamic prayer which may be interesting to further explore as potentially influencing the TOD effect.

Also, the lack of a TOD effect in both groups of participants (those who prayed and those who did not) may also indicate that other unobserved variables may have influenced the relationship between TOD and cognitive test scores in this cohort. Future research addressing the above-mentioned methodological considerations may allow to uncover these factors in a more controlled and valid manner.

9.5.4 Implications of the research findings

The present findings failed to report a significant interaction between TOD, daily five prayers and test scores in a sample of Muslim South Asian older adults. This indicated that the time a test was administered, did not influence cognitive test scores in participants who engaged in the daily five prayers, and in those who did not engage in this practice.

Although based on these findings it could not be concluded that engagement in the daily five prayers contributed to the lack of a TOD effect in this sample of Muslim South Asian older adults, the findings are novel and may have important implications for researchers using cognitive assessments.

The findings indicate that generalisations with regards to the TOD effect cannot be made conclusively. The results appear to suggest that there may be some, currently unknown, variables potentially influencing the TOD effect differently in Muslim South Asian older adults. This needs to be taken into consideration in future work which will be particularly important considering that the current research base in this field has been predominantly carried out in Caucasian samples, or samples were ethnicity has not been recorded.

9.6. Summary and conclusion

Previous literature in the field of TOD and cognitive screening highlights that clinicians and researchers should aim to deliver cognitive screening sessions at an individual's peak arousal time to minimise the effects of TOD and optimise the accuracy of the scores obtained (Evansova et al., 2020; Walters and Lesk., 2015).

For most older adults, peak cognitive arousal has been found to occur in the morning (Walters and Lesk, 2015). However, no advantage of morning testing was observed in the findings of chapter [8] in a sample of Muslim South Asian older adults. Based on this and considering that one of the salient characteristics of the present sample was that they were Muslims, the present research aimed to explore whether the lack of a TOD effect can be explained by engagement of this sample in the Islamic daily five prayers which take place across the day and may involve the use of various cognitive processes to complete (Williamson, 2018).

No significant interactions between TOD, engagement in the daily five prayers and cognitive test scores were found. This shows that the time of testing did not influence test scores in those who engaged in the Islamic prayer, and neither in those who did not engage in this practice. Although, no significant interactions between TOD and test scores were found in those who did not engage in prayer, these findings remain important. They further demonstrate that the notion that older adults should be tested in the morning, their optimal time, may not hold true for all populations equally. These are important findings which have practical and theoretical considerations for researchers using cognitive assessments as part of their diagnostic procedures.

The research findings highlight a need to further expand on these findings in more controlled experiments to better understand how the TOD effect may differ in people from across different cultures and religious practices.

9.7. Chapter highlights

- This chapter examined the interaction between engagement in the daily five Islamic prayers, TOD, and cognitive test scores as possibly explaining the lack of a TOD effect noted in chapter [8].

- No TOD effects were observed in participants who confirmed engagement in the daily five prayers, and neither in those who did not engage in this practice.

- Therefore, it could not be concluded that engagement in the daily five prayers was a contributing factor to the lack of a TOD effect observed in chapter [8].

- The findings remain important as they indicate that the TOD effect may not consistently apply to all populations equally which warrants further research to uncover the possible factors contributing to this.

Chapter 10: Engagement in the Islamic prayer and cognition

10.1. Introduction

The previous chapter looked at the interaction between engagement in the daily five prayers, TOD, and test scores to explore whether this may explain the lack of a TOD effect noted in chapter [8]. This chapter now aims to investigate whether engagement in the Islamic prayer, as an independent factor, may influence cognitive performance in this sample of Muslim South Asian older adults. Considering that the Islamic prayer may be a cognitively demanding task (see chapter [9]), engagement in this practice has potential implications for cognitive reserve and given that the sample tested was formed by Muslim South Asian older adults, makes it appropriate and valid to explore the general effect of engagement in the Islamic prayer on cognitive performance in the present cohort.

Also, statistics indicate that a large proportion of the UK's Pakistani and Bengali population identify as Muslims (ONS, 2011). According to the latest census data, 59.6% of the Muslim population in the UK originates from a South Asian background (ONS, 2011). These statistics further motivated the present study to explore the effect of engagement in Islamic praying practices on cognitive performance in this cohort.

In particular, the present chapter aims to explore the effect of four Islamic praying practices on cognitive test scores. These include engagement in the daily five prayers (also explored in chapter [9]), engagement in voluntary day prayers, voluntary night prayers and daily Quran recitation. Engagement in the daily five prayers was outlined in chapter [9], and the next section of this chapter provides a brief overview of the other praying practices being investigated.

10.1.1. Quran and voluntary prayers

Muslims around the world engage in the compulsory learning of Islam's holy book, the Quran, in its original Arabic version at a very young age (Akhtar, 2014).

As discussed in chapter [9], the Quran is formed by a complex grammatical structure and Muslims are required to recite the Quran with correct pronunciation by learning "Tajweed" which refers to the pronunciation rules of the Arabic text (Akhtar, 2014). As discussed in chapter [9], the daily five prayers require the recitation of Quranic verses from memory, however Quran can also be voluntarily recited at any time outside of the context of the daily five prayers (Williamson, 2018). Therefore, as well as performing the compulsory daily five prayers, Muslims may also engage in other voluntary prayers during the day and night which are discussed next.

Voluntary prayers are highly encouraged and recommended in the Quran (Sayeed and Prakash, 2013). As well as by reciting the Quran, these can also be prayed by praying additional units with or after the compulsory prayers in the same format and manner as the compulsory five prayers in units of two or four rakahs. Additionally, people may also engage in voluntary prayers in the form of a worship known as "dhikr" which involves the recitation of Quranic verses from memory as a form of remembrance of God (Sayeed and Prakash, 2013).

Muslims may also engage in voluntary night prayers by engaging in an act of worship known as "tahajjud" (Chodija, 2017). The word tahajjud means to stay awake at night and to spend the night in prayer by engaging in acts of worship involving salah and recitation of the Quran (Chodija, 2017).

10.1.2. The influence of prayer on mental health and cognition

Currently, there is a lack of literature investigating the impact of prayer, and in particular the Islamic prayer on cognitive performance. However, there is a wide range of literature investigating the effects of religion and prayer engagement on mental health and wellbeing in disorders such as anxiety, depression, and schizophrenia (e.g., Ghiasi and Keramat, 2018; Bonelli et al., 2012; Grover et al., 2014; Ironson et al., 2002).

One piece of study which explored the specific effects of the Islamic prayer on cognitive decline and AD was conducted by Inzelberg et al. (2013). They conducted door to door surveys in residents aged 65 years or over residing in the Wadi Ara village in northern Israel. The MMSE (Folstein et al., 1975) and Brookdale Cognitive Screening Test (for illiterate groups) (Davies, 1987) were used to assess cognitive functioning. Prayer engagement was assessed on a self-report lifestyle questionnaire. The sample was formed by 448 cognitively-healthy controls, 92 AD patients and 238 participants with MCI. Based on cognitive test scores, prayer was significantly associated with reduced risk of MCI, particularly in women. Inzelberg et al. (2013) concluded that prayer activity has the potential to reduce risk of MCI in women because the Islamic prayer actively engages individuals to use cognitive and motor components.

Inzelberg et al. (2013) also noted that they were unable to examine their aims in enough non-praying older male participants, as 94% of their male older adults responded engaging in prayer and therefore the findings may be gender biased. The study in chapter [9] of this thesis also reported a challenge in recruiting non-praying Muslim participants to establish more controlled comparisons between individuals who engage in prayer, and those who do not.

A further piece of research conducted by Coin et al. (2010) investigated the relationship between religiosity (Christianity) and the progression of cognitive impairment and behavioural disorders in MCI and AD. Their sample was formed by 64 AD patients who were assessed at baseline and 12 months later on the MMSE, the Behavioural Religiosity Scale and the Francis Short Scale (Francis and Stubbs, 1987) (measuring attitudes towards Christianity). Carers of patients were also questioned with regards to the patient’s daily functional abilities, behavioural disturbances, and stress levels. The results revealed that patients reporting low religiosity experienced a higher risk of cognitive impairment with an average decrease of three points in MMSE test scores over 12 months.

Doufesh et al. (2016) investigated the differences in mean gamma EEG power (neural oscillations in the human brain) between actual and mimic salah practices in a sample of 20 healthy male Muslim participants with a mean age of 26 years (authors do not specify ethnic background). As part of the inclusion criteria, participants were recruited if they were familiar with salah and had continuously performed salah, or daily five prayer, for 14(±5) years. In the actual salah group, participants were required to recite and perform salah as they would normally, whereas in the mimic practice they were requested to only perform the physical steps without recitation. The findings revealed that actual prayer engagement led to higher gamma powers as measured by an EEG in the frontal and parietal areas of the brain which are associated with attention and concentration. Doufesh et al. (2016) argued that salah actively engages working memory because those who engage in this practice must retrieve and recite verses from memory. Doufesh et al. (2016) concluded that the practice of salah with its specific set of movements and recitation from memory potentially enhances working memory which leads to improved attention and concentration. This has implications for cognitive assessment and performance which has not been previously explored.

The evidence discussed so far suggests that prayer may have the potential to enhance cognitive functioning (Doufesh et al., 2016; Coin et al., 2010). However, the present literature review failed to yield any studies which place a particular focus on investigating the impact of Islamic prayers (both salah and Quran recitation) on neuropsychological testing and cognitive performance in minority older adults. Considering that older adults are at a greater predisposition to suffer from cognitive decline (Sala Frigerio et al., 2019) and more likely to engage in prayer (Chaaya et al., 2006) supports the importance of exploring the effect of engagement in the Islamic prayer on cognitive performance in this cohort of Muslim South Asian older adults. The findings may have practical and theoretical implications for administering and interpreting test scores in clinical and research settings in people who engage in cognitively demanding praying practices.

10.2. The present study: Research aims

This study aims to explore engagement in the Islamic prayer as a factor which could influence cognitive performance. In particular, the aim is to explore the effect of engaging in the compulsory daily five prayers, voluntary day prayers, voluntary night prayers and daily Quran recitation on test scores in a battery of neuropsychological assessments in a sample of Muslim South Asian older adults.

Based on the cognitive demands of engaging in the Islamic prayer, it is hypothesised that there would be a significant effect of engagement in the daily five prayers, voluntary day prayers, voluntary night prayers and daily Quran recitation on cognitive test scores.

10.3. Methods

The present sample was formed by 45 participants aged 60 years and above from a Muslim South Asian background who confirmed proficiency in the Urdu language.

The same data and methods from chapter [8] were used to investigate the aims of this chapter. All participants completed a battery of neuropsychological assessments including DR, MoCA, PCS, LCS, DSF, DSB, SDMT, TMTA&B and DT. Prayer engagement was assessed on a self-report questionnaire requiring participants to state (“yes” or “no”) to whether they engaged in the daily five prayers, voluntary day prayers, voluntary night prayers and daily Quran recitation.

10.4. Results

The present study aimed to explore the main effect of engagement in the daily five prayers, voluntary day prayers, voluntary night prayers and daily Quran recitation on cognitive test scores in a sample of Muslim South Asian older adults.

10.4.1. Cognitive performance by prayer engagement group

To explore the aims, data on engagement in four different Islamic praying practices was collected through a self-report questionnaire. Engagement frequency for each praying practice investigated can be found in table one.

Table one – Engagement frequency in daily five prayers, voluntary day prayers, voluntary night prayers and daily Quran recitation

Prayer type	Frequency (Yes/No)
Daily five prayers	35/10
Voluntary day prayers	25/20
Voluntary night prayers	14/31
Daily Quran recitation	30/15

The data in table one indicates that as expected for an older adults' sample, there was a larger number of participants engaging in the compulsory daily five prayers and daily Quran recitation. This is likely to be because older adults tend to be more likely to hold traditional views and stronger beliefs in their faith making them more likely to engage in prayer (Chaaya et al., 2007). On the other hand, of all the prayer types investigated, engagement in the voluntary night prayers had the largest number of participants who reported not engaging in this practice, whilst the pattern was more balanced for engagement in the voluntary day prayers. The mean test scores on the battery of neuropsychological assessments administered by prayer engagement group are presented in table two.

Table two: Mean and SD (±) scores on the battery of neuropsychological assessments by prayer engagement group

Test	Prayer engagement	Daily five prayers	Voluntary day prayers	Voluntary night prayers	Daily Quran Recitation
DR	YES	2.77(±1.91)	3.08(±1.89)	3.21(±1.76)	2.70(±1.10)
	NO	3.00(±2.49)	2.50(±2.19)	2.65(±2.14)	3.00(±2.10)
MoCA	YES	16.86(±6.2)	18.36(±6.63)	19.57(±6.50)	16.97(±6.67)
	NO	15.30(±7.44)	14.20(±5.94)	15.13(±6.26)	15.50(±6.58)
PCS	YES	8.00 (±3.44)	8.28 (±3.13)	8.57(±3.20)	7.84(±3.31)
	NO	7.50 (±3.06)	7.40 (±3.59)	7.58(±3.39)	8.00(±3.51)
LCS	YES	5.86 (±3.09)	6.16 (±3.36)	5.86(±3.25)	6.00(±3.19)
	NO	5.80(±2.35)	5.45(±2.26)	5.84(±2.81)	5.50(±2.24)
DSF	YES	3.51(±0.78)	3.48(±0.82)	3.57(±0.76)	3.52(±0.77)
	NO	3.60(±0.70)	3.60(±0.68)	3.51(±0.77)	3.57(±0.76)
DSB	YES	2.60(±1.42)	2.76(±1.36)	3.07(±0.10)	2.55(±1.50)
	NO	3.00(±1.15)	2.60(±1.39)	2.52(±1.48)	3.00(±0.96)
SDMT	YES	8.40(±4.80)	9.28(±5.51)	9.43(±3.65)	8.65(±5.24)
	NO	9.50(±6.24)	7.85(±4.55)	8.29(±5.65)	8.64(±4.96)
TMT A	YES	3.40(±1.60)	3.06(±1.38)	2.78(±1.19)	3.42(±1.84)
	NO	4.20(±3.50)	4.24(±2.73)	3.94(±2.39)	3.93(±2.75)
TMT B	YES	4.16(±1.47)	3.83(±1.35)	3.58 (±1.23)	4.21(±1.71)
	NO	4.71(±2.65)	4.84(±2.11)	4.60(±1.91)	4.43(±1.99)
DT Ratio	YES	0.64(±0.14)	0.66(±0.12)	0.65(±0.10)	0.66(±0.11)
	NO	0.67(±0.15)	0.65(±0.17)	0.65(±0.16)	0.62(±0.19)

The findings in table two indicate that on average, participants performed better when they engaged in the daily five prayers on the MoCA and on assessments with a processing speed component which included the LCS, TMT A and TMT B (TMT B also taxes the domain of EF). Participants who engaged in the voluntary day prayers performed better on all cognitive assessments, except for test scores on DSF. With regards to engagement in the voluntary night prayers, participants who engaged in this praying practice performed better on all assessments when compared to those who did not engage in this practice. Lastly, participants who engaged in daily Quran recitation performed better compared to those who did not on the MoCA, PCS, LCS, SDMT, TMT A, TMT B and DT Ratio. The largest variance around the mean score values was given for test scores on the MoCA and SDMT, which are assessments of general cognitive function and EF, respectively.

10.4.2. Main effects of engagement in prayer on test scores

To assess the effect of engagement in the four prayer groups investigated on test scores, a MANCOVA analysis was carried out with each prayer group entered as a fixed factor (yes vs no) and cognitive test scores as the dependent variables. Age was controlled for in this model. The outcome for the main effects of each prayer group on test scores are reported in table three and significant main effects are graphically depicted in figures one and two.

Table three: Main effects of prayer group on cognitive test scores

Assessment	Daily five prayers	Voluntary day prayers	Voluntary night prayers	Daily Quran recitation
DR	n.s.	n.s.	n.s.	n.s.
MoCA	n.s.	n.s.	n.s.	n.s.
PCS	$F(1,41)=5.61$, $p<0.05$	n.s.	n.s.	n.s.
LCS	n.s.	n.s.	n.s.	Trend $F(1,41)=3.68$, $p= 0.06$
DSF	n.s.	n.s.	n.s.	n.s.
DSB	n.s.	n.s.	n.s.	n.s.
SDMT	n.s.	n.s.	n.s.	n.s.
TMT A	$F(1,41) =5.91$, $p<0.05$	n.s.	n.s.	$F(1,41)=7.81$, $p<0.05$
TMT B	n.s.	n.s.	n.s.	$F(1,41)= 6.60$, $p<0.05$
DT Ratio	n.s.	n.s.	n.s.	n.s.

The MANCOVA analysis revealed that there was a significant main effect of engagement in the daily five prayers and test scores on PCS and TMT A, which are assessments of processing speed. Significant main effects of engagement in daily Quran recitation and test scores were also found on the processing speed assessments of TMT A&B (part B also incorporates elements of EF), with a trend towards significance also reported in test scores on LCS, again another assessment of processing speed. All significant main effects are depicted in figures one and two which indicate that cognitive performance was significantly better in the group of participants who engaged in the daily five prayers and daily Quran recitation in assessments with a processing speed component.

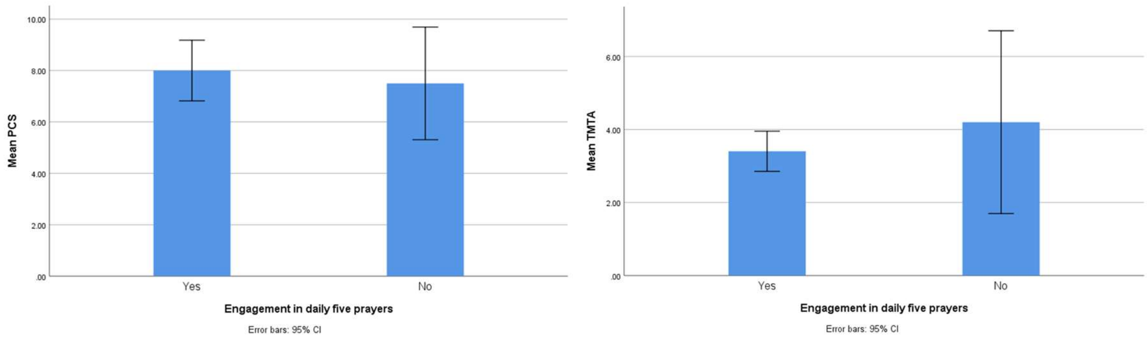


Figure one – Bar charts displaying the improved performance on test scores on the PCS in those who engaged in the daily five prayers and reduced time taken to complete the TMT A.

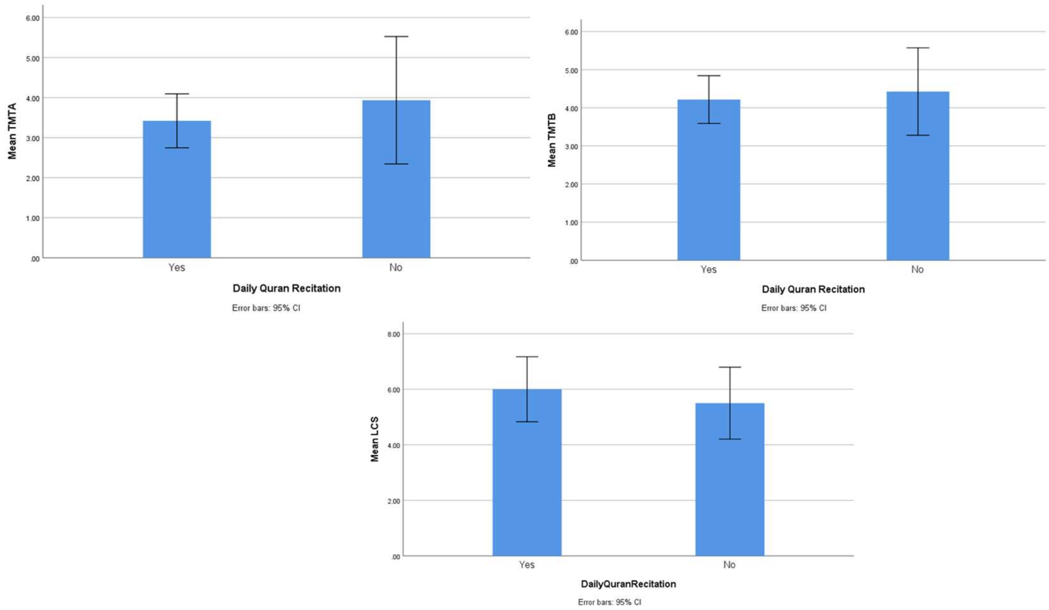


Figure two: Bar charts indicating that participants who engaged in daily Quran recitation took significantly less time to complete the TMT A&B. There was also a trend for significance on LCS scores, whereby test scores were higher in those who engaged in daily Quran recitation.

10.5. Discussion

The present study aimed to explore the effect of engagement in four different Islamic praying practices (daily five prayers, voluntary day prayers, voluntary night prayers and daily Quran recitation) on cognitive test scores in a sample of Muslim South Asian older adults.

10.5.1. Main findings

The analysis of the data revealed **(i)** a significant main effect of engagement in the daily five prayers on assessments of processing speed (PCS and TMT A) indicating improved test scores in those who engaged in this practice; **(ii)** a significant main effect of engagement in daily Quran recitation was also reported on test scores on the processing speed assessments of TMT A&B with a trend towards significance on LCS, whereby participants who engaged in this practice took significantly less time to complete the TMT A&B and scored higher on the LCS.

10.5.2. Engagement in prayer and cognitive testing

The daily five prayers and daily Quran recitation were the two praying practices that most participants reported engaging in and these were also the only two prayer types performed daily. Interestingly, main effects of engagement in prayer were only found in these praying practices on assessments with a processing speed component.

Previously discussed research by Doufesh et al. (2016) revealed increased gamma activity in the frontal and parietal areas of the brain in those participants who engaged in the Islamic Salah. These areas are argued to be associated with attention and concentration (Doufesh et al., 2016; Peers et al., 2005; Turken et al., 2008). Considering the role of the frontal and parietal areas in attentional processes required for processing speed, this may explain the enhanced performance of the present sample on assessments taxing this domain (PCS, LCS, TMT A&B).

Also, the findings in chapter [6] indicated that the sample of South Asian older adults were performing significantly closer to the population norms in assessments taxing processing speed when compared with the other cognitive domains assessed. This in conjunction with the present findings, appears to suggest that the adapted version of the TMT A & B (Kim et al., 2014) for lesser educated samples and the LCS and PCS may be more feasible to be used in a minority population with lower literacy levels.

There is also potential to argue that no significant main effects of engagement in the daily five prayers and daily Quran recitation were observed on any of the other assessments administered due to the higher reliance of those assessments on spoken language and education related skills and knowledge to complete as discussed in chapter [6]. Therefore, the non-significant findings for assessments measuring other domains further strengthens the argument that commonly used cognitive assessments may not be suitable to be implemented in populations who are less educated and may not have a good proficiency of the English language.

These findings may indicate that using assessments which may be biased by education and culture may also not be suitable to accurately explore the influence from external factors on test scores. This is due to the likelihood of performance not reflecting participants true levels of cognitive functioning implying that the effects of external factors on such assessments cannot be inferred with accuracy. This may potentially explain the lack of an effect in assessments such as the MoCA, SDMT, DSF, DSB and DT.

10.5.3. Prayer engagement and cognitive reserve

As discussed in chapter [9], the process of learning to recite the Quran involves learning to read and memorise complex structures in Arabic which may or may not be the learner's native language (Sayeed and Prakash, 2013). Further to this, the daily five prayers consist of a very structured process involving a particular set of movements which must be performed in a standard order (Doufesh et al., 2014). This indicates that the complex demands of the Islamic prayer may have the potential to contribute towards increased cognitive reserve, which may explain the enhanced cognitive performance on assessments of processing speed, which was the only domain incorporating an assessment adapted for lesser educated populations (TMT A&B).

Cognitive reserve is a concept which stipulates that complex cognitive activity can lead to structural changes in the brain which compensate for cognitive decline in normal ageing and even during brain damage caused by conditions such as AD (Hayakaw and Marian, 2019; Mondini et al., 2016; Stern, 2009). Cognitive reserve has been associated with factors such as higher education levels, skilled occupations, large social networks, bilingualism, and physical activity (Cosentinto et al., 2019; Zahodne et al., 2019; Mungas et al., 2018; Freedman et al., 2015). There is a potentially strong argument for engagement in the daily five prayers and Quran recitation increasing cognitive reserve particularly given that no significant main effects were observed for those who engaged in voluntary day and night prayers as these practices, unlike the daily five prayers and Quran recitation, may or may not be performed daily.

The role of engagement in prayer and the potential to develop higher cognitive reserve is therefore important to explore further. Higher cognitive reserve can mask neurodegenerative processes by compensating for the damage more efficiently, leading individuals to display adequate cognitive performance until the pathological damage has reached an advanced stage (Devita et al., 2019).

This indicates that researchers and clinicians may benefit from recording prayer engagement to control for the potential effects of higher cognitive reserve on neuropsychological test scores, which may otherwise not be sensitive enough to detect true levels of impairment. Devita et al. (2019) recommend the use of the Cognitive Reserve Index questionnaire (CRI-q) to supplement neuropsychological testing by measuring cognitive reserve. However, in its current format, the CRI-q does not measure cognitive reserve potentially acquired through engagement in the Islamic prayer, or any type of prayer in general. Therefore, if future research confirms an association between engagement in prayer and the development of higher cognitive reserve, assessments like the CRI-q offer the potential to be modified to incorporate a wider range of proxies of cognitive reserve to improve the sensitivity of neuropsychological assessments when implemented in populations who may engage in activities contributing towards higher cognitive reserve.

However, this cannot be asserted as currently there is no previous research exploring the effects of engagement in the daily five prayers and daily Quran recitation on cognitive performance, and on the development of cognitive reserve. The findings, however, provide the basis for future research to expand on this concept. It will be important to explore this using culturally appropriate assessment measures, as to the contrary, based on research findings in chapters [5-6] there is potential for cognitive test scores not being an accurate reflection of the sample’s true cognitive functioning for reasons other than cognitive reserve (e.g., language the tests area administered in, familiarity with the testing situation and the type of skills required to complete the tests). Subsequently, any analysis on the effects of engagement in prayer on cognitive performance and the development of cognitive reserve may also not be entirely accurate. This is particularly argued based on the present findings which only found significant effects of prayer engagement on assessments taxing the domain of processing speed which were also found to be more suitable in this thesis (see chapter [6]) for the present sample of South Asian older adults with lower levels of education.

10.5.4. Implications of the research findings

The results of this preliminary study have shown that participants who engaged in the daily five prayers and daily Quran recitation performed significantly better on tests of processing speed compared to those who did not engage in these practices. These are novel and interesting findings, which indicate that researchers may benefit from requiring participants to complete a detailed questionnaire with regards to their praying practices prior to completing neuropsychological assessments to improve the accuracy of the data obtained. Particularly, due to the potential of prayer leading to higher cognitive reserve.

Also, assessments taxing processing speed have been found to be suitable to differentiate between AD and Dementia with Lewy bodies (Peavy et al., 2013). This further highlights the importance of accounting and controlling for prayer engagement prior to a cognitive testing session involving the use of assessments of processing speed like the adapted TMT A&B to accurately differentiate between different types of dementias. Also, processing speed has been found to be sensitive to early decline (Lu et al., 2017), therefore if external factors which could influence performance on assessments taxing this domain are not accounted and controlled for, it may delay diagnosis.

10.6. Summary and conclusion

The Islamic prayer may be a cognitively demanding task involving the use of memory, attention, concentration, and motor skills which may have implications for cognitive reserve. Therefore, the present chapter aimed to explore engagement in the Islamic prayer as an independent factor which may influence cognitive performance in a sample of Muslim South Asian older adults.

The analysis of the data obtained indicated that engagement in the daily five prayers and daily Quran recitation had significant effects on cognitive test scores in assessments of processing speed, which is an important domain affected early in the development of AD (Lu et al., 2017). These findings have important implications for the interpretation of cognitive test scores and the accuracy of the subsequent diagnosis established in minority populations who engage in cognitively demanding praying practices. These findings are applicable to researchers conducting cognitive experiments using neuropsychological assessments in diverse populations.

As a preliminary piece of research, this paves for future research to be conducted in more controlled exploratory experiments to better understand how engagement in some Islamic prayers, and not others, may lead to enhanced cognitive performance in Muslim South Asian older adults. This may potentially be associated with the development of higher cognitive reserve, which requires testing in future research.

10.7. Chapter highlights

- The previous chapter [9] showed that the Islamic prayer may be a cognitively demanding task involving the use of memory, attention, concentration, and motor skills.

- The experiment in this chapter examined the effect of engagement in four different Islamic praying practices (daily five prayers, voluntary day and night prayers and daily Quran recitation), as independent external factors, on cognitive test scores in a sample of Muslim South Asian older adults.

- The results revealed a significant effect of engagement in the daily five prayers and daily Quran recitation on assessments with a processing speed component (LCS, PCS and TMT) indicating improved test scores in those who engaged in these two practices.

- The findings may be associated with the concept of cognitive reserve which warrants further research.

Chapter 11: General Discussion and Summary

11.1. Rational and motivation

According to statistics derived by the latest census data, South Asians of Pakistani, Indian, and Bangladeshi origin represent the largest ageing minority group residing in the UK (Hossain et al., 2018; Blakemore et al., 2018). With an increase in the ageing South Asian population, the number of individuals suffering from age related conditions, particularly AD and dementia, is also projected to increase (Blakemore et al., 2018).

In the UK, NICE (2018) recommend the use of brief assessments of general cognitive function to diagnose AD in non-specialist primary care settings. However, commonly used assessments of general cognitive function, like the MMSE, Mini-cog and the MoCA, have been developed and validated either with predominately White Caucasian samples or samples where ethnicity has not been stated/noted (Goudsmit et al., 2018). Some of the items within these assessments are affected by external factors such as culture, education levels and language (Blakemore et al., 2018; Filho et al., 2009). If these factors are not identified, noted, or controlled for, they may complicate the interpretation of clinical inferences derivable from neuropsychological test scores (Lesk et al., 2009; Walters and Lesk, 2016). It is crucial for cognitive test scores to be accurate because cognitive changes are a hallmark of AD, and accurately detecting these changes is vital, not only to infer an early diagnosis, but for evaluating the progression of symptoms, validating neuroimaging and fluid biomarkers, screening for research participants and evaluating the effectiveness of treatments in clinical trials (Cid et al., 2019).

Despite the importance of accurate cognitive screening, there is a lack of standardised neuropsychological assessment measures validated in minority populations (Goudsmit et al., 2018). South Asian older adults also remain largely absent in the field of cognitive and AD research (Blakemore et al., 2018).

This thesis aimed to address the lack of data on factors influencing cognitive testing in the increasing number of South Asian older adults residing in the UK. This was achieved by exploring a range of factors present at the time of testing to determine whether they had any influence on neuropsychological test scores in a sample of cognitively-healthy South Asian older adults.

11.2. Overall aims and methodology

The present thesis aimed to explore the potential influence of several external factors (e.g., testing language, education, type of skills required to complete tests, TOD, prayer engagement) on cognitive performance in a sample of cognitively-healthy South Asian older adults. In addition, the UNAS, an assessment of general cognitive function, and the SALT, an assessment of visual spatial associative memory, were also developed and evaluated as potential novel measures to improve the accuracy of neuropsychological test scores in less educated, culturally, and linguistically diverse populations.

All experimental chapters followed a quantitative methodology with cognitive performance assessed utilising a battery of cognitive assessments taxing different cognitive domains, all of which are commonly used in cognitive research settings. Cognitively-healthy participants were recruited for the experiments conducted as part of this thesis. However, the overall findings may have wider implications for the use of neuropsychological assessments both, generally and for the diagnosis of MCI and AD, particularly in underrepresented culturally diverse minority populations.

This chapter will summarise key findings from the experiments part of this thesis, examine the novel contributions of the studies to existing knowledge, and highlight implications for cognitive researchers, clinical practitioners, and policy makers. Lastly, recommendations for future research will also be made before drawing a final overall conclusion.

11.3. Key research findings and implications

A summary of the external factors investigated and the key findings from each experimental chapter are presented in this section. The implications and limitations of these findings are also discussed.

11.3.1. The influence of the testing language on cognitive performance

Chapter [5] explored the influence of the language in which the MMSE and the RUDAS were administered in, as a factor affecting cognitive performance. The results revealed that the sample of cognitively-healthy South Asian older adults scored within the cognitive impairment spectrum, both on the MMSE and the RUDAS, when administered in both English and Urdu, a language that the sample was proficient in. Both assessments were found to be affected by education, with higher levels of education correlating with better performance. This was despite the RUDAS claiming to be free from the cultural and educational bias associated with the MMSE (Storey et al., 2004).

These findings indicated that the MMSE and RUDAS were not suitable for identifying cognitive impairment in South Asian older adults with fewer years of education. In clinical settings, scores on cognitive assessments which are below the normality cut-off scores would have been an indication of a clinically significant cognitive impairment prompting referrals to specialist memory clinics or psychiatrists (NICE, 2018), which may not have been necessary. Considering that the present sample was formed by cognitively-healthy older adults and language bias was minimised by administering the assessments in a language that the sample was proficient in, implies that the lower test scores may not necessarily reflect true cognitive impairment. These may be more reflective of the sample's lower education levels (average of 4 years).

Some items in the MMSE and RUDAS may have been challenging to complete for participants with a lack of formal education. Both tests have a visuo-constructional test which requires participants to draw a cube (RUDAS) or a pentagon (MMSE). Further items in the MMSE require participants to read a written command, carry out a subtraction or spell the word "world" backwards.

This indicates that some of the items on the MMSE and RUDAS require familiarity with geometric figures, an understanding of Western numbers and the ability to read and write. Therefore, even if these items are translated for non-English speaking populations, like in the present study, less educated individuals are unlikely to have the ability to complete items requiring them to use skills typically learnt through Western education systems (Ardila et al., 2010).

These findings are important because, although the MMSE is no longer recommended for use in primary care settings by the NICE (2018) dementia guidelines, the items on other shorter assessments recommended in the new guidelines are derived from items in the MMSE (ADI, 2011). Moreover, as highlighted in chapters [4-5], despite the limitations of the MMSE, it continues to be used in a wide range of contemporaneous literature in the field of cognitive and AD based research (Devous et al., 2021; Arevalo-Rodirguez et al., 2015). This may lead to inaccurate interpretations of test scores which could inaccurately guide the inclusion and exclusion of South Asian older adults with lower levels of education from research and clinical trials. This would be of concern considering that South Asian older adults are already largely absent in the field of cognitive research (Blakemore et al., 2018).

It is also important to note that the RUDAS was developed as a culturally and linguistically fair cognitive screening tool for use in people from across different cultural backgrounds (Nielsen et al., 2019). The present study did not find that the RUDAS was more suitable when compared with the MMSE. The poor performance on the RUDAS in Urdu indicated that simply developing items which can be linguistically adapted is unlikely to remove the cultural bias in its entirety. Considering that minority ageing populations, like the South Asian, tend to be less educated (Blakemore et al., 2018; Goudsmit et al., 2018) implies that more emphasis should be given to developing assessments which do not rely on the completion of items that require education related knowledge to complete.

The findings also indicated that until more adequate screening measures are available, when assessing ethnically diverse and less educated populations, clinicians and researchers using cognitive tests should engage in detailed history taking which aims to identify factors such as language, education, and ethnic background to ensure that these variables are taken into consideration and accounted for when interpreting cognitive test scores.

11.3.2. Brief battery of domain specific assessments

Based on the recommendations by NICE (2018) to implement brief assessments of general cognitive function to diagnose AD in primary care settings, and the unsuitability of the MMSE and the RUDAS in the South Asian older adults' sample, in chapter [6] an alternative battery of brief domain specific assessments with lower reliance on language and education was put together. This included the assessments of DR, PCS, LCS, DSF, DSB, SDMT, adapted TMT A&B and DT.

It was proposed that developing a short battery of domain specific assessments with little reliance on language and influence from education may prove to be more suitable for populations like South Asian older adults. The assessments forming this battery, to our knowledge, had not previously been administered to this cohort of participants.

Chapter [6] explored how South Asian older adults would perform on these assessments based on comparisons with normative data sources. This chapter also explored the influence of the type of skills required to complete the tests on cognitive performance. Additionally, chapter [6] compared the global performance on the battery of domain specific assessments to an established assessment of general cognitive function, the MoCA, to determine whether global or general cognitive function could be better assessed by one single assessment of general cognitive function or by a battery of several domain specific short assessments. This, to our knowledge, had not been assessed by any previous literature in this group or any other minority populations.

Test scores obtained on the MoCA and the assessments part of the brief battery of domain specific tests were converted to z-score means using population norms. Z-score transformed means provide a standard measure of performance for assessments with different scoring systems facilitating comparisons between different tests (Mielke et al., 2017).

The analysis of the data revealed that participants performed below the population norms (therefore indicating poorer performance) on all assessments, except for test scores on the adapted TMT A&B. The TMT A&B was the only assessment in the battery which was conceptualised and validated for use in a less educated Korean sample (Kim et al., 2014). The results also indicated that cognitive performance was closer to the population norms on the single assessment of general cognitive function, the MoCA, when compared with the global cognitive test scores from the battery of brief domain specific cognitive assessments. Therefore, indicating that in this sample of cognitively-healthy South Asian older adults, general cognitive function was better assessed by a single assessment of general cognitive function. The results also revealed that test scores were closer to the population means in the domain specific assessments with a processing speed component (PCS, LCS, TMT&B and SDMT). Participants also performed significantly closer to the population norms in assessments with a non-verbalised response component (TMT A, TMT B, SDMT) and the furthest away in assessments with a verbalised response component (DR, PCS, LCS, DSF, DSB, DT).

These findings suggested that when attempting to reduce educational bias in neuropsychological testing, it is not sufficient to simply minimise items requiring the use of language and literacy skills, but the method in which cognitive assessments are administered may also have important implications for performance (Goudsmit et al., 2018; Kosmidis, 2018; Ardila et al., 2010). It transpired that abilities such as simply copying numbers in the SDMT, or just taking part in assessments may have significantly influenced cognitive test scores in South Asian older adults. This may indicate that even when tests do not appear to have an obvious requirement for education related knowledge, the way assessments are conducted and solved may still be affected by academic and cultural related experiences and attitudes.

Considering that the normative data sources used were also not culture specific, highlights that the poor cognitive performance of South Asian older adults may also be reflective of the lack of suitable normative data for culturally diverse populations. This has important implications for cognitive research as the results highlight the importance of developing more accurate normative data in older and ethnically diverse populations which considers, not only age and education related factors, but also cultural and ethnic differences in cognitive performance. This is important because the use of inappropriate norms and cognitive measures which do not account for cultural differences in cognitive testing may potentially lead to diagnostic errors (Ryan et al., 2020). To address this, it is proposed that test items should be developed or adapted by developing normative data obtained specifically for each population being tested (Ryan et al., 2020; Ostrosk -Solis et al., 2007).

The lack of normative data is also an important issue in clinical settings. The current shorter cognitive assessments recommended by the updated NICE (2018) dementia guidelines do not have any corresponding norms for less educated and culturally diverse populations. This is the case because these assessments have not been widely validated and the recommendations are largely based on opinions of what constitutes good practice (Larner, 2018). This means that in the absence of appropriate norms, there is a potential for increased risk of misdiagnosis in primary and specialist care settings where these assessments are commonly used.

Overall, these findings highlight the need to develop population specific norms and alternative measures of cognitive performance which are more reflective of the cultural living contexts of South Asian older adults.

11.3.3. Development of the UNAS and SALT

Chapter [7] aimed to address some of the issues identified in previous chapters with regards to the effects of external factors on cognitive performance in South Asian older adults and the lack of standardised cognitive assessments validated for minority populations. This was achieved by developing a new assessment of general cognitive function, the UNAS, and an assessment of visual spatial associative memory, the SALT. These were developed by building on the limitations of existing assessments like the MMSE, RUDAS and the MoCA.

An assessment of general cognitive function was developed because research findings from chapter [6] revealed that South Asian older adults performed closer to the population norms on the MoCA, which is a single assessment of general cognitive function, when compared with the global cognitive scores on assessments part of a brief battery taxing different domains. Also, cognitive decline characteristic of conditions like AD is progressive in nature, and it cannot be explained by impairment of a single domain (Duong et al., 2017). This makes assessments of general cognitive function more appropriate because they allow the assessment of a wide range of cognitive domains within one single test. A single assessment is also more likely to be easier to administer in time constrained clinical settings.

The UNAS was designed to incorporate items assessing processing speed, a domain known to be affected early in the pathology of AD (Lu et al., 2017). Currently, processing speed is not assessed by commonly used assessments like the MMSE, MoCA or the RUDAS (Hoops et al., 2009). This has implications for the early identification of cognitive impairment in conditions like AD. Research shows that individuals with phosphorylated tau pathologies, which are biomarkers in the early stages of AD (chapter [2)], experience a significant decline in processing speed abilities (Ho and Nation, 2018; Haworth et al., 2016). Tau is one of the earliest pathological biomarkers to develop in AD, and ongoing treatment trials call for reliable and quantifiable tau biomarkers to improve treatment effectiveness (Cumming et al., 2018). The National Institute on Ageing and Alzheimer's Association has also incorporated the presence of tau biomarkers in their research criteria for the diagnosis of AD in its earlier stages (Jack et al., 2018).

This evidence supports the claim that the absence of processing speed items in existing assessments can lead to a failure in accurately detecting early pathologies and cognitive changes in a timely manner. Moreover, findings from chapter [6] indicated that the sample of cognitively-healthy South Asian older adults performed closer to the population norms in assessments with a processing speed component which further supported its incorporation into the new assessment.

An assessment of spatial associative memory, the SALT, was also developed because this type of memory has shown to be sensitive to decline in the earliest stages of AD (Parra et al, 2010; Della Sala et al., 2012; Rubino and Andres, 2018). Associative memory is defined as the ability to learn and remember the association between unrelated items (e.g., the name of a person with a particular aroma) (Suzuki, 2005) and it is argued to be mediated by the activity of the medial temporal lobe which is shown to experience atrophy in the early stages of AD (Howett et al., 2019; Spaan, 2016). This area has also been associated to play a crucial role in memory function (Feczko et al., 2009), navigation (Laczo et al., 2009) and has been implicated in MCI and early AD (Chen and Chang, 2016; Della Sala et al., 2012; Amariglio et al., 2012).

Despite evidence supporting the assessment of spatial associative memory, to our knowledge, there is little to no mention of any papers in the literature investigating this cognitive domain in South Asian older adults. Also, assessments of general cognitive function currently recommended by NICE (2018) do not incorporate any items assessing associative memory. This implies that despite this being a domain sensitive to early decline, it is currently not a standard practice to assess this in primary care settings. Based on the lack of implementation of assessments of associative learning as a standard measure of cognitive decline, chapter [7] aimed to develop and pilot the use of the SALT as a novel test of spatial associative learning and a construct of episodic memory in the underrepresented South Asian older adults.

Although the UNAS and SALT were administered together in chapter [7], it was not suggested that this should be the standard practice. Both assessments were being piloted as novel measures, and future research is required to establish how they can best be used to assess early cognitive decline in minority samples.

The use of the UNAS and SALT was piloted in a sample of cognitively-healthy South Asian older adults, and test performance on the UNAS was compared with the established assessment of general cognitive function, the MoCA. The results revealed that the sample of South Asian older adults scored significantly higher, and therefore better, on the UNAS when compared with test scores on the MoCA. Based on the average test scores data, participants scored within the cognitive impairment spectrum on the MoCA (<26/30), however mean scores on the UNAS were significantly higher than those on the MoCA and much closer to the maximum scores. Although test scores on the SALT were not comparable to any existing assessments, participants did perform above chance level and closer to the maximum scores. There was no significant effect of education on the UNAS or SALT, however test scores on the MoCA, both at baseline and re-test, increased significantly with increasing number of years in education. The UNAS and the SALT achieved a good level of internal reliability as measured by a Cronbach Alpha analysis and good test re-test reliability as measured by a Pearson correlation. This preliminary data indicated that the UNAS and SALT were suitable for the present cohort of less educated South Asian older adults.

These initial preliminary findings supported the claim that the UNAS and SALT may have minimised the cultural and educational bias associated with commonly used assessments like the MMSE, RUDAS and MoCA. This has important implications for the cognitive screening of culturally diverse and less educated populations. In particular, the UNAS and SALT have demonstrated good psychometric properties and in conjunction, both measures cover domains known to be affected in the early stages of cognitive impairment (e.g., processing speed, EF, memory). This implies that with future investigations to establish these assessments, they have the potential to not only allow to infer a more culturally fair assessment, but they may also facilitate the detection of symptoms in a timely manner when treatment interventions have increased potential to ameliorate symptoms and slow down the progression of further decline (Insel et al., 2018). The UNAS and SALT are relatively easy and quick to administer without the need for specialist training which implies that they can be used by a range of different people with convenience, both in clinical and research settings. Also, with future research, there is potential that the UNAS and SALT can be combined into one single assessment which may make it more convenient for use in time constrained clinical settings.

11.3.4. TOD effects on neuropsychological test scores

Cognitive performance is also known to vary with circadian cycles, which are a series of physical, cognitive, and behavioural changes that the human body experiences during the typical 24-hour daily cycle (Newman et al., 2020). Research has shown that this leads to fluctuations in cognitive performance throughout the day, known as the TOD effect (Walters and Lesk, 2015; Singh et al., 2016). It is generally accepted that older adults reach their peak cognitive arousal in the morning (Walters and Lesk, 2015) and assessing cognitive performance during this time is considered optimal to obtain the most accurate reflection of an individual's cognitive abilities (Walters and Lesk, 2015, 2016; Blatter et al., 2007).

Chapter [8] explored the TOD effect in a sample of Muslim South Asian older adults. To our knowledge, this was the first study to explore the TOD effect in this cohort and in a BAME group. Prior to this research, there was no data specifically exploring the TOD effect in individuals from different cultural and ethnic backgrounds.

The analysis of the data gathered in chapter [8] revealed that contrary to the existing literature, no TOD effects were noted in this sample of Muslim South Asian older adults. This indicated that the time a cognitive test was administered did not have an influence on test scores in this sample.

In the absence of previous research in this group of participants suggesting otherwise, this preliminary data indicated that there does not appear to be an advantage for scheduling cognitive testing sessions for Muslim South Asian older adults in the morning hours. This has implications for memory clinics trying to meet the increased demand for their services. If memory clinics do not have to be restricted to be conducted in the morning to optimise the performance of their older patients, it implies that a higher number of individuals can be tested across the day reducing waiting times. Subsequently, quicker cognitive screening would also increase the likelihood of cognitive impairments being detected earlier.

The implications of these findings also extend to research which recruits children or younger adults from a Muslim South Asian background, or potentially from other minority backgrounds. At present, research recommends that young adults, regardless of ethnicity, should be assessed during their optimal time, which for this age group tends to be in the afternoon or evening (Van der Vinne et al., 2017; Schmidt et al., 2007; Hasher et al., 2005). Based on this, the teaching of critical subjects and examinations in the early hours of the morning may disadvantage the performance of children and teenagers because of the circadian dependent fluctuations in cognitive performance during the day (Van der Vinne et al., 2015; Haraszti et al., 2014; Hasher et al., 2002). However, based on the current preliminary findings, there is potential that there may be cultural differences in the variations of cognitive performance based on circadian dependent fluctuations.

This may have implications for education policy makers as it indicates that adopting the view that all young students will benefit from testing later in the day may not be true for people from across different backgrounds, and potentially for those with varying religious beliefs and practices. However, at this stage, it is not possible to make concrete conclusions with this regard, as to our knowledge, this was the first piece of research exploring the chronotype-dependent cognitive performance in an ethnic minority sample of Muslim South Asian older adults which requires further testing.

11.3.5. Daily five Islamic prayers and TOD interactions

Based on the lack of a TOD effect in the Muslim South Asian older adults' sample observed in chapter [8], it was important to explore why this might be the case. One possible explanation could be engagement of Muslim South Asian older adults in the cognitively demanding daily five Islamic prayers. These Islamic prayers take place across the day and are likely to influence the sleep-wake cycle, and subsequently the mechanisms by which circadian rhythms operate to allocate resources for optimal cognitive performance.

Chapter [9] explored the interaction between engagement in the daily five prayers and TOD to determine whether prayer engagement may explain the lack of a TOD effect in Muslim South Asian older adults.

The results indicated that there were no significant interactions between engagement in the daily five prayers and TOD on any of the cognitive tests administered in both, the group of participants who confirmed engagement in the daily five prayers, and neither in those who did not engage in this practice. This was an indication that, in this sample of Muslim South Asian older adults, the time of testing, again, did not influence cognitive test scores.

Based on the non-significant findings in both groups, it could not be concluded that prayer engagement may explain the lack of a TOD effect in this cohort. However, these are novel and interesting findings as they further support the claim that generalisations with regards to the influence of time of testing on cognitive test scores cannot be made conclusively in this cohort.

This has implications for researchers and clinics, as well as implications for education planning as discussed in section [11.3.4]. However, as a preliminary piece of study, further research is required to gain a more enhanced understanding of the potential impact engagement in cognitively enhancing activities has on influencing the TOD effect (or the lack of influence).

In particular, the present sample of non-praying Muslims was relatively small (10/45) compared to the number of people confirming engagement in the daily five prayers, which would be expected from an older adults' cohort (Chaaya et al., 2006). The small sample size in the non-praying group may have potentially contributed towards the lack of significance in this group which requires to be studied further in a larger and more equal sample of praying and non-praying participants. However, it is important to acknowledge that recruiting non-praying older adults is challenging and this is discussed later in this chapter.

11.3.6. The Islamic prayer and its influence on cognition

Chapter [10] investigated whether engagement in the Islamic prayer, as an independent external factor, may influence cognitive performance in a sample of Muslim South Asian older adults. Considering that the Islamic prayer may be a cognitively demanding task (see chapter [9]), engagement in this practice has potential implications for cognitive reserve and given that the sample tested in chapters [8-9] was formed by Muslim South Asian older adults, made it appropriate and valid to explore the effect of engagement in the Islamic prayer on cognitive performance in this cohort. Also, statistics indicate that Islam is the most practiced religion by UK based South Asians (ONS, 2011) which further motivated the aims of this research.

Chapter [10] explored the effect of four Islamic praying practices on cognitive test scores. These included engagement in the daily five prayers (also explored in chapter [9]), engagement in voluntary day prayers, voluntary night prayers and daily Quran recitation.

The results revealed that cognitive performance was significantly better in the group of participants who engaged in the daily five prayers and daily Quran recitation on assessments with a processing speed component (PCS, TMT A&B, and a trend towards significance on LCS).

This indicated that engagement in the daily five prayers and daily Quran recitation may be potential external factors which may influence the accuracy of neuropsychological test scores in Muslim South Asian older adults, particularly in assessments with a processing speed component. This raises the question as to whether research participants should be required to complete a detailed questionnaire with regards to their praying practices prior to completing neuropsychological assessments to control for the influence from these factors and improve the overall accuracy of the scores obtained.

This chapter also highlighted the importance of using culturally appropriate assessments when exploring the effects of external factors on cognitive performance. Significant effects were only found in assessments with a processing speed component, which were also the same assessments that were found to be more suitable for this cohort in chapter [6]. This indicates that there is potential that no significant effects were observed on any of the other assessments used due to their potential lack of suitability for this sample.

11.4. Wider implications

Currently, there are no disease modifying or curative treatments for AD (Livingston et al., 2017). Existing medications are only effective in temporarily alleviating and slowing down the progression of cognitive symptoms in mild to moderate stages of the disease (Livingston et al., 2017). Therefore, early diagnosis is currently a national priority to facilitate a timely access to treatment interventions (Mukadam et al., 2011).

The current NICE (2018) dementia guidelines recommend the use of neuropsychological assessments to identity cognitive impairment in primary care settings, which tend to be the first point of contact for people with complaints regarding their cognitive abilities (Alzheimer’s Society, 2021). Effective screening of cognitive performance using neuropsychological assessments is therefore critical for the early identification of impairment and for the optimal management of AD (Black et al., 2019). Neuropsychological test scores are also commonly used to diagnose and research other medical conditions including Parkinson’s disease (Herbozo and Bustamante, 2020), Huntington’s disease (Martinez-Horta et al., 2020), schizophrenia (Kraus et al., 2019), autism (Matsuura et al., 2014), depression (Mayer et al., 2021) and to assess child development trajectories amongst others (Linsell et al., 2018). Therefore, neuropsychological testing is used in a wide range of different research and medical settings to diagnose and map cognitive impairment trajectories overtime and across the lifespan.

Although this thesis has predominately focused on the implications of some external factors on cognitive performance with relevance to AD and MCI in an older adults’ cohort of South Asians, the findings and their respective implications are also likely to extend to any type of research or clinical setting using cognitive testing measures. The results are also likely to apply to any cohorts of participants with lower levels of education, and not only to those from ethnically diverse minority backgrounds.

The promising preliminary findings with regards to the use of the UNAS and SALT in South Asian older adults have also suggested that an assessment which reduces the educational, linguistic, and cultural bias from testing may prove to be more suitable for application in older adults from ethnically diverse and less educated backgrounds. With future continuations of the validation of these assessments in clinical samples, there is potential that these may become suitable for use in clinical settings to diagnose conditions like AD. This, subsequently, may also have policy implications for NICE (2018) who acknowledge the impact of culture and education on cognitive testing, however, currently fail to offer advice on alternative measures which may be more suitable in such circumstances. Nonetheless, it is acknowledged that although these initial findings are positive, these assessments may need some alterations and further work to enhance their properties.

Another important implication of the research presented, is that it highlights the existence of discrimination based on culture/race within the diagnostic pathways for AD and other conditions using neuropsychological assessments. This is argued because as observed, the sample of cognitively-healthy South Asian older adults performed within the impairment spectrum on commonly used and established assessments like the MMSE, RUDAS, MoCA as well as on assessments which were proposed to have lower reliance on education and language (DR, PCS, LCS, DSF, DSB, SDMT, DT). This was found despite the assessments being delivered in a language that the sample was proficient in.

Considering the education bias present in these assessments and the enhanced performance on the UNAS, suggests that commonly used standard assessments of cognitive performance may put certain groups of patients at a disadvantage due to their protective characteristics (e.g., race, disability, age, sex – Equality Act 2010). Individuals who are less educated and from a non-English speaking background appear to be disadvantaged by the items on commonly used assessments which may have negative repercussions on their timely diagnosis and access to adequate services pre and post diagnosis. There is an important legal issue attached to this for which NICE have previously been scrutinised (Davey and Jamieson, 2004).

In the past, the NICE dementia guidelines widely recommended the use of MMSE test scores to grade cognitive decline and decide which patients were eligible for AD treatment (Davey and Jamieson, 2004). However, NICE were involved in Judicial Review proceedings as this practice was found to be discriminatory against those whose first language was not English and were not able to complete assessments like the MMSE for reasons beyond the level of deficits in their cognitive functioning (Mitchell, 2009). Following this, NICE amended their guidance on eligibility for treatment. However, again the amendments suggested very vague solutions whereby clinicians were simply told to implement different measures other than the MMSE where equality of treatment was prevented due to linguistic and communication issues (Davey and Jamieson, 2004). This means that there is potential to argue that the cultural and educational bias noted in commonly used assessments in South Asian older adults may be discriminatory which could potentially raise further legal issues for NICE. This issue can potentially be addressed by developing more representative and accurate population based normative data sources and exploring the use of alternative assessments, such as the UNAS and SALT, and validate their use in ethnic minorities.

11.5. Future directions

The future directions discussed in this section are being proposed by building on from the strengths and limitations as well as the methodological considerations for each experimental chapter.

The findings from chapters [5-6] indicated that currently available assessments of cognitive function were influenced by the sample's education level and familiarity with Western constructs. This highlighted the need for future research to account and control for the effects of these variables to improve the interpretation of test scores when assessing South Asian older adults. Also, in view of the lack of normative data available for ethnic minority populations and the enhanced cognitive performance observed on the UNAS and SALT in chapter [7], it may be more important for future research to focus on the development of alternative assessments which are developed with minority populations and account for cultural variance in cognitive performance. This may help minimise the need to conduct detailed history taking practices to identify and control for the effects of subtle external factors which could reduce overall appointment times for cognitive testing sessions.

Future research should also explore the use of measures which assess processing speed and EF, such as the adapted TMT A&B (Kim et al., 2014) as these processes have been demonstrated to be affected in the early stages of decline in AD (Lu et al., 2017; Daugherty et al., 2020). However, the NICE (2018) dementia guidelines do not routinely advocate the use of measures which tax these domains. Future research in cognitively-healthy controls and clinical samples targeting these domains may offer insightful knowledge with potential implications for NICE (2018) to update their dementia assessment guidance.

Chapter [8] failed to report a TOD effect on cognitive test scores in a sample of Muslim South Asian older adults. These preliminary findings support future research to be conducted in a more controlled manner. This should be done by recording participants' subjective levels of tiredness and sleep patterns which modulate circadian rhythms and may alter TOD effects (Bugg et al., 2006). Prior caffeine intake is also known to affect circadian rhythms and TOD effects (Walters and Lesk, 2015, 2016) and it should also be noted and controlled for in future continuations of this study. Walters and Lesk (2016) also found an interaction effect of caffeine with TOD on cognitive performance suggesting that prior caffeine intake and TOD may need to be studied in combination in South Asian older adults. To our knowledge, there is currently no papers in the literature which explore this interactive effect in a minority sample of South Asian older adults. This is an important future direction considering that caffeine is one of the most consumed beverages across the world (Fredholm et al., 2017), implying that it is likely to be prevalent during a typical cognitive testing session.

The interaction between engagement in the daily five Islamic prayers, TOD and cognitive test scores was also explored due to the potential the Islamic prayer has on modulating the sleep-wake cycle. This confirmed that the group of Muslim South Asian older adults who engaged in the daily five prayers did not experience a TOD effect. However, this was also the case for the small number of people who did not report engaging in the daily five prayers. Therefore, future research is required in different age groups and in an equal number of participants who do not engage in prayer to establish more controlled and accurate comparisons.

However, as noted in this thesis, it was challenging to recruit older adults who did not engage in prayer. To address this, prior to expanding future research in different age groups, it may be beneficial to work with South Asian religious leaders (e.g., Mosque imam’s, Hindu, and Sikh leaders) as this could help to gain a better insight into praying practices and factors affecting levels of religiosity in different age groups to target the recruitment of people who engage and those who do not engage in prayer.

Moreover, to facilitate the recruitment of underrepresented South Asian older adults in cognitive research and to improve the representation of the different ethnicities forming a part of this group, future research could also benefit from liaising with community leaders, such as community development workers. This is important to improve the sample size and heterogeneity of the South Asian sample being studied to produce more representative findings. Community leaders are likely to have established links with the local community, and as a result they are likely to be a trusted source which can act as a mediator to facilitate the recruitment of South Asian older adults in research. This is particularly important as South Asian older adults are underrepresented in research due to being a hard-to-reach group (Blakemore et al., 2018; Waheed et al., 2019) and encouraging their participation considering the novel findings in this thesis can facilitate the development of more enhanced and culturally suitable cognitive screening measures.

The findings with regards to the pilot of the UNAS and SALT were also preliminary and future research in larger and more diverse samples is required before it can be concluded that these assessments are suitable for all South Asian older adults. In particular, the South Asian population is very heterogenous and is formed by people who follow different religions (Islam, Hinduism, Buddhism, Sikhism) and speak a range of different languages. For example, religion statistics derived from the Office for National Statistics (ONS, 2020) indicate that after Christianity, the most followed religions in the UK are Islam (4.8%), Hinduism (1.5%) and Sikhism (0.8%) which are identified as predominately South Asian religions (Peach, 2006). Moreover, UNICEF (2019) found that speaking two or more languages was a norm rather than an exception in most parts of South Asia due to the linguistic diversity within these countries. For example, Hindi is the official language in India, however it is not the only national language, but it is part of the 22 constitutionally recognised official languages (UNICEF, 2019; Aarti and Kopparapu, 2018). Pakistan, the country from which a large part of the current sample originated from, is estimated to have 72 recognised languages with the most commonly spoken being Urdu, Punjabi and Pashto (UNICEF, 2019). In Bangladesh, Bangla is the officially recognised language, however it is divided into different local dialects. Moreover, Bangladesh has many Urdu speakers because it was part of East Pakistan before becoming an independent state following the 1971 war (UNICEF, 2019). A report by Samad (2010) titled "Muslims and community cohesion in Bradford" also highlighted that there are marked differences within those in the Pakistani community based on clan and village alliances (e.g., Mirpuris, Pathans, Chahchis, etc). The report also identified that Pakistani Muslims are also further sub-categorised because mosques are often divided by sect type (Barelwi, Deobandi, Ahmadiya, etc).

This indicates that there is a large diversity amongst South Asians based on language, religion, and village alliances in their home countries. However, the present thesis failed to capture this diversity within the South Asian sample, which was predominately formed by Pakistani participants. This heterogeneity within the South Asian population suggests that future research validating the use of the UNAS and SALT should be conducted with all the potential different groups and sub-groups of South Asians. This will be necessary before it can be confirmed that these assessments are suitable for all the diverse South Asian population groups residing in the UK.

Research implementing the UNAS, and SALT is also needed in clinical samples with a diagnosis of MCI and AD to explore their ability to identify clinically significant cognitive impairments and distinguish between MCI and AD. This will be important to determine whether the current items require any alterations or adjustments, and to develop appropriate cut-off scores for impairment based on performance comparisons between healthy controls and clinical samples.

As the UNAS and SALT aim to be universal assessments for people from across different ethnic backgrounds and education levels, future research is needed in other BAME groups, such as Africans, Eastern Europeans and East Asians residing in the UK to investigate the suitability of these assessments as standard universal scales.

Also, the paper version of the SALT may have some practical issues attached, particularly in that it is more time consuming to deliver. However, this was only a preliminary study, and it is proposed that future continuation studies should aim to explore the potential to develop an electronic version whereby instructions are provided verbally in a selection of languages and the task merely requires participants to make touch selections to identify the location of the relevant stimuli. A test trial should also be incorporated into the electronic version to ensure that participants understand how the task will work to minimise the likelihood of participants becoming overwhelmed by being requested to use an electronic device, which they may not have previous experience with.

Ideally, the UNAS and SALT should be combined to consist of one assessment to make the tests more suitable for clinical use where time constraints are a major concern. Although it is acknowledged that the use of a single test score may not be adequate to determine the overall outcome, if the assessment is successful at measuring cognitive domains known to be affected early (e.g., EF and processing speed), this could improve the validity and reliability of the results obtained and the implementation of a longer battery of tests may not be required.

It is also important to highlight that the present thesis has focused on some external factors relevant to South Asian older adults that may affect cognitive performance. However, there remain many other factors which could influence test scores. The present thesis did note other additional factors including caffeine intake, bilingualism, alcohol intake, smoking, occupation, and sleep. Some analysis was carried out to explore the influence of prior caffeine intake on cognitive test scores based on research findings by Lesk et al. (2009) and Walters and Lesk (2016) as well as the influence of bilingualism.

However, the findings did not reveal any results of significance. As a result, this data was not reported in the present thesis. These factors were only noted but not adequately controlled for which may have contributed to the lack of significant findings. Considering that previous research has found an influence of prior caffeine intake (Walters and Lesk, 2016; Lesk and Womble, 2004) and bilingualism (Kousaie and Phillips, 2011) on cognitive test scores, these are important factors that should be continued to be explored in future in more controlled experiments.

11.6. Overall summary of the discussion

The experiments forming part of this thesis have highlighted a lack of general cognitive research in ethnically diverse populations, such as the South Asian older adults, or that inclusion of such groups is not being reported. This thesis has aimed to address this issue by conducting novel research exploring the influence of several factors, which are particularly salient for this cohort, on cognitive performance by using a battery of established and validated assessments of cognitive function commonly used in the present cognitive research literature.

This thesis also developed two new tests, the UNAS and SALT, to improve the accuracy of cognitive screening in an underrepresented minority group. The preliminary findings have shown that these assessments may be more suitable for this cohort. This is an important finding considering that the sample of cognitively-healthy participants performed below the population norms on existing neuropsychological assessments.

However, the overall sample in this thesis was predominately formed by Pakistani Muslim South Asian older adults which may not be representative of the wider South Asian community in the UK. Nonetheless, the present sample was formed by participants with lower levels of education and evidence indicates that less educated migrants are a hard-to-reach cohort (Waheed et al., 2019; Shaghaghi et al., 2011). Recruiting this sample has therefore allowed to produce novel data on cognitive screening in an underrepresented and hard-to-reach group. However, the recruitment of a larger and more heterogenous group of South Asian older adults will be required to improve the overall generalisability of the research findings and rise the standards of cross-cultural research within the field of cognitive screening.

11.7. Thesis conclusion

The results presented in this thesis raise questions about the routine use of currently established neuropsychological assessments in research and clinical settings in South Asian older adults with lower levels of education.

Currently established assessments of general cognitive function, the MMSE, MoCA and the RUDAS were found to be significantly influenced by education and language and some of the items in these assessments required a certain level of acculturation with Western based concepts. The sample of cognitively-healthy older adults, on average, performed below the published population norms on all assessments administered, except for the adapted TMT A&B, which was the only assessment in the battery specifically developed and validated with a lesser educated sample. This also indicated that performance on commonly used assessments may be a direct reflection of the present cohort's limited experience and familiarity with the testing situation. The format of neuropsychological assessments resembles education-based tasks and the skills assessed are often absent, or trained to a lower level, in people with lower levels of education (Kosmidis, 2018). This may imply that neuropsychological assessments, as currently administered, may be measuring factors which are extrinsic to the assessment itself. This may lead to errors in healthy older adults with lower levels of education which resemble to those associated with AD. This may have led the present cohort of cognitively-healthy older adults to score within the impairment spectrum, despite the battery of cognitive assessments used being delivered in Urdu, which was a language that the sample confirmed fluency in.

A new assessment of general cognitive function, the UNAS, and an assessment of visual spatial associative memory, the SALT, were developed by the researcher and piloted in a sample of South Asian older adults with the aim to provide solutions which align with the issues expressed within the cognitive assessments used in this thesis. The preliminary evaluation of these novel assessments has shown that these may be more suitable for the assessment of cognitive functioning in minority less educated samples. No education bias was reported for both assessments which were also found to have a good level of reliability. These are important findings considering that the present cohort scored poorly on exiting neuropsychological assessments. However, future research in clinical and more diverse samples is required to identify whether any alterations may be necessary and to develop appropriate normality cut-off scores for the UNAS and SALT.

The work presented in this thesis was also, to our knowledge, the first one to explore the TOD effect and engagement in the Islamic prayer as factors which may influence cognitive performance in a minority underrepresented group. Contrary to the existing literature, no TOD effects were observed in this cohort, and engagement in some Islamic praying practices (daily five prayers and daily Quran recitation) significantly influenced test scores in assessments with a processing speed component (PCS, LCS and TMT A&B). Although it was not possible to make conclusive decisions with regards to the influence (or lack of influence) of these factors on cognitive performance, these are novel findings which provide the basis for future research to explore further. The influence of prayer on cognition may also lead to hypotheses to be drawn regarding the wider field of cognitive reserve.

Although the thesis has focused on the assessment of several factors and their influence on neuropsychological testing in an older adults' cohort, the findings have wider implications in the field of experimental psychology and cognitive research in general. The effects of external factors on cognitive test scores are important for any paradigm which uses cognitive testing measures as part of their methodology in people from across different age groups and for the diagnosis or monitoring of different conditions.

In conclusion, currently available neuropsychological tests administered to detect cognitive decline characteristic of AD are developed from a very particular cultural, political, and clinical context which is problematic in terms of universality in implementing with diverse populations. It is important to highlight the idea that cognitive functioning cannot be understood independent of the cultural and linguistic context of the person being assessed. Therefore, neuropsychological tests are required to be tailored towards the needs of different cultural groups. This thesis has highlighted some issues present in the cognitive screening of South Asian older adults. However, as an underrepresented group, further research in this cohort continues to be vital to validate culturally appropriate tests, such as the UNAS and SALT, and understand how diagnosis is established and what can be done to account for cultural variance in cognitive performance to improve the accuracy of neuropsychological test scores, and ultimately of the final diagnosis established.

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