

**DEMOGRAPHIC AND ETHNICITY EFFECTS ON
NEUROPSYCHOLOGICAL TEST PERFORMANCE:
IMPLICATIONS FOR DEMENTIA ASSESSMENT IN
CARIBBEAN POPULATIONS**

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ABSTRACT

Prevalence rates of dementia are increasing worldwide and more so in developing countries. Early and accurate diagnosis of dementia then assumes critical importance. Cross-cultural neuropsychological assessment of dementia depends on the use of instruments that have been appropriately normed and validated for target populations. While culture and ethnicity have been acknowledged as variables which significantly impact cognitive performance, they are not usually included in normative and validation studies. The main aim of this dissertation was to standardise and identify the role played by ethnicity in performance on a number of instruments used in the assessment of dementia and identify the role and interaction of ethnicity with other common demographic variables on performance for Caribbean populations. Performance on the Mini Mental State Exam (MMSE) was influenced by age, education and ethnicity and a validation of corrected scores yielded a cut-off that resulted in a 35% reduction in false positive rates among non-AD persons. The Alzheimer's Disease Assessment Scale-cognitive section (ADAS-cog) was influenced by education and was resistant to effects of ethnicity. Cut-off scores were lower than traditionally suggested, perhaps due to higher educational levels, but resulted in very high sensitivity (89%) and specificity (89%) rates. Education influenced scores on most measures: digit span, digit cancellation, logical memory, semantic and phonemic fluency and Raven's Coloured Progressive Matrices. Ethnicity also influenced scores on digit span backwards, digit cancellation, semantic fluency and Raven's Matrices. Ethnic differences in performance may be attributed to differences in attention, working memory and also to differences in cognitive styles. Differences in educational attainment across cultures and generations renders earlier norms invalid and highlight the needs for norms to be periodically revised in order to be considered representative of current populations. The provision of culturally relevant and contemporary norms yielded in this study can be regarded as invaluable tools in the assessment and diagnosis of dementia in diverse populations.

*With love to the Khan women: Leila, Zaida and Nisha (and the twosome Stella and Lily)
My achievements are a testimony to your unwavering support, constant encouragement and
enduring faith. You inspire me to embody the words:*

*“You are not here merely to make a living. You are here in order to enable the world to live more amply, with
greater vision, with a finer spirit of hope and achievement. You are here to enrich the world, and you
impoverish yourself if you forget the errand.”*

Woodrow T. Wilson

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CHAPTER 1

AN OVERVIEW OF DEMENTIA

1.1 A BRIEF EVOLUTION OF THE CONCEPT OF DEMENTIA

From as early as the 7th century B.C., the issue of cognitive decline in the elderly had been recognized. Pythagoras, in describing the stages of the life cycle, identified the last two stages (starting at 63 and 81 years respectively) as the senium or ‘old age’ which were characterised by decline and decay of the human body and regression of mental capacities (Halpert, 1983). In the Greco-Roman period, Hippocrates, Plato, Aristotle, and Cicero also made mention of mental decline in old age in their writings, with deterioration seen as an almost inevitable consequence of the ageing process (Halpert, 1983; Karenberg and Forstl, 2006).

The first classification of dementia as a mental disorder came in 2nd century AD when the Roman physician Galen included it (he used the term ‘morsis’) in his list of mental diseases. Galen’s description of ‘morsis’ is indeed evocative of the symptoms encountered in dementia: “[there are] some in whom the knowledge of letters and other arts are totally obliterated; indeed they can’t even remember their own names...” (Torack, 1983, p 24 as cited in Berchtold and Cotman, 1998).

Following this period, little was written about senile cognitive decline until the 16th century, with the exception of Francis Bacon in the thirteenth century who reiterated the theme of mental decline in old age. Critical also, was his attribution of memory and thought processes to the brain and not to the heart, which was popularly held to be the seat of the soul and mental processes at that time (Torack, 1983 as cited in Berchtold and Cotman, 1998).

Dementia continued to be regarded as an inevitable feature of ageing. Advancements in the conceptualization of cognitive disorders as well as the increasing trend towards dissection and a search for underlying physiological changes in the brain as a cause for mental disorders further influenced and refined the concept of dementia (Berchtold and Cotman, 1998). The 17th century physician and anatomist Willis reasoned that ‘stupidness, or morosis or foolishness’ was due to a defect in intellect or judgement and identified a number of causes: congenital factors, age, head injury, alcohol and drug abuse, disease and prolonged epilepsy (Berrios, 1987, p 831)

In the nineteenth century, the humanitarian efforts of French physician Pinel led to the acceptance of ‘madness’ as a disease and not a crime and ensuing reforms in mental health institutions enabled clinical and pathological observation of mental disorders (McGrew, 1985). Pinel’s student Esquirol, made refinements to the categories of dementia, differentiating between dementia and amentia: “A man in a state of dementia is deprived of advantages which he formerly enjoyed; he was a rich man who has become poor. The idiot, on the contrary, has always been in a state of want and misery” (Hunter and Macalpine, 1982, pg 733). The nineteenth century also saw the discovery of the first aetiological basis for dementia in which a reduction in brain weight due to atrophy of brain cells was seen to be associated with some dementias (Berrios, 1994). Improvements in microscopy and histochemical techniques also enabled unprecedented etiological development (Berchtold and Cotman, 1998). The observation of the accumulation of substances into plaques in a number of cases of senile dementia led this neuropathology to be considered a marker for senile dementia (Fischer, 1907 as cited in Berchtold and Cotman, 1998).

In 1907, the use of the Bielschowsky stain to identify neurofibrillary tangles made Alois Alzheimer famous. In describing the pathology of the brain of a deceased 51 year old woman who had developed an unusual dementia, Alzheimer felt he had come across

something unique. The widespread presence of neurofibrillary tangles, neuronal degeneration and plaques seemed similar to the pathology described in senile dementia. However, this case stood out from other dementia cases which were the result of neurosyphilis or vascular disease. The young age of onset, rapid course of progression and unique neuropathological features led Alzheimer to believe that he had encountered a previously undefined disease. This notion was officially endorsed when Emil Kraepelin included 'Alzheimer's disease' in his classic Textbook of Psychiatry in 1910, listing it as a subtype of senile dementia-presenile dementia (Berchtold and Cotman, 1998). This inclusion and its designation as a separate subtype has often been criticised as being premature and inspired by political rather than scientific reasons (Amaducci, Rocca, Schoenberg, 1986). The validity of the claim of Alzheimer's disease as distinct from senile dementia spurred observation at the histological and behavioural level and drove research for the next several decades (Berchtold and Cotman, 1998).

1.2 GLOBAL IMPACT OF DEMENTIA

Despite having been mentioned in Egyptian and Roman literature thousands of years ago, dementia was considered a rare occurrence. Few people would have survived to an advanced age, and as such, few persons would have been affected and thus the disease was not subjected to much investigation (Ineichen, 1998). The first dementia prevalence survey was published in 1948, in the United Kingdom (Sheldon, 1948). This was followed by a steady progression of further studies: Scandinavia, Far East and North America in the 1950s, Australia and New Zealand in the 1960s and Russia in the 1970s (Henderson, 1994). It was not until the 1980s that the first prevalence study in Africa was undertaken (Ben-Arie et al, 1983) and in India, prevalence studies were only first published in the 1990s (Wadia, 1992). While surveys from developing countries are fewer, attempts have been made nonetheless to estimate the worldwide prevalence of dementia.

In 2001, 24 million persons were estimated to be living with dementia and this figure is expected to double every 20 years, increasing to approximately 80 million by the year 2050 (Ferri, Prince, Brayne et al, 2005). Utilising a Delphi consensus approach using a systematic review of published works on dementia prevalence, Ferri and colleagues (2005) obtained prevalence rates for the fourteen regions of the world as defined by the World Health Organisation. Specifically, predictions for increases in dementia prevalence are associated with three regions- developed regions who are among the regions with highest prevalence are expected to increase moderately (100%) by 2040, Latin America and Africa who have much lower prevalence rates are expected to have rapid and large increases (235%-393%) and China, India and other south-Asian and western-Pacific countries which have relatively high prevalence are also expected to have relatively large, rapid increase (314- 336%). See Table 1.1

One key explanation for the projected increase in dementia cases has been attributed to unprecedented ageing of the world's population in which the increasing proportion of older persons (over age 60) is accompanied by a concurrent reduction in the proportion of children (under age 15). While the world's population is increasing at a rate of 1.1% per year, the over 60 age group is advancing at a rate of 2.6% (United Nations, 2007). This has profound consequences for many sectors of society including epidemiology and health-care services.

The worldwide cost associated with dementia has been estimated at US\$315 billion (Wimo, 2005) and includes a consideration of both formal and informal care. Given the expected increase in prevalence, the costs associated with dementia are expected to rise considerably. Ferri et al (2005) note that any such calculation is dependent on accurate estimates of persons living with dementia which in turn relies on representative epidemiological surveys from the different regions of the world.

Table 1.1

Number of people with dementia in 2001, projections for 2020 and 2040, and percentage increases, by WHO region

		Population (millions),aged 60 years (2001)	Consensus dementia prevalence (%) at age >60	Estimated annual incidence per 1000	New dementia cases (millions) per year, 2001	Number of people (millions) with dementia, aged >60			Proportionate increase (%) in number of people with dementia	
						2001	2020	2040	2001–2020	2001–2040
Western Europe	(A)	89.6	5.4	8.8	0.79	4.9	6.9	9.9	43	102
Eastern Europe	(B)	27.4	3.8	7.7	0.21	1.0	1.6	2.8	51	169
Eastern Europe	(C)	44.6	3.9	8.1	0.36	1.8	2.3	3.2	31	84
North America	(A)	53.1	6.4	10.5	0.56	3.4	5.1	9.2	49	172
Latin America	(B/D)	40.1	4.6	9.2	0.37	1.8	4.1	9.1	120	393
North Africa and Middle East	(B/D)	27.5	3.6	7.6	0.21	1.0	1.9	4.7	95	385
Developed western Pacific (Japan, Australia, NZ)	(A)	34.5	4.3	7.0	0.24	1.5	2.9	4.3	99	189
China and developing western Pacific	(B)	151.1	4.0	8.0	1.21	6.0	11.7	26.1	96	336
Indonesia, Thailand, and Sri Lanka	(B)	23.7	2.7	5.9	0.14	0.6	1.3	2.7	100	325
India and south Asia	(D)	93.1	1.9	4.3	0.40	1.8	3.6	7.5	98	314
Africa	(D/E)	31.5	1.6	3.5	0.11	0.5	0.9	1.6	82	235
TOTAL		616.2	3.9	7.5	4.6	24.3	42.3	81.1	74	234

Table adapted from Ferri et al (2005)

At present, 60% of persons living with dementia come from developing countries and this is expected to rise to 71% by 2040. See Figure 1.1. The impact of this pattern is expected to take a greater toll on developing countries given their faster pace of ageing, less time to adjust to the consequences and overall lower levels of socio-economic development.

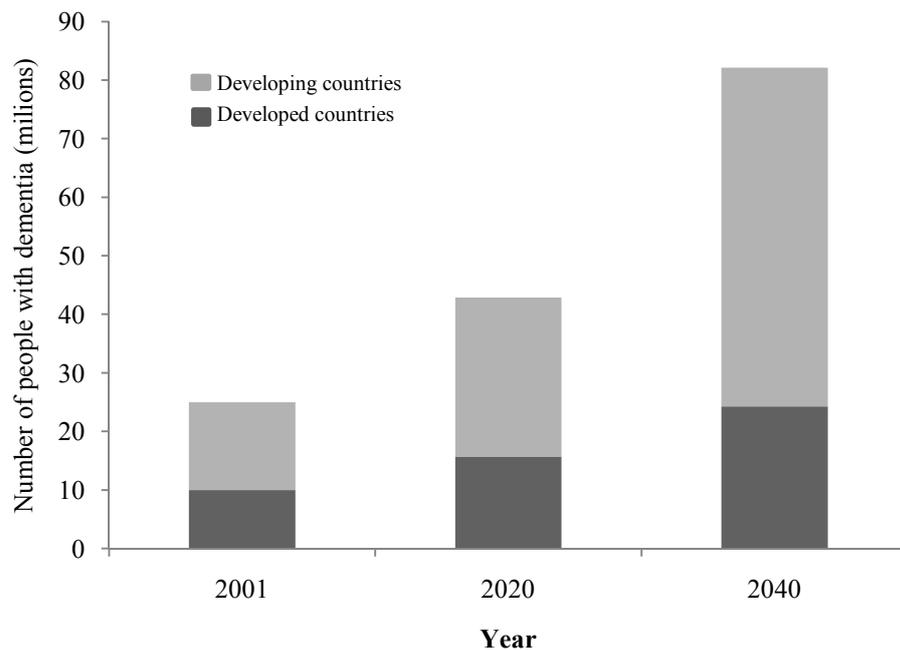


Figure 1.1 Graph showing distribution of persons with dementia in developing and developed countries.

Ineichen (1998) also outlines the practical problems of investigating dementia populations in developing countries: shorter life spans and as such fewer people reaching old age, the influence of poverty, poor health and little education make measurement, diagnosis and interpretation difficult, lack of physical and human resources to conduct research and difficulty in diagnosis given the absence of standardised culture-free tests (Chandra et al., 1994; Pollitt, 1996). As these challenges highlight, dementia poses a huge burden worldwide and remains a critical priority for governments and policy makers worldwide.

1.3 DEMENTIA DEFINITIONS AND SUBTYPES

The term dementia refers to a clinical state and on its own is not indicative of aetiology or prognosis (Geldmacher, 2004). Modern definitions and explanations of dementia place more emphasis on its identifying clinical features (Cantley, 2001).

Different definitions of dementia are outlined below in Table 1.2.

Table 1.2

Definitions of dementia

Author	Definition
Roth (1980, p24)	‘the global deterioration of the individual’s intellectual, emotional and cognitive faculties in a state of unimpaired consciousness.’
Lishman (1978, p6)	‘an acquired global impairment of intellect, memory and personality but without an impairment of consciousness.’
The Royal College of Physicians Committee on Geriatrics (1981)	‘the global impairment of higher cortical functions including memory, the capacity to solve problems of day-to-day living, the performance of learned perceptuo-motor skills, the correct use of social skills and control of emotional reactions, in the absence of gross clouding of consciousness.’
Munro, Saxton and Butters (2001, p523)	‘a clinical syndrome of acquired intellectual disturbances produced by brain dysfunction’
Mesulam (2000a, pg 444-445)	‘ a chronic and usually progressive decline of intellect and/or comportment which causes a gradual restriction of customary daily living activities unrelated to changes of alertness, mobility or sensorium’

There are over 70 different types of dementia (Cress, 2007) with symptoms overlapping among different types as well as with changes associated with normal ageing. Differential diagnosis becomes very important for at least two reasons: selection and management of increasingly available treatment options and also with respect to accurate and appropriate selection criteria for research purposes (Della Sala and Venneri, 2000; Geldmacher, 2004). Other benefits associated with accurate diagnosis are outlined in Table 1.3.

Table 1.3

Benefits of determining the specific cause of dementia

Choose drugs that are known to be effective in that particular disease
Avoid drugs that are not appropriate for that disease, known to be ineffective, or are contra-indicated
Know what disease complications to expect
Avoid unnecessary evaluations when a new symptom consistent with the disease develops
Plan for future care based upon the known clinical course of the specific disease
Educate caregivers about the cause of the disease, its symptoms, and recent research advances
Answer (sometimes unspoken) questions about family risk based upon genetics of the disease

Table adapted from Herholz, Perani, Morris (2006).

Dementias can be characterised as either primary (neurodegenerative) or secondary depending on known aetiology. Primary dementias are not thought to be due to any other disease or disorder and are characterised histologically by neuronal loss, gliosis and abnormal protein deposition (Josephs, Ahlskog & Parisi et al, 2009). These histological features occur in varying degrees for each neurodegenerative disease. The most common neurodegenerative disorders that cause dementia include Alzheimer's disease, Lewy body disease and frontotemporal lobar degeneration (Josephs, Ahlskog & Parisi et al, 2009). Primary neurodegenerative dementias are thought to be progressive and irreversible.

Secondary dementias are caused by a specific physical disorder or injury. They are the result of some neurodegenerative primary condition that is etiologically responsible for the dementia syndrome. Many secondary dementias can be reversible or remediable if the underlying aetiological condition is treated (Sultzer and Cummings, 1994, Geldmacher, 2004). Table 1.4 lists the most commonly occurring primary and secondary dementias.

Table 1.4

Types of Dementia

Primary or Neurodegenerative	Secondary
Alzheimer's disease	Vascular brain disease
Frontotemporal dementia	Endocrinological deficits (hypothyroidism, hyperthyroidism, Addison's disease)
Dementia with Lewy bodies	Metabolic Deficits (kidney or liver pathology)
Corticobasal degeneration	Inflammatory diseases (HIV, multiple sclerosis, encephalitis)
Parkinson dementia	Vitamin or other deficiencies
	Toxic state (drugs, metal, alcohol abuse)

Table taken from Venneri (2009).

The relative distribution of the most commonly occurring dementia subtypes based on UK data is shown in Figure 1.2. However, a caveat must be made as these figures refer only to the UK. Distributions are likely to vary across countries and regions where the proportion of cases attributed to vascular dementia, mixed dementia, or HIV dementia (as in the case of sub-Saharan Africa) may be increased (Wong et al, 2007). Notwithstanding the variation, Alzheimer's disease remains the most prevalent type of dementia worldwide. The more common types of dementia will be discussed in further detail in the next section.

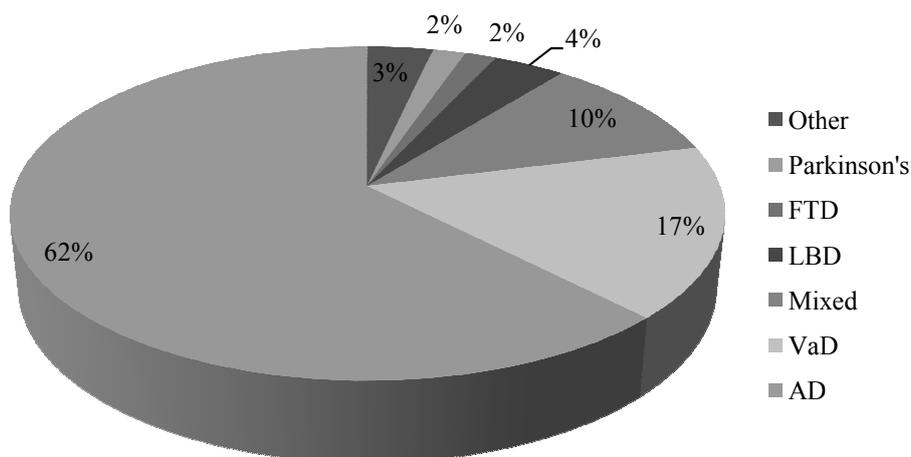


Figure 1.2: Distribution of prevalence of dementia subtypes (Alzheimer's Society, 2007)

1.4 ALZHEIMER'S DISEASE

The most well-known of the primary neurodegenerative dementias is Alzheimer's disease (AD). AD is thought to account for the majority of dementia cases with figures ranging from 42% to 74% (Brunnstrom, Gustafson, Passant et al, 2009; Kawas, Gray, Brookmeyer et al, 2000; Lobo, Launer and Fratiglioni et al, 2000). AD is characterised by progressive degeneration of nerve cells within the cerebral hemispheres which is accompanied by deterioration of intellect and personality (Lezak, 2004). Symptoms may vary widely and as such there is considerable clinical, pathological and aetiological heterogeneity among AD patients (Cummings, Vinters, Cole & Khachaturian, 1998). In advanced cases, diagnosis can be made readily but in early cases diagnosis can prove to be very challenging.

At autopsy, the presence of amyloid plaques and neurofibrillary tangles are usually indicative of a diagnosis of AD (Lezak, 2004). In the living patient, diagnosis is usually by exclusion due to the lack of accurate, definitive diagnostic methods (Monczor, 2005). Advancements in neuroimaging have refined techniques of *in vivo* brain imaging. The discovery of the use of the Pittsburgh Compound-B (PIB) to image beta-amyloid protein deposits in the brains of living persons using PET has significant implications for the use of PIB in screening for amyloid pathology and as a diagnostic agent in AD (Klunk, Engler, Nordberg et al, 2004). Mesulam (2000a) however, emphasises the need for clinical examination of patients and states that no radiological, neurophysiological or other laboratory investigation can rule out the need for a clinical examination of the patient's mental state.

A number of cognitive impairment patterns are seen as characteristic and are used to aid the diagnosis of AD (Mesulam, 2000a). The most distinctive is a relatively

severe verbal memory disorder with other accompanying deficits in orientation, praxis, psychomotor performance, language and speech fluency, complex reasoning and judgment (Lezak, 2004). In addition to cognitive difficulties, the Alzheimer's patient may also experience psychiatric symptoms such as depression, psychosis, agitation and personality change. They may also suffer functional impairment in which there is poor performance of activities of daily living such as feeding, dressing, performing household tasks and managing money (Mohs, 2000).

Mesulam (2000a) outlines the progression of the clinical presentation of AD in three stages: initial, intermediate and final. Memory impairment characterises the initial stages, with the patient forgetting names or misplacing objects. Deficits are often selective with memory for remote events and recent highly emotive events usually remaining intact. Voluntary recall is affected, but the use of clues or multiple choices may aid retrieval. The initial picture of AD may present with a patient who is healthy, capable and independent. However certain changes may become more apparent: a withdrawal or disengagement from regular professional, social and recreation activities or a decrease in eating, drinking or libido. In the conduct of such professional and social activities, the patient may become increasingly less decisive and in need of more assistance.

Deficits in multiple other domains become more apparent in the intermediate stage. Memory impairments worsen but there concurrent deficits in language, reasoning, spatial orientation and executive functioning also develop (Mesulam, 2000a). Attention and language deficits disrupt thought processes and communication and judgment and insight may deteriorate with poor awareness of impairments. Independence in daily activities wanes, and neglect of personal hygiene and etiquette may occur and the patient may become increasingly reliant on a spouse or carer. Sleep

disturbances may emerge in the intermediate stage as a result of disruption in circadian rhythms due to pathological changes in the suprachiasmatic nucleus caused by AD (Stopa, Volicer, Ku-Leblanc et al, 1999; Swaab, Fliers & Partiman, 1985).

Sundowning, which refers to the exacerbation of cognitive and behavioural symptoms towards the end of the day, is an increasingly frequent occurrence (Bliwise, Carroll, Lee et al, 1993; Volicer, Harper, Manning et al, 2001). Psychiatric symptoms may also become more apparent in this stage with the patient exhibiting possible delusions, hallucinations, irritability, agitation, aggression, rituals and belligerence. (Jost & Grossberg, 1996; Lopez, Becker and Sweet et al, 2003).

In the final stages, symptoms worsen significantly with cognitive, behavioural and psychiatric function most affected. Patients may be unable to recognise family members, become incontinent and lose the capacity to speak, feed themselves or control movement. Mesulam (2000a) points out that while primary sensory and motor functions may remain spared until very late, extrapyramidal deficits including myoclonus, rigidity, cogwheeling, hypomimia and gait instability are quite frequent. Death may result due to infection or cardiopulmonary arrest.

1.4.1 ALZHEIMER'S DISEASE RISK FACTORS

A number of risk factors are associated with AD. These are described below:

1.4.1.1 Genetic Factors

Certain genetic risk factors are associated with AD. Lezak (2004) notes that having an affected first-degree relative doubles one's chances of developing AD. This is substantiated by results from twin studies which show concordance rates of 21% to 67% (Breitner et al, 1995; Gatz et al, 2006). Some persons develop the familial form

of AD which is caused by three kinds of mutations: the *presenilin-1* gene on chromosome 14, the *presenilin-2* gene on chromosome 1 and the *amyloid precursor protein* (APP) on chromosome 21 (Andreasen, 2001). Apart from the rare cases caused by mutations, it is a complex interaction of genes and environmental factors that modulates the susceptibility to AD (Farrer, 2000).

Many genes have been implicated in AD, for example SORL1 (sortilin-related receptor) and GAB2 (GRB2-associated binding protein 2). The most compelling evidence has been provided by studies of the epsilon 4 allele of the apolipoprotein E (ApoE) on chromosome 19 which is associated with a risk of developing AD of 2.7 - 3.2 for those carrying a single copy and a risk of 12.5 to 14.9 for those homozygous for the allele (Farrer, 2000).

The pathological changes associated with AD have also been found in many persons with Down's syndrome (Malamud, 1966) although all do not go on to develop Alzheimer's disease (Zigman, Silverman and Wisniewski, 1996). The clinical prevalence of Alzheimer's disease in persons with Down's syndrome is also much greater than that of the normal population with rates of 9% in persons aged 40-49 years, 36% in those 50-59 years and 55% in those 60-69 years (Prasher, 1995). Heyman et al (1983) also found increased occurrences of Down's syndrome in families who have a history of Alzheimer's disease than those without.

1.4.1.2 Demographic Factors

Age is the major and most consistently reported risk factor for Alzheimer's disease with most cases occurring after age 60 and prevalence rising as age increases (Lezak et al, 2004). The prevalence of dementia is estimated at 1% at 60 years increasing to 25% at age 85. Some studies also predict prevalence rates of 62 – 77% at

age 95, suggesting an exponential increase in prevalence from age 60 (Jorm, Korten and Henderson, 1987). However, these studies and others have been criticised for not including sufficient numbers of persons in the very old age groups. Ritchie and Kildea (1995) found that rather than displaying an exponential increase, the prevalence rates of dementia resemble a flattened S curve which indicates that in the very old, prevalence rates begin to fall. Thus, by age 95, prevalence rates are estimated to be around 40% (Ritchie and Kildea, 1995). Gao et al (1998) also found a levelling off of prevalence rates in very old age, showing that for every five-year increase, the incidence of Alzheimer's disease triples before age 64, doubles before age 75 but then slows down to an increase of 1.5 times by age 85. In this regard, it is thought that AD should be conceived as 'age-related' - referring to a specific age range, rather than 'ageing-related' - an inevitable consequence of ageing.

Women have also been found to have an increased risk for Alzheimer's disease with an odds-risk ratio of 1.56 (95% CI: 1.16-2.10) relative to men (Gao et al, 1998). One explanation for this implicates hormonal factors since hormone replacement therapy resulted in a 54% reduction in risk of women in a 16 year longitudinal study (Kawas et al, 1997). McCullagh, Craig, McIllroy and Passmore (2001) also suggest that since males have an increased risk of vascular dementia they are less likely to develop a pure form of Alzheimer's disease.

Low educational and occupational attainment has been implicated in an increased risk for developing Alzheimer's disease (Ott et al, 1999). Katzman et al (1993) studied a sample of elderly residents in rural Italy and found having fewer than three years education was associated with an OR of 1.8 (95% CI 1.0 – 3.4) for Alzheimer's disease. Higher education is associated with cognitive reserve which is

thought to delay onset and compensate for neuropathological changes (Lezak, 2004, McCullagh et al, 2001). Education may also be associated with better brain perfusion resulting in higher levels of regional cerebral blood flow in certain regions of the brain (Chiu, Lee, Tsiao and Pai, 2004). However, education and schooling has also been linked to a faster rate of cognitive decline in Alzheimer's patients. Roselli et al (2009) found patients with more than 8 years of schooling showed more rapid decline in MMSE scores than patients with fewer than 8 years of education.

1.4.1.3 Vascular Factors

Vascular factors may also play a role in the development of Alzheimer's disease. Insulin-dependent diabetes, vascular disease, hypertension and myocardial ischemia have all been associated with acquiring Alzheimer's disease (Stewart, Prince and Mann, 1999). The studies on the effect of smoking are mixed. Current and former smokers were found to have an increased risk (Launer, Andersen and Dewey et al, 1999). However other studies have found a protective effect of smoking (e.g. Fratiglioni and Wang, 2000) but these studies may be a reflection of having a lower proportion of smokers due to selective survival. Indeed, when cases examining incidence of AD and longitudinal studies investigating smoking and cognitive impairment are used, the protective factor of smoking is no longer found (Ford, Mefrouche, Freidland et al, 1996; Launer, Feskens, Kalmijn et al, 1996; Wang, Fratiglioni, Frisoni et al, 1999). The risk of smoking may also interact with the presence of the ApoE ϵ 4 allele with smokers lacking the ApoE ϵ 4 allele exhibiting a modest risk (Kukull, 2001; Ott, Slooter, Hofman et al., 1998).

1.4.1.4 Traumatic Brain Injury

Traumatic brain injury (TBI) has been associated with an increased risk of developing Alzheimer's disease. Many studies show persons with AD reporting a history of frequent incidences of TBI (Lye and Shores, 2000; Schofield et al, 1997), however some studies fail to find the same association (Mehta, Ott, Kalmijn et al, 1999). ApoE ϵ 4 may also be implicated in TBI as some research find that the risk of AD subsequent to a TBI is greater in those lacking the allele (Guo et al, 2000; Jellinger, Paulus, Wrocklage et al, 2001).

1.4.2 NEUROPATHOLOGY OF ALZHEIMER'S DISEASE

Amyloid plaques (AP) and neurofibrillary tangles (NFT) are the hallmark characteristics of AD neuropathology (Braak et al, 1999; Mesulam, 2000b; Zubenko, 1997). Amyloid precursor protein (APP) is the precursor protein of amyloid beta (A β) which is found in senile AP in AD (Glenner, 1984, Kang, 1987). AP consists of a core of amyloid protein surrounded by astrocytes, microglia and dystrophic neurites (Brion, 1998; Cumming and Back, 1998; Morris, 1997). The implication of APP and A β involvement in AD are supported along three lines of genetic evidence (Yankner, 1996). Firstly there is an association with AD and many of the APP mutations: namely mutation of A β PP on chromosome 21 can cause early-onset AD and mutation of presenilin 1 on chromosome 14 and presenilin 2 on chromosome 2 can lead to greater production of the neurotoxic form of A β (Selkoe, 1994, Yankner 1996). Secondly, the overexpression of APP in Down's syndrome is associated with AD. Trisomy 21 leads to an increase in APP and A β levels which leads to the early manifestation of AD. Also, evidence of the neurotoxicity of A β suggests its involvement in AD. In vitro, A β is neurotoxic to cells and promotes the phosphorylation of tau and in transgenic mice,

overexpression of mutations of A β PP promotes AP deposits, neuronal loss and tau phosphorylation (Yankner, 1996).

The hypothesis that AP causes AD was refuted however on the basis of evidence which showed that the severity of AD was predicted more accurately by the distribution of NFT rather than plaque density (Morris, McKeel, Storandt et al, 1991; Yankner, 1996). Additionally the finding of significant presence of AP in brains of non-demented adults furthered the argument that AP did not lead to AD (Katzman et al, 1988; Dickson et al, 1991). Differences in composition and structure of AP in demented and non-demented individuals as well as the role of ApoE in mediating vulnerability may explain the lack of causation by A β itself but does not rule out its role in AD pathology (Mesulam and Geula, 1994).

The distribution patterns of AP and NFT are different and occur independently of each other (Braak and Braak, 1991, Arriagada et al, 1992). While the distribution of AP appears to be unrelated to the progression of the disease, the sequence of development of the NFT shows a pattern that corresponds to the progression and severity of AD (Braak and Braak, 1991). Although NFT are also found in autopsied brains of non-demented elderly, they are much more abundant in AD patients (Yamamoto and Hirano, 1985).

NFT consist of paired helical filaments consisting of abnormal, highly phosphorylated tau protein accumulating in the neuronal perikarya, dendrites and axon and their deleterious effect occurs through disruption of the microtubule network and axoplasmic flow (Brion, 1998; Cummings, 2003). NFT are found in the early stages in the transentorhinal cortex and then the entorhinal cortex, hippocampus and other regions of the temporal lobe, progressing to other limbic cortical regions and finally

into the neocortex in advanced stages of AD. This pattern of NFT formation is very stereotypical and has resulted in a six stage neuropathological staging of AD (Braak and Braak, 1991).

1.4.3 NEUROPLASTICITY IN AD- A UNIFYING THEORY

While genetic evidence for AD suggests a causative hypothesis surrounding AP, clinical and pathological data point to an explanation involving NFT. The gaps left by separate explanations have prompted researchers to search for a common theory that unifies both concepts. A number of authors have suggested flawed neural plasticity as the underlying mechanism causing AD (Mesulam, 1999; 2000b; Buell and Coleman, 1979; Arendt et al, 1998; Neill, 1995). This process is used to explain how the interaction of different factors and genes can result in a common clinical and neuropathological phenotype (Teter and Ashford, 2002).

Neuroplasticity is distributed unevenly throughout the brain and in AD pathology, the areas that are most affected include those that are more structurally and functionally plastic and involve the acquisition of new epigenetic information, such as the limbic system (Mesulam, 2000b; Teter and Ashford, 2002). It is thought that the different genetic profiles and risk factors (Amyloid, presenilins, ApoE, estrogen, age) exert their influence on AD by impacting the process of plasticity (Mesulam, 2000b). Neuroplasticity is described by Teter and Ashford (2002) as:

...both a substrate of learning and memory and a mediator of responses to neuronal attrition and injury... It is a continuous process in reaction to neuronal activity and neuron injury, death and genesis which involves modulation of structural and functional processes of axons, dendrites and synapses. The varied structural elements that embody plasticity include LTP, synaptic

efficacy, synaptic remodelling, synaptogenesis, neurite extension including axonal sprouting and dendritic remodelling, and neurogenesis and recruitment (p 403).

Plasticity can be separated into either downstream or upstream processes: the former takes place at the level of the axons, dendrites and synapses and the latter at the level of the perikaryon. Mesulam (1999; 2000b) proposes that AD risk factors cause the disruption of neuroplasticity at the downstream level and results in intensified, compensatory upstream plasticity activity. Over a period of years, the increased neuroplasticity burden and chronic upregulation becomes unsustainable and increases the vulnerability of the system to the formation of NFT (Mesulam, 2000b, Teter and Ashford, 2002). Specifically, high plasticity results in the upregulation of the expression of tau resulting in its phosphorylation and the subsequent polymerization of tau into NFT. Since the neurons in the limbic system have the highest baseline level of plasticity, it is expected that they would be the earliest and most affected.

Injury and denervation can also induce plasticity and result in the upregulation of A β PP in sites which have high plasticity burdens. Soluble A β diffuses into extracellular fluid and excess levels results in the formation of inert diffuse plaques which have neurotoxic, neurite-inhibiting and LTP-inhibiting properties (Mesulam, 2000b; Freir et al., 2001; Dewachter et al., 2002). The initial inertness as well as the uneven accumulation of A β PP may explain the asynchronous distribution with NFT as well as the lack of concordance with the clinical features of AD (Mesulam, 2000b).

As such, Mesulam (1999; 2000b) proposes genetic mutations and environmental risk factors do not cause AD but rather accelerate and exacerbate the processes that result in excessive and maladaptive plasticity. Increasing age is

associated with a decreased capacity for plasticity and thus increasing life span coupled with AD promoting factors serves to increase the brain's susceptibility to AD pathology.

1.4.4 DISEASE COURSE, PROGRESSION AND STAGING

Braak and Braak (1991) were the first to suggest a neuropathological staging of AD based on the distribution patterns of NFT. They suggest that the sequence of degeneration follows the inverse pattern of cortical myelination and as such, late myelinating areas are affected by the disease earlier and more intensely than early myelinating areas (Braak et al, 1999). Using post mortem analyses to identify location and severity of AD pathology, six stages were identified (Braak and Braak, 1991; 1999). Mesulam (2000a) furthered the work of Braak and Braak, who had confined their work primarily to the medial temporal lobe. Mesulam examined whole brain sections and enhanced the staging proposed by Braak and Braak. These stages along with the contributions by Mesulam are briefly outlined below:

Transentorhinal stages I and II (Mesulam's low limbic stage): The first two stages correspond to mild or severe changes in the transentorhinal layer. There is little involvement of the entorhinal region. These stages represent the preclinical phase of the disease and do not manifest any clinical symptoms.

NFT are fewest in this stage and while their number may increase in older patients, their distribution does not. NFT clusters are located in limbic areas (nucleus basalis, entorhinal-transentorhinal cortex, hippocampus, amygdala and temporopolar cortex). Isolated tangles may be found in the hypothalamus, insular, orbitofrontal cortex and parolfactory gyrus and start to appear in the nucleus locus coeruleus.

The distribution of NFT in this stage is found in most nondemented subjects over the age of 60 and does not characterise a diagnosis of AD (Braak and Braak, 1996). Mesulam (2000a), however, argues against considering their presence a benign or normal aspect of ageing and rather an abnormal, though common, feature of ageing.

Limbic stages III and IV (Mesulam's High limbic stage): Key features include involvement of both the transentorhinal and the entorhinal cortex. Functional disturbances and clinical symptoms first appear in these stages and patients may manifest slight mental deterioration or subtle personality changes.

There is a distinct increase in the concentration of NFT in the limbic and paralimbic cortices and they begin to appear in the thalamus and substantia nigra. The prefrontal, posterior parietal and occipital cortex, however, remain free of NFT.

In this stage, daily functioning may be normal, however performance on neuropsychological tests may yield abnormal scores especially in memory function. Braak and Braak (1996) note that while there may be subjective reports of cognitive difficulties and some slight personality changes may occur, these are not usually severe enough to warrant a diagnosis of dementia and instead may be associated with conditions such as 'mild cognitive impairment' or preclinical AD.

Neocortical stages V and VI (Mesulam's low and high neocortical stages): Brain lesions spread from inferior temporal regions into multimodal association areas of neocortex. Initial AD diagnosis is usually made in these stages. Primary motor field, primary sensory areas and unimodal secondary fields may remain unaffected initially but in the last stage may also be affected. In the final end stages, cortical atrophy, distinctive ventricular widening and loss in brain weight occur. Patients become severely demented and destruction of the limbic loop hampers autonomic functions.

In Mesulam's low neocortical stage, NFT density is intensified in all limbic areas. Memory deficits and other clinical impairments underscore a diagnosis of dementia due to AD. In the high neocortical stage, all areas of the association neocortex show a high density of NFT and the concurrent presence of densely distributed neocortical plaques reaffirm a diagnosis of dementia caused by AD. Cognitive and behavioural deficits are extensive and extrapyramidal symptoms appear in this terminal stage. Figure 1.4 below shows the progression of AD through the brain.

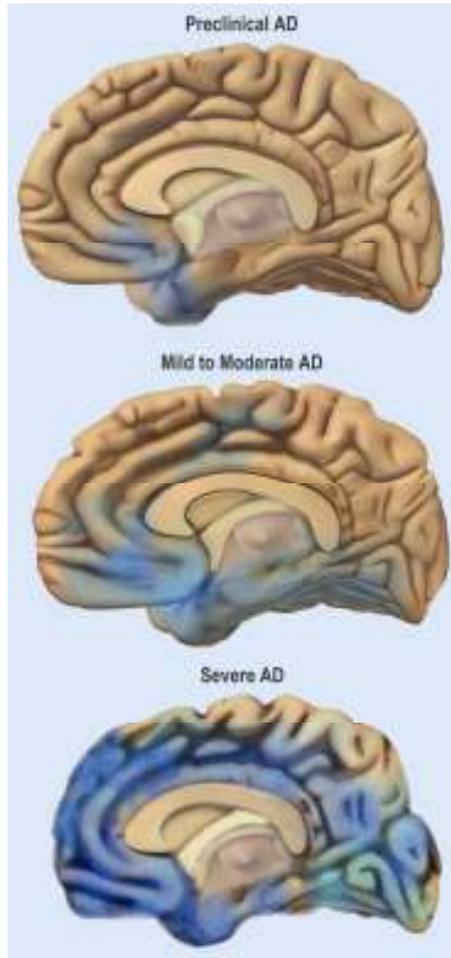


Figure 1.4 Progression of Alzheimer's disease through the brain. Image courtesy of the National Institute on Aging/National Institutes of Health

1.4.5 EFFECTS OF ALZHEIMER'S DISEASE ON COGNITION

The progression of AD is thought to be slow, gradual and insidious. Abrupt changes may warrant consideration of an alternative diagnosis such as structural damage as from a stroke, acute injury or intoxication. Since decline is so gradual, and in the early stages most fundamental abilities are preserved, it is often difficult to ascertain onset of clinical symptoms (Braak and Braak, 1999; Lezak, 2004). Kasniak, Sadeh and Stern (1985) note that early symptoms such as inattentiveness, mild cognitive dulling, social withdrawal, emotional blunting or agitation may be mistaken

for depression and AD patients are commonly treated for depression before a diagnosis of AD is made.

Memory is often the first cognitive function to deteriorate, along with complex mental tracking and verbal fluency (Albert, Moss, Tanzi and Jones, 2001). Delayed recall of verbal and visuospatial memory has a rapid deterioration early on, thus Locascio, Growdon and Corkin (1995) suggests the use of measures which show steady linear decline for clinical staging of AD: these include immediate recall, category fluency and confrontational naming. Symbol substitution and construction tests also show steady decline (Lezak, 2004). While some patients often exhibit self-awareness and are cognisant of their problems and their illness, the majority are not. They may have insight into their deficit but it may be for a fleeting moment (Vasterling et al, 1997; Wagner et al, 1997). Perseverations and intrusions in speech and actions may also occur (Monsch, Bondi, Salmon et al, 1995; Salmon, Granholm, McCullough et al, 1989).

Midstage deficits include poor fluency, paraphasias, bizarre word combinations and intrusions. Aphasia, apraxia and agnosia may also worsen considerably (Chobor and Brown, 1990). In late and very late stages, it may be difficult to measure many functions as the patient is no longer able to comprehend task instructions or can no longer perform the tasks themselves. Au, Albert and Obler (1988) note that in very late stages, speech becomes non-fluent, repetitive and non-communicative with limited auditory comprehension. After the initial presentation of memory impairment, further cognitive decline may not occur for nine months to almost three years (Haxby, Raffaele, Gillette et al, 1992). However Lezak (2004) notes that once non-memory functions become impaired, mental deterioration seems inevitable.

While the cognitive changes in AD are well established, the pattern varies from patient to patient; however, in all, there is usually a consistent progression of cognitive deterioration. Many functions are affected by AD and these impairments are described in greater detail below.

1.4.5.1 Memory and Learning

Many studies show memory problems occurring early in the course of Alzheimer's disease and often even before a clinical diagnosis is justified (e.g. Albert, Moss, Tanzi and Jones, 2001; Backman et al, 2001). Different types of memory are differentially affected throughout the course of AD (Perry and Hodges, 1999). Changes in the medial temporal lobe structures often occur early and these adversely affect episodic memory (Braak and Braak, 1991). Delayed memory is also affected with AD patients displaying rapid forgetting (even after acquisition) on verbal and visual learning trials (Larrabee, Youngjohn, Sudilovsky et al, 1993). Retrieval problems are seen in poor performance on verbal fluency tasks and defective remote memory (Wilson, Kasniak and Fox, 1981). Learning and retrieval tasks are the most severely impaired early in Alzheimer's disease with poor performance on acquisition, retention and rote learning tasks (Grafman, Weingartner, Lawlor et al, 1990; Hodges, 2000). Patients may also have a tendency to produce many intrusions errors on both verbal and nonverbal memory tests (Butters, Granholm, Salmon et al, 1987; Gainotti and Marra, 1994; Kramer, Levin, Brandt et al, 1988; Jacobs, Brandt, Salmon et al, 1991; Manning et al, 1996).

Performance on recognition can be normal for mildly impaired patients, but for those past the early stages, performance on both visual and verbal tasks are significantly below normal (Moss, Albert, Butters and Payne, 1986). Common errors include patients giving a high number of false positive responses (Deweer, Pillon,

Michon et al, 1993). Working memory is impaired in many mild to moderately affected Alzheimer's patients (Belleville et al, 1996). The addition of a distracter task often worsens performance (Morris and Kopelman, 1986).

Research also suggests a temporal gradient in accessing memories with older memories more available than newer ones. This pattern applies both to personal and publicly available information (Fama, Sullivan, Shear et al, 2000; Fama, Shear, Marsh et al, 2001; Kopelman, 1989; Nebes, 1992). Knowledge of general information and current events may be adversely affected in early stages and deteriorates as the disease progresses (Brandt, Folstein and Folstein, 1988).

Some learning tasks remain intact in AD. These include those involving simple (but not complex) motor and skill learning (Bondi and Kaszniak, 1991, Eslinger and Damasio, 1986); thus procedural memory, like memory for a pleasurable task like playing a musical instrument may be maintained (Beatty, Winn, et al, 1994). Performance on implicit memory tasks may vary depending on difficulty (Gabrielli, Vaidya, Stone et al., 1999; Meiran and Jelicic, 1995) and Lezak (2004) note that such differences in learning patterns reflects the 'selectivity of cortical degeneration' (pg 216) of the disease.

1.4.5.2 Attention

Many aspects of attention become impaired in Alzheimer's disease. After memory, attention is the first other cognitive domain to be affected- before language and visuospatial functions (Perry and Hodges, 1999). Selective attention may become impaired in AD, with patients performing worse than controls on tasks which require them to disengage and shift attention from one stimulus to another. Defective focusing and shifting are apparent in earlier stages while arousal and responsive

focusing are impaired later on in the disease with performance worsening as the tasks grow more complex (Baddeley et al, 2001; Nebes and Brady, 1989; Perry and Hodges, 1999). Performance also worsens in the presence of distractors due to impaired inhibitory mechanism (Perry and Hodges, 1999).

In a timed digit cancellation task which is used as measures of selective attention, Della Sala et al (1992) found AD patients exhibited passive or slow scanning in which they were ‘looking but not seeing’ and were also slow to make a decision. The Stroop task requires response inhibition and involves the ‘supervisory attentional system’ which allows cognitive flexibility by modulating ‘automatic’ thoughts or actions and facilitating the ability to perform novel actions (Norman and Shallice, 1986). The Stroop test is very sensitive to AD patients in the early stages of AD (Fisher, Freed, Corkin et al, 1990; Grady, Haxby, Horwitz et al, 1988; Haxby, Grady, Koss et al, 1990; Spieler, Balota, Faust et al, 1996), however Perry and Hodges (1999) assert that it is unclear whether the poor performance among AD patients is due to the difficulty of the task or a defect in response selection or response inhibition.

Simple attention span (like that required in the Digits Forward task) is relatively normal (Wilson and Kaszniak, 1986) and in patients in early and intermediate stages of AD, alertness is relatively intact (McKhann et al, 1984; Nebes and Brady, 1993). Vitaliano et al, (1984) point out the real life implications of these impairments in increased social dependency and worsening personal habits.

1.4.5.3 Executive Functioning

AD patients are thought to be impaired on a number of tasks that involve executive functioning including everyday tasks that are assumed to involve executive functioning (choosing appropriate clothes for an occasion, planning a trip). However,

there is some disparity in the literature as to when impairment becomes apparent. AD patients with mild or moderate AD have shown impaired performance on some neuropsychological tests including: verbal fluency, delayed alternation, Self Ordering Pointing Test, Wisconsin Card Sorting Test, Hukok Logical Matrices and, Trail Making Test (Bhutani, Montaldi, Brooks and McCulloch, 1992; LaFleche and Albert, 1995).

However other authors surmise that it is only when AD worsens that patients may encounter difficulty with complex tasks that require planning and flexible thinking (Brugger, Monsch, Salmon and Butters, 1996; Mack and Patterson, 1995). Broks, Lines, Atchison et al (1996) propose that executive functions are spared in early AD and deteriorate as a function of the severity and duration of the disease. Pillon, Dubois, Lhermitte, and Agid (1986) also suggest that executive dysfunction is a symptom of moderate or severe cognitive impairment.

1.4.5.4 Language Functions and academic skills

There is considerable decline in the quality of verbal functions in Alzheimer's disease. Braak and Braak (1991) note that as AD neuropathology extends beyond the medial temporal lobe to the association cortices of the temporal, frontal and parietal lobes, certain higher-order cognitive abilities become affected. AD patients may develop a semantic memory deficit demonstrated by a loss of general knowledge and impaired language abilities (Salmon and Bondi, 2009). Confrontation naming, semantic categorisation and verbal fluency including word generation in letters, categories and situations are often impaired (Bayles, Salmon, Tomoeda et al, 1989; Binetti, Magni, Cappa et al, 1995; Chan, Salmon, Butters, 1995; Hodges, Patterson, Graham et al, 1996).

Category fluency shows greater deterioration than letter fluency in AD and category fluency is often the most sensitive measure of semantic memory in AD (Hart, Smith and Swash, 1988; Hodges and Patterson, 1995; Martin and Fedio, 1983; Monsch, Bondi, Butters et al, 1992). Forbes-McKay, Ellis, Shanks et al, (2005) compared the performance of AD patients and controls on a category fluency task and found AD patients generated fewer and shorter items, more typical and frequent items and items which had an earlier age of acquisition.

Impaired semantic processing also impacts on spoken language with AD patients exhibiting anaphora, paraphasias, word finding difficulties, circumlocutions and diminished vocabulary (Croisile, Ska, Brabant et al, 1996; Hier, Hagenlocker, Shindler, 1985; McNamara, Obler, Au et al, 1992). Deficits are also seen in comprehension of spoken and written language, with diminished reading skills and an impaired ability to recognize emotional tones in speech (Allender and Kaszniak, 1989; Bayles et al, 1989; Martin and Fedio, 1983; Storandt, Stone and LaBarge, 1995). In advanced cases of AD, there may also be a loss of spontaneous speech in conversation and in extreme cases there can be muteness (Naugle, Callum and Bigler, 1997).

Writing skills are also affected in AD as patients suffer damage to both the central and peripheral levels of writing. Motor output, phonology and syntax may be preserved, but writing may be spatially disordered and show graphemic paraphasias (Horner, Heyman, Dawson et al, 1988). Sentences are also shorter, less grammatically complex, contain fewer words and more spelling errors (Horner et al, 1988; Neils, Boller, Gerdeman et al, 1989; Pestell et al, 2000). Sentences may appear unintelligible, irrelevant or redundant (Bayles, 1988; Devlin, Anderson, Seidenberg, 1998). Surface dysgraphia is seen in AD patients and as the disorder progresses, the phonological system may also become impaired (Platel, Lambert, Eustache, et al, 1993). In severe

cases, AD patients also experience difficulty with letter formation, stroke placement and revert to writing in print rather than cursive (Forbes, Shanks, and Venneri, 2004).

Arithmetic skills are also affected in the early stages of AD, deteriorating as the disease progresses (Deloche et al, 1995). Oral arithmetic performance on the Weschler Intelligence scales correlate highly with sentence repetition scores and digit span (forward and backward) and Roselli, Ardila, Arvizu et al (1998) suggested that patients may experience difficulty in keeping the question in their minds long enough to complete the task and thus the deficit in arithmetic skills may be secondary to a working memory deficit.

1.4.5.5 Visuospatial functions, construction and praxis

Impairment in visuospatial functions is found in different tasks: left-right discrimination involving rotation, (Brouwers, Cox et al, 1984; Flicker, Ferris, Crook et al, 1988) left sided inattention (Freedman and Dexter, 1991) and line orientation judgment (Ska, Poissant, Joannette, 1990). Patients also show defective constructional abilities in both simple and complex tasks such as clock drawing (Cahn-Weiner et al, 1999), copying of a complex figure, copying the intersecting pentagons in the Mini Mental State Exam (Binetti, Cappa, Magni et al, 1998; Brandt, Folstein, Folstein, 1988; Brouwers, Cox, Martin et al, 1984) and block design (Bozoki, Giordani, Heidebrink et al, 2001). Poor performance on these tasks may also be associated with patients getting lost, wandering aimlessly, being unable to recognise familiar surroundings (Henderson, Mack and Williams, 1989) and being unable to use a map (Beatty and Bernstein, 1989).

Patients also exhibit ideomotor and ideational apraxia, showing difficulty in pantomiming (Bayles, Boone et al, 1989; Schwartz et al, 2000), copying finger

movements (Willis, Behrens, Mack et al, 1998) and making tool-action associations (Dumont, Ska, Joannette, 2000). Ideomotor apraxia often parallels speech problems making it difficult for patients to complete intentional acts including speech (Lezak, 2004).

1.4.5.6 Sensorimotor status

Visual dysfunction may manifest as reduced contrast sensitivity or in inferior visual fields (Gilmore and Whitehouse, 1995; Trick et al, 1995). Studies have shown a common occurrence of visuo-perceptual deficits in AD patients which show up on tests measuring visual discrimination, analysis, spatial judgment and perceptual organisation (Cogan, 1985; Eslinger and Benton, 1983; Mendez, Mendez, Martin et al; 1990). Object recognition is also impaired while auditory skills and tone perception are relatively unchanged (Kurylo, Corkin, Growdon, 1996; White and Murphy, 1998).

Olfactory acuity is also affected and is associated with NFT and cell loss in olfactory nuclei as well as reduction in hippocampal volume (Esiri and Wilcock, 1984; Murphy et al, 2003). Devanand, Michaels-Marston, Liu et al, (2000) suggest that olfactory deficits may predict the future development of AD in patients with mild cognitive impairment. Apart from the very late stages, motor skills are not frequently impaired although patients perform better on less complex tasks (Mesulam, 2000; Kluger, Gianutsos et al, 1997).

1.4.5.7 Neuropsychiatric symptoms, personality and psychosocial behaviour

Neuropsychiatric symptoms are common in Alzheimer's disease and negatively affect prognosis (Cummings, 2003). Symptoms include depression, anxiety, irritability, apathy, agitation, delusions, hallucinations, aberrant motor behaviour, disinhibition, euphoria, overactivity and aggression (Hope, Keene, Fairburn et al,

1997; Lyketsos, Breitner, Rabins, 2001). AD patients are more prone to apathy, irritability, anxiety depression, and psychotic symptoms (delusions and hallucinations) (Cacabelos, Rodriguez, Carrera, et al, 1996; Mega, Cummings, Fiorello, et al, 1996). Apathy may range from passivity and lack of interest to decreased spontaneity and anergia (Bozzola, Gorelick and Freels, 1992). Prevalence of neuropsychiatric symptoms in AD ranges from 60% to 80% depending on whether the patient is community dwelling or institutionalised (Lyketsos, Lopez and Jones et al, 2002; Lyketsos, Sheppard, Steinberg, 2001; Zuidema, Koopmans and Verhey, 2007)

Patients may also experience sleep disruptions and incontinence (Cacabelos, Rodriguez, Carrera, et al, 1996). Wandering, outbursts of violence, suspiciousness and paranoia may also be present and pose a problem for caregivers (Haley, Brown and Levine, 1987; Rabins, Mace and Lucas; 1982; Swearer, Drachman, O'Donnell et al, 1988). As the disease progresses, self-care becomes limited and deteriorating hygiene and inappropriate dressing are common problems (Haley, Brown and Levine, 1987).

One disorder which results in many erroneous diagnoses of dementia is depression, leading to the development of terms 'pseudodementia' and 'depressive pseudodementia' to describe such cases (Roose and Devanand, 1999). Depression is one of the most common reasons for psychiatric referrals in the elderly with dementia having the higher incidence only after age 75. While Wells (1979) suggested that the two can be differentiated on the basis that in pseudodementia, the mood changes manifest first, the nature of the relationship between the two is still difficult to ascertain as similar signs and symptoms appear in both (apathy, disrupted sleep patterns, complaints of memory impairment) (Kaszniak and Christensen, 1994). Indeed many older patients may show atypical presentations with little affective disturbance and with cognitive symptoms common to dementia such as impaired

memory, concentration, orientation and faulty knowledge of current events (Hart and Semple, 1994)

Also, research has yielded conflicting results with one study showing depressed persons more likely to show signs of Alzheimer's disease during follow-up (Devanand, Sano, Tang et al, 1996), while another shows persons with Alzheimer's disease having low rates of major depressive disorder (Weiner et al, 2002). Depressive illnesses may also co-exist with Alzheimer's disease, further complicating the diagnostic picture.

1.4.6 DIAGNOSTIC STRATEGY FOR ALZHEIMER'S DISEASE

The diagnostic criteria for dementia (due to Alzheimer's disease) used most commonly in the UK are those found on the International Classification of Diseases (10th revision). The other widely used sets of criteria are those outlined by the DSM-IV TR and NINCDS-ADRDA which both provide operational criteria to assist in diagnostic definition.

A diagnosis of Alzheimer's disease is based on the criteria outlined by the DSM IV-TR (American Psychiatric Association , 2000) and/or the National institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) (McKhann, Drachman, Folstein et al, 1984). Both sets of criteria require the identification of a dementia syndrome and then the application of criteria based on the clinical features of AD. The DSM IV-TR criteria require the presence of memory impairment and cognitive deterioration in at least one other area such as language, perception, motor skills or executive functioning (APA, 2001). The NINCDS/ADRDA has three different categories for classification: definite (clinical diagnosis with a histologic confirmation of Alzheimer's disease),

probable (clinical diagnosis without histologic confirmation) and possible (atypical symptoms, no alternative diagnosis and no histologic confirmation) (McKhann, Drachman, Folstein et al, 1984). See table 1.5 for more details.

Table 1.5

NINCDS-ADRDA Criteria for Definite, Probable, and Possible AD

Diagnosis	Clinical Criteria
	Clinical criteria for Probable AD
Definite AD	Histopathologic evidence of AD (autopsy or biopsy)
Probable AD	Dementia established by clinical examination and documented by mental status questionnaire Dementia confirmed by neuropsychological testing Deficits in two or more areas of cognition Progressive worsening of memory and other cognitive functions No disturbance of consciousness Onset between ages 40 and 90 Absence of systemic or other brain diseases capable of producing a dementia syndrome
Possible AD	Atypical onset, presentation, or progression of a dementia syndrome without a known etiology A systemic or other brain disease capable of producing dementia but not thought to be the cause of the dementia is present There is a gradually progressive decline in a single intellectual function in the absence of any other identifiable cause
Unlikely AD	Sudden onset Focal neurological signs Seizures or gait disturbance early in the course of the illness

Adapted from McKhann et al. (1984)

Sensitivity for these criteria range from 65% to 95% while specificity in differentiating dementia due to AD against other types ranges from 23% to 88% (Petrovitch, White, Ross et al, 2001; Varma, Snowden and Lloyd et al, 1999; Kazee, Eskin, Lapham, 1993). Dubois, Feldman, Jacova et al, (2007) call for revised AD and

non-AD dementia diagnostic criteria to address the low specificity rates. These revised criteria would enable diagnosis at the onset of symptoms, before full-blown dementia and thus facilitate earlier intervention at the prodromal stage.

Another set of criteria that may be used to rate dementia is the Clinical Dementia Rating Scale (CDR) which was developed by Morris in 1979 primarily for use among patients with probable AD and is commonly used to assess severity of the disease and focuses on cognitive symptoms. It can, however, also be used to classify other dementias. It uses a five point rating scale which classifies persons as having no cognitive impairment, very mild dementia, mild, moderate and severe dementia. Using a structured interview, individuals are assessed on six domains: memory, orientation, judgment and problem solving, community affairs, home and hobbies and personal care. Their rating in each area is based on their ability to function in each domain. The cognitive functioning associated with each stage is shown below in Table 1.6.

1.5 VASCULAR DEMENTIA (VAD)

VaD is a degenerative cerebrovascular disease which presents with an acute onset and a stepwise decline in cognitive functioning (Mathias and Burke, 2009). Vascular dementia (VaD) is one of the most commonly occurring dementias, accounting for 10% to 50% of all dementia cases (Brayne, 1995; Lobo et al, 2000; Rocca, Hofman, Brayne, 1991; Rockwood et al, 2000). In Western countries it is second only to AD and in many Asian countries it is thought to be the leading cause of dementia due in large part to the higher incidence of stroke (Desmond, 2004).

Table 1.6

Clinical dementia rating scale

Rating	Symptoms	Functioning
CDR 0	No cognitive impairment	No evidence of dementia
CDR 0.5	Very mild dementia	Mild consistent forgetfulness or slight problems with two or more other cognitive areas
CDR 1	Mild dementia	Moderate difficulty with recent recall which interferes with daily activities or mild forgetfulness with mild to moderate impairment in three or more other cognitive areas including requiring prompting for personal hygiene
CDR 2	Moderate dementia	Severe or moderate memory loss with severe impairment in three or more other cognitive areas including requiring assistance with dressing or personal hygiene
CDR 3	Severe dementia	Severe memory loss with only memory fragments, orientation to person only, inability to make judgments or problem solve, no independent function, inability to perform personal care, incontinence.

Table adapted from Lezak, 2004.

Compared to other dementia subtypes, patients with VaD show marked impairment in executive functioning and overall fluctuations in cognitive performance (Looi & Sachdev, 1999; Walker, Ayre, Cummings et al, 2000). It is characterised by ‘patchy’ deficits with areas of strengths and weaknesses varying among patients (Reichman, Cummings, McDaniel et al, 1991). There is significant overlap between VaD and AD with shared symptomatology and neuropathology and they may also coexist in what is referred to as mixed dementia. In one study, 30% of patients with confirmed AD had cerebrovascular disease and 40% of confirmed VaD patients showed AD pathology on autopsy (Kalaria and Ballard, 1999). Also as previously

mentioned, vascular factors are implicated in the acquisition of AD (Stewart, Prince and Mann, 1999). Thus, the distinction between VaD and AD may not be very clear and some regard the two as existing as pure forms on either extreme of a continuum (See Table 1.5).

1.5.1 RISK FACTORS FOR VAD

Stroke and ischemic heart disease are thought to be responsible for the development of VaD as one or more ischemic strokes are associated with a greater risk of developing VaD (Kiyohara, 1994). Also, a number of studies have shown patients meeting the criteria for a diagnosis of dementia three months after suffering a stroke with the dementia attributed primarily to the stroke (Desmond, 2000; Pohjasvaara et al, 1998).

Table 1.7

The continuum of patients in which pure vascular dementia (VaD) and pure Alzheimer’s disease (AD) represent the two extremes. CAA= cerebral amyloid angiopathy.

<i>Description</i>	<i>Identifying Features</i>
Pure AD	Plaque and neurofibrillary pathology only
Plaque only AD	Lack of neurofibrillary pathology
AD with severe CAA	Profound vascular amyloid deposition
CAA with plaques	Mild AD with vascular involvement
AD with vascular lesions	Vascular lesions include microinfarcts
AD with cerebrovascular disease	Mixed dementia
VaD with AD changes	Mixed dementia or coincidental AD pathology
VaD with small-vessel disease	Prominent microvascular changes
Pure VaD	Infarction only and white matter lesions

Figure adapted from Kalaria et al (2002).

Other risk factors include prior stroke, history of cerebrovascular disease, hypertension, atherosclerosis, vasculitis, hyperlipidemia, diabetes mellitus and smoking (Hodges and Graham, 2001; Roman, 2003). Advanced age, usually after 70

years, fewer years of education as well as non white ethnicity are also associated with higher risk of VaD (Desmond, 2000). The prevalence of VaD is also usually higher in men than women.

In the last two decades, research on genetic factors involved in VaD has gained ground. Patients with the ApoE ϵ 4 allele are three times more likely to have both AD and VaD than those without (Kalaria, 1997). Another study found a higher frequency of ApoE ϵ 4 alleles in patients with dementia and stroke when compared to controls. Also, ApoE ϵ 4 homozygotes had a seven-fold increased risk and ApoE ϵ 4 heterozygotes had a two-fold increased risk of dementia with stroke present when compared to ApoE ϵ 3 homozygotes (Slooter, Tang, van Duijn et al, 1997).

Another related but extremely rare condition is CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) which has a presenile onset and results in multiple subcortical infarcts (Salloway and Hong, 1998). CADASIL is regarded as a hereditary form of VaD, and is attributed to a mutation on Chromosome 19. Symptoms may include migraines or an ischemic event in early adulthood and following recurrent ischemic events, stepwise decline and resulting dementia syndrome (Chabriat, Vahedi, Iba-Zizen et al, 1995; Desmond, Moroney, Lynch et al, 1999).

1.5.2 NEUROPATHOLOGY AND PROGRESSION OF VAD

VaD may be due to small vessel and/or large vessel disease. Large vessel disease results from many multiple strokes resulting in multi-infarct dementia (MID) while small vessel disease causes lacunar strokes and Binswanger disease (Roman, 1993; 2002). In small vessel disease, impairments in executive function are thought to be due to lacunar infarctions affecting structures like the thalamus and caudate nucleus

and disrupting connecting pathways of frontal-subcortical circuits (Wolfe, Linn, Babikian et al, 1990). Patients with subcortical VaD may also experience disinhibition and other neuropsychiatric symptoms (e.g. apathy, abulia) consistent with frontal lobe dysfunction. Small deep white matter infarctions may also cause an abrupt change in behaviour with symptoms of fluctuating alertness, inattention, memory loss, apathy, abulia and psychomotor retardation. Location of the infarct impacts cognitive performance differentially; left-sided infarcts were associated with verbal memory loss while right-sided infarct was associated with impairment of visuospatial memory (Tatemichi, Desmond, Prohovnik, 1995).

MID has been associated with a stepwise course of cognitive decline and dementia. However, Desmond (2004) notes that a single large cortical infarction can have a less deleterious clinical impact than a strategically located subcortical infarction because its effects are limited to the region of the infarction while the subcortical infarction can have disproportionate effects to its location and size due to the disruption of metabolic pathways. Thus some patients with multiple infarcts may exhibit symptoms due to stroke- aphasia and spatial neglect but fail to meet criteria for MID. In cases where VaD and AD coexist, the clinical picture will often be determined by the progression of AD.

1.5.4 EFFECTS ON COGNITION AND DIFFERENTIAL DIAGNOSTIC ISSUES IN VAD

As mentioned, VaD is marked by an acute onset, worse impaired executive function but superior memory test performance than that observed in AD patients. Executive functions that are affected include planning, sequencing, mental processing speed and performance on unstructured tasks (Villardita, 1993; Almkvist, Backman,

Basun et al, 1998; Mendez, Cherrier and Perryman, 1997; Mendez and Ashla-Mendez, 1991). Attention may also be impaired (Doody, Massman, Mawad et al, 1998).

Compared to AD, VaD patients may exhibit poorer verbal fluency and increased perseverations but primary language functions remain largely preserved (Doody, Massman, Mawad et al, 1998; Lamar, Podell, Carew, 1997; Starkstein, Sabe, Vazquez et al, 1996). AD patients tend to show greater impairments than VaD on tests assessing memory functions (Villardita, 1993) showing more intrusion errors (Loewenstein, D'Elia, Guterman et al, 1991; Barr, Benedict, Tune et al, 1992), faster rates of information decay (Carlesimo, Sabbadini, Fadda et al, 1995; Carlesimo, Fadda, Bonci et al, 1993), decreased benefits from cues (Del Re, Pennese, Ciurlino et al, 1993; Yuspeh, Vanderploeg & Kershaw, 1998) and poorer naming (Villardita, 1993; Powell, Cummings, Hill et al, 1988; Barr, Benedict, Tune et al, 1992). Despite these findings, some earlier studies fail to find patterns distinguishing cognitive impairment in AD and VaD (Erkinjuntti, Laaksonen, Sulkava et al, 1986).

1.6 DEMENTIA WITH LEWY BODIES (DLB)

Lewy bodies consist of abnormal protein aggregates which develop within cells and were first identified by Frederick Lewy in 1914 who identified them in the substantia nigra of patients with Parkinson's disease. Cases of dementia with Lewy bodies were later described in the 1960s and thought to be very rare and it wasn't until the 1980s that the immunocytochemical methods were developed to identify the disease and more cases were diagnosed.

DLB is a progressive dementia that is characterised by cognitive decline and may account for 0 to 35% of all dementia cases (Zaccai, McCracken and Brayne,

2005). There are three defining clinical features (Rampello, Ceresa, Alvano et al, 2004):

(1) pronounced fluctuations in attention and alertness and other aspects of cognitive functioning including frequent drowsiness, lethargy, lengthy periods of time spent staring into space, or disorganized speech (Lezak, 2004).

(2) complex visual hallucinations (for example, patients may describe a scenario with dwarfs or supernatural creatures (McKeith, Galasko, Wilcock et al, 1996).

(3) parkinsonian motor symptoms, including rigidity and impairment of spontaneous movement, bradykinesia, stooped posture and shuffling gait (Walker, Allen, Shergill et al, 1997).

Repeated falls, syncope, systemic delusions and hallucinations as well as behavioural disruption in REM sleep have also been suggested as features supporting a diagnosis of DLB (Rampello et al, 2004, Ferman, Boeve, Smith et al, 2002).

1.6.1 RISK FACTORS IN DLB

The average onset occurs between ages 60 to 68 years. While many studies report no sex differences, some suggest that DLB may occur slightly more frequently in men (Weiner, Risser, Cullum et al, 1996; Rosenberg et al, 2001). A relationship with DLB and the genotype Apoε4 exists but only when AD is also present.

1.6.2 NEUROPATHOLOGY AND PROGRESSION OF DLB

Pathological criteria for DLB are established by the presence of Lewy bodies. The number of Lewy bodies in five cortical areas (transentorhinal, cingular, temporal, frontal and parietal) are counted and assigned a score of 0 to 2 for each area with a

sum of 7-10 being indicative of DLB (Mizutani, 2000). The localization as well as density of the Lewy bodies are thought to correspond to the severity of the symptoms (e.g. Lewy bodies in brain stem are related to movement disorders), however other studies suggest that no great correlation exists (Greicius et al, 2002).

Although up to one third of AD patients also show Lewy bodies at autopsy, greater neuronal loss in the substantia nigra, innominata and locus coeruleus, lower cortical choline-acetyltransferase activity as well as the rare occurrence of NFT in DLB may help distinguish the two (Gibb et al, 1989, Burkhardt et al, 1988; Weiner, 1999).

1.6.3 EFFECTS ON COGNITION AND DIFFERENTIAL DIAGNOSTIC ISSUES IN DLB

Rampello et al (2004) advise that a differential diagnosis between AD and DLB based solely on clinical features is risky. But while there is some overlap of symptoms, certain features occur more frequently in DLB than AD. These include more Parkinsonian symptoms, hallucinations, manic symptoms, agitation.

Parkinsonian symptoms may be present in up to 70% of DLB patients. Significant memory impairments may not be present in the early stages, but they become more apparent as the disease progresses (Rampello et al, 2004). Deficits in visuospatial ability and attention are more likely to be prominent and this can be seen in poorer copying of pentagonal figures and block designs than AD patients (Ala et al, 2001; Hansen et al, 1990) and in acute confusional states and decreased forward and backward digit spans (Gnanalingham et al, 1997; Hansen et al, 1990). Given the impaired attention and constructional abilities in DLB patients, the MMSE is useful in helping to distinguish DLB from AD (Ala et al, 2002).

Depression may be present in up to one half of DLB patients and disturbed REM sleep also occurs (McKeith and Burn, 2000; Ferman, et al, 2002; Grace et al, 2000). Behavioural disturbances such as aggression, rebellion and agitation may occur more frequently in DLB patients. However, patients with DLB may show marked neuroleptic sensitivity which may exacerbate behavioural and extrapyramidal symptoms.

1.7 FRONTOTEMPORAL DEMENTIA (FTD)

Initially identified by Arnold Pick, the discovery of rapid atrophy in the frontotemporal regions was described as Pick's disease in the 1920s. However, by the 1980s and 1990s, scientists discovered variants of the disease and it became known by many different names including Frontotemporal lobar degeneration (FTLD) and Frontotemporal dementia. The concept has expanded beyond that of Pick's disease and is now associated with pathological and genetic heterogeneity (McKhann et al, 2001). FTD is thought to encompass three syndromes: 1) the frontal variant, previously known as Pick's disease which is characterised mainly by striking changes in behaviour and judgment, 2) progressive nonfluent aphasia and 3) semantic dementia which is distinguished by fluent aphasia with impaired word knowledge (Geldmacher, 2004).

1.7.1 RISK FACTORS IN FTD

FTD can affect persons between the ages of 35 and 75 years and affects both sexes equally (McKhann et al, 2001). Approximately 20%- 50% of cases have a family history of FTD (Higgins and Mendez, 2000; McKhann et al, 2001) in which the FTD is transmitted by autosomal dominant inheritance. Tau pathology and tau mutation on chromosome 17 is also implicated in many cases (Higgins and Mendez,

2000). Traumatic brain injury has also been suggested as a possible risk factor but existing evidence suggests its influence may be weak (Mortimer and Pirozzolo, 1985).

1.7.2 NEUROPATHOLOGY AND PROGRESSION OF FTD

FTD involve progressive degeneration of the frontal and temporal neocortex, with the parietal and occipital lobes and the posterior parts of the superior temporal gyrus remaining relatively spared (Lezak, 2004). The main cellular changes are microvascular changes and/or severe gliosis in astrocytes with or without the presence of Pick bodies. Unlike AD, NFT and AP are absent. Frontal metabolism and blood supply are reduced, however EEG readings are normal.

FTD follows a gradual course of deterioration, with duration ranging from 2 to 17 years (Neary and Snowden, 1991). Social behaviours and judgment are impaired in earlier stages and as the disease worsens, apathy and cognitive dysfunction are seen. In late stages, mutism and motor rigidity may be present (Lezak, 2004).

1.7.3 EFFECTS ON COGNITION AND DIFFERENTIAL DIAGNOSTIC ISSUES IN FTD

While FTD is much less prevalent than AD, differentiating between the two can be a challenge as many verbal and behavioural symptoms are common to both conditions. However, the hallmarks of FTD are the behavioural changes: poor personal and social judgment, perseveration, stereotyped behaviours, executive dysfunction characterized by poor planning and goal setting as well as apathy and disinhibited behaviour. Unlike the pattern seen in AD, executive dysfunction is more prevalent in FTD than memory impairment (Mathuranath et al, 2000; Thompson, Stopford, Snowden et al, 2005). Anosognosia may also occur (Geldmacher, 2004; Lezak, 2004). Performance on verbal fluency may be worse than AD but visuospatial

orientation and praxis as well as arithmetic skills remain unaffected (Mathuranath et al, 2000; Thompson et al, 2005). Performance on screening tests can also assist with differentiation as MMSE scores in FTD are often regular or show minimal impairment while in AD, poor scores are usually associated with the level of impairment (Hodges, 2001; Geldmacher, 2004). It is also quite rare for FTD onset to occur after age 75 years (McKhann et al, 2001).

Despite the differences in neuropsychological profiles, differentiating between FTD and AD remains a challenge and some studies provide inconsistent results or fail to distinguish between them. Thompson et al, (2005) suggest a qualitative examination of scores to help differentiate between FTD and AD. In their study, the groups were not differentiated by scores on a naming task, repetition task or Weigl's block test; however scrutiny of the error types increased the predictive ability of the tasks. For instance, perseverations were predictive of FTD and phonological errors of AD in the naming task, concrete responses in the repetition task were predictive of FTD while phonological errors indicated AD and dismantling behaviour in the block task was predictive of FTD. Thompson et al (2005) conclude that neuropsychological test scores may obscure differences between dementia groups and an examination of performance characteristics and error types can augment differentiation between FTD and AD.

A summary of the prominent clinical features of the most common types of dementia are described in Table 1.8.

Table 1.8

Summary of cardinal clinical features of the common neurodegenerative dementias

Executive and Attentional Dysfunction	Amnesia	Aphasia	Visuospatial Disturbance	Behavioural disturbance
AD				
Often present but rarely present in history in early stages	Common at presentation Manifests as forgetfulness May remain isolated	Common at presentation typically fluent and anomic	Often present at presentation may not be prominent in history	uncommon
Vascular Dementia				
Prominent early feature. Manifests as slowing of cognition	Mild: usually due to attentional/executive factors	Uncommon	Uncommon	uncommon
FTD				
Common at presentation but usually overshadowed by language/behaviour	uncommon at presentation but usually overshadowed by language/behaviour	Seen in 50% of cases at presentation; fluent or non-fluent syndromes; latter may evolve to become consistent with AD or DLB	Uncommon	Seen in 50% of cases at presentation; protean manifestations include disinhibition, obsessiveness and aboulia
DLB				
Present and may be prominent in history	Not prominent; may reflect dual pathology if present	Uncommon	Common and prominent in history at presentation	Fluctuating cognitive state and hallucinosis common; personality change rare

1.8 DIAGNOSIS AND ASSESSMENT OF DEMENTIA

All therapies available for the treatment of dementia are based on an early diagnosis. The first step of diagnosis usually involves the use of a screening test. Screening is critical for identifying persons with undiagnosed dementia and thus may allow persons and their families to access care at an earlier stage (Boustani et al, 2003). A positive screen on a test usually leads to a referral for specialist assessment, either to a memory clinic or to a geriatric psychiatrist. Different methods may be employed to assist in a diagnosis of dementia including neuropsychological assessment, brain imaging and biomarker analysis.

1.8.1 NEUROPSYCHOLOGICAL ASSESSMENT

A diagnosis of dementia due to a specific cause can be quite difficult especially in the early stages. Neuropsychological assessment can be very useful in this regard. Miller and Morris (1993) highlighted three goals of assessment in dementia. Firstly, it is used to aid the diagnosis or identification of persons with dementia and the discrimination between the different types of illness. The findings can help to identify neuropsychological impairment, identify impairment in persons with high pre-morbid functioning or rule out the presence of clinical problems in the worried well.

A second goal of neuropsychological assessment is the measurement of change in performance in which initial assessments are used as a baseline measure for subsequent re-testing. The rate or pattern of decline can help to facilitate differential diagnosis. Finally, neuropsychological assessment can be used to analyse levels of functioning and identify relative strengths and weaknesses in order to facilitate

decisions about management, care and treatment (Morris, Worsley and Matthews, 2000).

The recognition of the importance of early dementia screening has led to the development of a number of screening instruments for use in research and clinical settings (Ritchie & Hallerman, 1989). Some commonly used screening instruments include the Mini-Mental State Examination (MMSE) (Folstein, Folstein & McHugh, 1975), Abbreviated Mental Test Score (AMTS) (Qureshi and Hodkinson, 1974), Blessed Information-Memory-Concentration Test (BIMC), (Blessed, Tomlinson and Roth, 1968), Blessed Orientation-Memory-Concentration Test (BOMC) (Katzman, Brown, Fuld et al., 1983), Short Test of Mental Status (STMS) (Kokmen, Naessens, Offord, 1987) and the Clock Drawing Test (Critchley, 1953). Neuropsychological test batteries are more detailed, take more time to administer and measure a wider range of cognitive domains than screening tests. Cognitive domains include orientation and perception, memory, language functions, aphasia, visual motor constructional ability (praxis), attention, abstract reasoning and executive functioning (Lezak, 2004).

However, while neuropsychological assessment may possess good sensitivity and can detect impairment, they can possess low specificity in failing to differentiate between neurological and psychiatric disorders (Morris, Worsley and Matthews, 2000). Another major problem arises from the finding that the application of psychometric instruments standardised on whites resulted in a larger than expected number of false-positives on both psychopathological and neuropsychological variables in non-white populations. The dilemma posed by the lack of standardised instruments and use of inappropriate norms among ethnic populations not only

places restrictions on the use of the instruments among diverse cultures but also limits the theories explaining cognitive functioning (Ardila, 1995; Greenfield, 1997).

The advent of neuro-diagnostic techniques (such as brain imaging and laboratory analyses) has shifted the attention of neuropsychological testing away from diagnosis and towards patient management and ascertainment of strengths and weakness (Lezak , 2004).

1.8.2 BRAIN IMAGING

Brain imaging is a non-invasive procedure and consists of either structural (computerised tomography (CT), magnetic resonance imaging (MRI)) or functional imaging (functional MRI, positron emission tomography and single photon emission computerised tomography (SPECT)). Imaging has become increasingly useful in confirming a diagnosis of dementia, in monitoring the progression of the disease and for research purposes (O'Brien, 2010). A further list of the reasons for brain imaging is provided in Table 1.9.

Table 1.9

Reasons for imaging in dementia

-
1. To exclude a space-occupying lesion as a cause for the cognitive impairment (for example, tumour, abscess, subdural haematoma, normal pressure hydrocephalus)
 2. To improve the accuracy of differential diagnosis (in particular, to look for vascular pathology to help with the diagnosis of vascular dementia which would exclude a diagnosis of Alzheimer's disease, to look for focal atrophy such as frontal atrophy in frontotemporal dementia)
 3. For monitoring the disease process or disease progression (for instance, if clinical diagnosis is unclear, repeat imaging after two to three years can show clear progression in cases who have progressive dementia, while those with static cognitive impairment will show no change between scans)
 4. For research purposes (in particular, structural imaging is used to investigate the earliest brain regions affected by the disease process, while functional imaging is used to investigate the variety of chemical and other systems that may be involved).
-

Table adapted from O'Brien, 2010.

In AD, CT and MRI scans are used to establish the degree of cerebral atrophy. Scanning along the axis of the temporal lobe allows better visualisation of the medial temporal lobe and hippocampus which are earliest and most affected in AD (Jobst, Barnetson and Shepstone, 1998). CT has limited sensitivity with some AD patients having normal scans, however MRI offers higher resolution scanning and the ability to differentiate grey and white matter as well as vascular changes in white matter (O'Brien, 2010). In longitudinal studies of AD, the earliest changes in MR were seen in the posterior cingulate, entorhinal cortex and hippocampus (Scahill, Schott, Stevens et al, 2002).

Serial MRI scanning has been used to track the progression of brain atrophy in different dementias (although different dementias may show different regional atrophic patterns) and has also been used as an outcome measure in clinical trials of anti-dementia drugs (Fox, Freeborough, Rossor, 1996; Jack, Lowe, Weigand et al, 2009; O'Brien, Paling, Williams, Lloyd et al, 2000; Venneri, 2007). Barber, Gholkar, Scheltens et al (1999) estimate that hippocampal atrophy can be detected in 80-90% of cases of AD using MRI.

Functional imaging with SPECT and PET scanning shows bilateral, bitemporal and biparietal hyperfusion in AD and these changes are observed even in persons who possess a genetic risk of developing AD but have not yet developed symptoms (Kennedy, Rossor, Fracowiak, 1995). Studies have also investigated the role of nicotinic receptors in the differential diagnosis of dementia (VaD, AD and DLB) using nicotinic SPECT scans (O'Brien, Colloby, Pakrasi et al, 2007, 2008). The use of fMRI is proving promising for diagnosis and monitoring of disease especially with respect to predicting AD in patients with mild cognitive impairment (Scheltens and Korf, 2000).

Brain imaging however is not an infallible procedure in dementia diagnosis. Chaves, Ilha, Maia et al, (1999) assessed the diagnostic value of brain measures (obtained from CT scans) and cognitive functioning (based on neuropsychological assessment) in AD and multiinfarct patients and found higher sensitivity and specificity among the cognitive measures. A meta-analysis of SPECT use in dementia diagnosis by Dougall, Briggink, Ebmeier (2005) found that while SPECT had higher specificity than clinical criteria in differentiating AD and other dementias, clinical criteria had higher sensitivity.

1.8.3 BIOCHEMICAL MARKERS

Biochemical markers are usually used as diagnostic or prognostic indicators in illness and may involve either imaging or fluid analyses. A vast amount of research has been conducted on biomarkers in dementia with limited success and finding definite diagnostic biomarkers has proven to be a significant challenge. Wiltfang, Lewczuk, Riederer et al (2005) support the analysis of cerebrospinal fluid (CSF) biomarkers in the diagnosis in dementia. CSF biomarkers have been implicated in differential diagnosis of AD, DLB and FTD (Gómez-Tortosa, Gonzalo, Fanjul et al, 2003; Hampel, Buerger, Zinkowski et al., 2004) and there has been mixed results with some studies reporting differences between AD and VaD (Fredman, Wallin, Blennow et al., 1992) and others finding no difference (Nagga, Gottfries, Blennow et al, 2002).

In AD, areas of biomarker research include investigations of (CSF), peripheral tissue markers, pharmacologic and neuroendocrine probes and behavioral and biochemical correlates (Sunderland, Molchan, Zubenko, 2000). Studies of levels of choline acetyl transferase (CAT) acetylcholinesterase (AChE), and

butylcholinesterase (BuChE) in CSF report mixed findings among AD patients and controls, with some showing decreased levels in AD patients and others showing no difference (Appleyard, Smith, Berman et al, 1987; Atack, May, Kaye et al., 1988; Ruberg, Yillageois, Bonnet et al, 1987). Another potential biomarker for AD lies in peripheral tissue (e.g. platelets, blood cells, skin fibroblasts, and peripheral vessels) and the alterations that take place during the disease (Zubenko, Cohen, Growdon, 1984).

Research has also focussed on the role on neurotransmitters and neurohormones in AD including cholinergic, serotonergic and GABAergic systems (Lawlor, Sunderland, Mellow et al., 1989; Raskind, Peskind, Veith et al. 1989).

Research investigating anatomical substrates of behavioural correlates in AD, such as depression and psychosis, aim to further develop understanding of the disease. For example, one study found an association with depression and degeneration of the locus coeruleus and dorsal raphe nuclei in AD (Zweig, Ross, Hedreen et al., 1988), and another study found an association between psychosis and increased cortical densities of AP and NFT and preservation of norepinephrine in the substantia nigra (Zubenko, Moossy, Kopp, 1990). Both psychosis and depression were associated with a decrease in serotonin in the hippocampus (Zubenko, Moossy, Kopp, 1990).

While biomarker analysis is very promising in terms of refining sensitivity and specificity in dementia diagnosis, there are a number of challenges that limit its use. High intra and inter- person variability can affect the levels and interpretation of potential biomarkers and markers identified in one group cannot be reproduced by other groups (Cedazo-Minguez & Winblad, 2010). Also, the lack of a standardized method of analysis caused by inconsistencies in data analysis of CSF sample due to

differences in sample collection, transportation and storage limit its application (Anoop, Singh, Jacob et al., 2010, Cedazo-Minguez & Winblad, 2010).

1.9 LIMITATIONS TO THE ASSESSMENT OF DEMENTIA

The use of different methods of assessment of dementia often depends on the prescribed strategy and availability of methods for diagnosis. In the UK, a patient's first point of contact is usually with a general practitioner and other primary care medical personnel. At the primary care phase, a full history and routine physical and blood examinations should be conducted to assist in the differential diagnosis or treatment of dementia. McKeith and Fairbairn (2001) recommend referral to specialist secondary services especially when there are complicating factors including atypical presentation, rapid deterioration, significant behaviour problems and need for anti-dementia drug advice. Specialist services will usually involve the assessment of the patient using different scales and while brain scanning is more routine in an American context, it is less so in the UK and is based upon the merits of individual cases. Larner (2007) recommends an integrated care pathway which includes multiple disciplines to deal with the heterogeneity of presentation of dementia patients. Depending on the presentation, patients would be referred to an old-age psychiatrist, geriatrician, neurologist or clinical geneticist who would promote more accurate diagnosis, treatment and prognosis.

The strategies for diagnosis in developing countries however may be different and the use of different methods may be affected by practical reasons of cost and availability. The Australian Academy of Science notes the prohibitive cost of MRI which can cost millions of dollars. In Australia, this cost is subsidized by the government; however, people in poorer countries may not have access to such

expensive procedures. Given the limited public funding of health and social care in developing countries, it is likely that such cost constraints will continue to impact the kinds of assessments available to patients (Prince, 1997). Puongvarin, Viriyavejakul, Komontri (1991) also highlight the practical difficulties that may be encountered in the use of neuro-diagnostic technologies:

With highly refined technologies becoming increasingly available worldwide, physicians must be selective in applying these to patients. The cost constraint [however] is greater in developing countries. Investigative procedures in neurology, notably computerised brain scanning and magnetic resonance imaging, are prohibitively expensive in both the initial investment and the maintenance, requiring careful consideration in their acquisition and usage (p 1565)

In Africa, Ogun, Oluwole, Aogunseyinde et al (2001) bemoan the lack of brain imaging facilities. Although they refer to its application in stroke diagnosis, their comments also likely apply to use in dementia diagnosis. They note that the technology is not readily available in sub-Saharan Africa and access by patients is furthered hampered by distance and cost constraints. This cost limitation also applies to use of biomarker analysis in dementia diagnosis in developing countries (Anoop, Singh, Jacob et al, 2010).

The limitations of brain scanning and biomarker analyses may preclude their use in routine diagnostic strategies in developing countries, and as such it is likely that neuropsychological testing will remain the most important tool for dementia assessment. This assertion is corroborated by Chaves, Ilha, Maia et al (1999) who maintain “cognitive evaluation still seems to be the best method to screen individuals from the community, especially for developing countries, where the cost of brain

imaging precludes its use for screening and initial assessment of dementia” (p 1133).

The lack of sufficient data on dementia prevalence in developing countries and the possibility of undetected dementia in community populations also strengthen the argument for neuropsychological screening and testing (Jitapunkul, Chansirikanjana, Thamarpirat, 2009).

However, the use of neuropsychological instruments in diverse, cross-cultural settings warrants careful consideration since validation and standardised norms applicable to one culture cannot be assumed to apply to another culture. Comparison across cultures is also only possible with the use of common, standardised procedures (Prince et al, 2000). A detailed discussion of the factors influencing use of and performance on neuropsychological tests in dementia assessment across cultures will be undertaken in the next chapter.

CHAPTER 2

**CULTURAL INFLUENCES ON DEMENTIA AND
DEMENTIA ASSESSMENT**

**2.1 DEMENTIA ACROSS ETHNICITIES AND CULTURES:
EPIDEMIOLOGICAL DIFFERENCES**

Regional and ethnic differences in the prevalence of dementia have been reported in the literature. Prevalence rates range from a low of 1.6% in Africa to a high of 6.4% in North America. A 2005 Delphi consensus study estimated prevalence rates for different WHO regions and these are ranked according to dementia prevalence in table 2.1 below.

Table 2.1

Dementia prevalence ranked across WHO regions

Rank	Country	Prevalence Rate/%
1	North America	6.4
2	Western Europe	5.4
3	Latin America	4.6
4	Developed western Pacific (Japan, Australia, NZ)	4.3
5	China and western Pacific	4.0
6	Eastern Europe	3.9
7	Eastern Europe	3.8
8	North Africa and Middle East	3.6
9	Indonesia, Thailand, and Sri Lanka	2.7
10	India and south Asia	1.9
11	Africa	1.6

Table adapted from Ferri et al (2005)

Some studies (based on research in India and Nigeria) suggest lower prevalence of dementia in developing than in developed countries and attribute this, not simply to reduced survival, but to decreased incidence (Hendrie et al, 2001; Chandra et al, 2001). The determination and comparison of prevalence rates across

different regions has been hampered by a lack of published studies from low and middle income countries in Latin America, Africa, Middle East, Eastern Europe and Russia (Ferri et al, 2005).

A 10/66 Dementia Research Group study of approximately 15000 persons investigated the dementia prevalence in seven low and middle income countries in Latin America, China and India and compared the rates to existing published data. Rodriguez et al (2008) found that with the exception of urban Latin America, which had prevalence rates similar to those in Europe, prevalence rates in Latin America and India were relatively lower than that reported for Europe. Similar findings were reported by Kalaria et al (2008) who included more recent large scale prevalence studies and reported large variation in prevalence rates within developing countries. They attributed these findings to differences in population age structure, genetics, lifestyle, reduced survival after diagnosis and difficulty in standardising dementia assessment. Rodriguez et al (2008) also suggested that underestimation of prevalence rates may be due to informants being less likely to report cognitive decline or social impairment.

2.2 PREVALENCE OF DEMENTIA SUBTYPES

Differences in distribution are also noted by cause or subtype of dementia. For instance, in white populations in the United States and Europe, vascular disease is less common and as such, mixed or vascular dementia is much less frequent than Alzheimer's disease (Jorm, 1991). However in Japan, vascular disease is more common and as such there is an increased proportion of vascular dementia cases (Ueda, Kawano, Hasuo & Fujishima, 1992). However, subsequent studies suggest this pattern may be changing and the ratio of vascular dementia to AD is

approximately 1:1 and this may be the result of a decline in vascular dementia, an increase in AD or both (Kiyohara, 1994).

Within country differences among different ethnicities have also been noted; for example, in the United States, Alzheimer's disease accounts for 90% of dementia cases among Caucasian middle class populations (Evans et al, 1989) while in African Americans, vascular dementia accounts for approximately 50% of dementia cases (Folstein, 1985; Wallace, 1993). A comparison of Japanese American men in Hawaii and Japan revealed higher rates of Alzheimer's disease in the American sample than the Japanese sample (5.4% vs 2%), (White et al, 1996). While North American and Africa report the highest and lowest dementia prevalence rates (6.4% and 1.6% respectively), the prevalence rates for white and African American groups in North America show a converse pattern. In adults aged 71 years and over, African Americans were twice as likely as whites ((21.3% vs 11.2%) to have AD and other dementias (Potter, 2009). Also, a special report focussing on race, ethnicity and Alzheimer's disease published by the Alzheimer's Association of the United States (2010) concluded that African-Americans and Hispanics are more likely than whites to have AD and other dementias and many published studies confirm these findings (Stern et al, 1994; Dilworth-Anderson et al, 2008, Lopez et al, 2003; Manly et al, 2004).

2.3 COGNITIVE PERFORMANCE IN ETHNIC MINORITIES

Differences in performance on measures of cognitive performance between ethnic groups have also been well established. The performance of ethnic minority groups is often found to be lower than that of comparable white populations in both community and clinical samples even after correcting for education and socio-

economic differences. Manly et al., (1998) found scores of African-Americans to be significantly lower than whites on measures of verbal learning and memory, figure memory, abstract reasoning, language and visuospatial ability. The African American group had significantly fewer years of education but after this was controlled for, ethnic differences remained. Controlling for occupational attainment also did not remove the effect of ethnicity and scores by whites were still significantly higher than that of African-Americans. A subsequent sample of whites and African Americans matched for education also yielded significant differences with African Americans obtaining lower scores on measures of figure memory, verbal abstraction, category fluency, drawing and figure matching. Manly et al. also took into consideration differences in the frequency of medical conditions between the groups. However after comparing groups with hypertension, diabetes, cardiac disease and thyroid, the significant effect of ethnicity still remained.

Results from a Health and Retirement study in the United States which surveyed over 16 000 respondents found levels of cognitive impairment varied by ethnicity. Whereas 8.8% of whites were deemed impaired, the prevalence among African Americans was 23.9% and in Hispanics, 17.5% (HRS, 2010). These differences were even greater in younger age groups, with African Americans and Hispanics aged 55 - 64 being four and two times respectively more likely than whites to have cognitive impairment as compared to two and 1.6 times more likely in the over 85 age group.

Stewart et al (2001) reported normative data for a test battery for cognitive functioning in African Caribbean elderly in the UK and found that like African American groups, they yielded lower scores than those obtained from white populations. Richards et al. (2000) also investigated cognitive performance in

elderly African- Caribbeans and found significantly lower scores among African Caribbeans than whites on most tests. When assigned cognitive ratings of normal, impaired or demented, a greater percentage of African Caribbeans were rated as impaired and demented (22% and 34% respectively) when compared to whites (9% and 4% respectively). Richards et al. also adjusted for the effects of education, occupational social class, and the presence of hypertension or diabetes and African Caribbeans still had an elevated odds risk ratio for being rated as impaired or demented OR=5.0 [1.3 – 18.5] and OR=5.9 [0.9 – 38.1] respectively.

2.3 FACTORS INFLUENCING ETHNIC DIFFERENCES IN COGNITIVE PERFORMANCE AND DEMENTIA PREVALENCE

Given the variation in rates of dementia, a number of reasons have been postulated to account for the differences across ethnicities. Richards, Abas, Carter et al (1999) suggest that different patterns of experience can influence cognitive functioning and while some of these like education and occupation can be formalised, equating these, even across societies with similar socio-economic backgrounds still poses a great challenge. Irvine (1979, as cited in Irvine and Berry, 1988) theorised that differences in group performance may be attributed to four types of causes:

- *Intra-hominem*: differences attributed to structural differences in brain or its biochemistry or neurology (e.g genetic factors)
- *Extra-hominem*: differences attributed to ecological press and particular demands of environment (e.g. migration, assimilation, culture)
- *Inter-hominem*: differences in that which is taught- e.g. language, education, values and behavioural norms

- *Ad-hominem*: a common sense explanation that has heuristic value but is unscientific. They can however lead to revaluations of research.

These differences need not operate on a level of mutual exclusivity. Indeed one or more or a combination of these causes may prove the most comprehensive explanation for the existence of ethnic differences in cognitive performance. Some of the factors explaining these differences are outlined in greater detail below.

2.3.1 GENETIC FACTORS

Underlying genetic factors may play a role in conferring different levels of susceptibility to different ethnic populations. Most of the studies on genetic factors in dementia have been based on Caucasian populations but Farrer (2000) notes that the picture varies among ethnicities. Having one or more copies of the $\epsilon 4$ allele of the apolipoprotein E as compared to having the ApoE $\epsilon 3$ allele is associated with a greater risk for Alzheimer's disease in Caucasians but not in African Americans or Hispanics. In the absence of the ApoE $\epsilon 4$ allele, Hispanic Americans and African Americans seem to develop AD at the same rate as Caucasian Americans, but among those who lack the variant, Hispanic Americans and African Americans develop the disease at two and four times the rate of Caucasians respectively (Tang, Stern et al, 1998). In Japanese Americans, the effect of the ApoE $\epsilon 4$ allele is even stronger than in Caucasian Americans in which those who are heterozygous for the $\epsilon 4$ allele are 5 times more at risk and in those homozygous for the allele, the risk is 30 times more than that for Caucasian Americans (Farrer, 1997).

Ineichen, (1998) further purports that genetic arguments based on common ancestry to explain findings in African-Americans and African diasporic minorities may be compromised especially in light of European interbreeding and contrasting

cultural experiences. Thus, explanations for minority ethnic group differences may also be sought in other factors.

2.3.2 EDUCATIONAL FACTORS

As mentioned in chapter one, low education is associated with a higher risk for many dementias, with illiteracy and fewer years of education conferring a two or three fold risk of dementia than for more highly educated persons (Ott, Breteler, Vanhaskamp et al, 1995; Mortimer et al, 1993; Katzman et al, 1993; Stern et al, 1994). Studies show persons with lower education, literacy and numeracy tend to perform more poorly on cognitive screening instruments and as such can result in false positive screens for dementia for persons who are cognitively normal (Chandra et al, 1994; Ganguli, 1995). This has implications for dementia screening in developing countries and among migrant populations as countries that are lesser developed economically, tends to have fewer students enrolled in primary and higher education. Although enrolment rates in higher education have increased in developing countries over the last two decades, the rates in industrialized countries are still five times higher (World Bank, 2000).

Attempts are usually made to accommodate the impact by statistically controlling for years of education, however results should be cautiously interpreted as subsequent analysis which reanalysed ethnic groups matched for education resulted in a reduced effect of ethnicity on cognitive performance (Manly et al, 1998). Indeed, studies which show worse performance by African Caribbeans than whites in the UK, acknowledge that the African Caribbean sample were more likely to have fewer years of full time education than the white group (Richards et al, 2000; Stewart et al, 2002). Fratiglioni et al (1993) point out variable performance among

countries might be due to different educational levels or different curricula at the same schooling levels in different countries.

2.3.3 ENVIRONMENTAL FACTORS

Nazroo (2004) notes that different cultures and ethnic groups may have different levels of risk for different diseases associated with dementia. For example, in the UK, African Caribbeans have a higher risk of stroke and coronary heart disease than whites. In the US, environmental factors such as stroke, hypertension, diabetes and smoking may also occur at higher levels in African American populations and as such may account for higher levels of vascular dementia in these populations (Gorelick, Freels, Harris et al, 1994; Snowdon, 1997). Other factors may include lifestyle behaviour such as diet, alcohol consumption, sedentary lifestyles and environmental exposure to toxins (eg, air pollution, harmful metals, and pesticides). In addition to these, Nazroo (2004) also suggests a possible role for migration in which experiences prior to and related to migration may have an impact on health and lead to ethnic inequalities in ethnic minorities in later life.

2.4 CULTURAL INFLUENCES ON COGNITIVE ABILITIES

Cultural factors shape intellectual and cognitive abilities and this has been recognised for many decades. Irvine (1984, as cited in Irvine and Berry, 1988) questions whether cross-cultural differences lie in both the instruments used to measure intelligence/cognitive abilities and in the concept or dimension itself being measured. In relating culture and intelligence, two extreme positions may be adopted which views intelligence either as a concept which operates as a function of culture or intelligence as equal regardless of culture, see Figure 2.1. These extreme positions are represented on one pole by Berry's (1974, as cited in Irvine and Berry, 1988))

This extreme constancy position however has its critics. An area that has attracted considerable research is Piaget's theory of cognitive development which has long been regarded as universal but subsequently challenged by findings from cross-cultural research. Dasen and Heron (1981, p296) reported "a rather odd but consistent finding, that in some populations a proportion of the children and adults do not seem to reach the last sub-stage of the concrete operational stage, which constitutes an important limitation to the universalist position." This finding was evidenced by Greenfield's (1966) classic study of the Wolof of West Africa in which she performed conservation experiments with beakers of water. When subjects responded that changing water levels were suggestive of changing *amounts* of water, they reasoned it was because "You poured it". Greenfield attributed this assertion to a magic-fixation among the Wolof, a view that the experimenter had performed magic to change the amount of water in the beakers. This assertion was later challenged by Irvine (1978) who revisited the Wolof. Having received similar responses of 'You poured it' in response to the water beaker experiment, she invited further explanation and showed that the Wolof were indeed capable of conservation and discounted Greenfield's assertion of magical thinking suggesting instead that Greenfield's explanations were the result of an ignorance of the 'cultural conventions governing the organization of talk'. Greenfield's defence was that Irvine had obtained her results by changing the original experimental context and as such had invalidated the clinical interview.

Irvine (1978, p309) concludes, "formal experimental equivalence of operations is no guarantee that different cultural groups will interpret the experimental stimuli in the same way or that they will be motivated by the same concerns...The results of cross-cultural experiments are therefore suspect, since the

performance elicited by these tests are not comparable manifestations of subjects' cognitive abilities." This challenge is highlighted by Richard and Abas (1999) who also refer to factors that are more subtle and as such may be difficult to quantify, equate or eliminate. Serpell (1976) has long studied culture and intelligence and notes:

Cultures vary in their readiness with which they will display their intellectual skills to strangers and in their familiarity with the conventions of information elicitation outside the context of practical activities. If the assessment of cognitive function is to be undertaken in a cross-cultural setting, test items should have comparable meaning, familiarity and salience across cultures (p 107).

Another example of the need to acknowledge the underlying role of cultural factors in cognitive processing can be seen in Scribner's (1974) work on clustering in free recall among the Kpelle in Africa. Since environmental influences would dictate perceptions of and responses to stimuli, Scribner suggested that the clustering effect would be eliminated if there was no associative grouping among objects. As such, objects that could be clustered among Euramericans may not necessarily be grouped by the Kpelle. After observing the Kpelle community, Scribner assembled an object list that was culture consonant for the Kpelle and subsequent clustering in responses confirmed this. A lack of clustering would have posed a dilemma as to the cause; did a lack of clustering indicate a lack of clustering strategies among the Kpelle or a lack of clustering potential among items? Irvine and Berry (1988) surmise that this is the task left to psychometric or Piagetian task users- how to account for inadequate performance. They continue:

“Central to our argument is the proposition that Spearman’s law of positive correlation among all [cognitive] tasks has to be reconciled with Ferguson’s law of cultural differentiation. Ferguson’s law predicts differences in human performance that are functions of ecological press to learn skills and strategies of adaptation. We consider the definition of ability to be incomplete without accounting for cultural and biological differences...” (pg xiv)

The law of cultural differentiation regards skills as adaptive functions, thus changes in ecology may cultivate or render certain skills superfluous. Irvine and Berry (1998) illustrate one such example suggesting that the introduction of calculators in schools will suppress the development of computational strategies and it seems a given consequence that children from third world countries will soon show ‘superior’ paper and pencil computational skills when compared to Euramericans.

Other authors also address the issue of attitudes to time and time orientation and how they may affect performance on tests that are timed or contingent on processing speed. Byrd, Touradji, Tang et al (2004) suggests that in cultures whose perceptions of time are less rushed, as is found in African American and Hispanic cultures, the approach to task performance may be one that favours accuracy at the expense of speed. On timed tests therefore, interpretation may be contingent on a determination of whether lower time scores are the result of ability or cognitive style.

A critical component of any discussion of influences on cognitive performance is how societies view ageing and to what extent they may label the symptoms of dementia as abnormal or pathological or normal and expected during old age. Richards and Abas (1999) note that the cultural expectations of the elderly

vary across cultures. In societies where the elderly routinely take on the tasks of younger adults such as domestic activities and financial management, an older person with such difficulty would be easier to recognise and be labelled as impaired. However in other societies where the elderly assume less functional responsibility, changes in performance may be harder to detect and may not be recognised as a form of impairment. For example, Cohen (1995) states that among the people of Benares in India, relatives are more likely to identify personality changes, rather than memory loss, as a signs of senile decline.

The works of Luria (1976) and Vygotsky (1962) also suggest a significant role for culture and by extension the impact of development of society on the cognitive skills of its people. Words and language may be regarded as the tools needed for the cognitive skills of generalization and abstraction (which would be required for a task like semantic fluency). Language, however, and the role it plays in everyday life and functioning is a product of, and determined by, sociohistorical development. They suggest therefore, that cognitive styles are a function of the mode of production in a society and there would exist differences in cognitive styles in less developed or developing as compared to modern, industrial or developed societies.

An example of this is illustrated in Luria's research with the Uzbek people in pre-industrialized Russian society in the 1930s which revealed that different groups of people at different levels of modernization performed cognitive tasks in different ways. Groups not exposed to formal education were unable to form categories and instead grouped objects based on their real world functions. For example, when shown pictures of hammer, saw, log, hatchet and asked to group objects together, a common reply would be that they all go together, that all were needed. When prompted that the hatchet, saw and hammer would go together because they were

tools, the reply was: “yes, but even if we have tools, we still need wood-otherwise we can’t build anything” (Luria, 1976, pg56). Concrete or situational thinking was used to form groups and when more abstract categories were suggested, eg, ‘tools’, they were rejected on the basis of not reflecting the real relationship between objects. Those who did acknowledge the grouping based on an abstract category did so reluctantly but maintained that that form of group: ‘tools’, was not important. In these illiterate groups, words were not interpreted as symbols for abstract categories; they were interpreted solely within practical realms. Classification based on practical experience was valued whereas classification based on abstract terms was deemed inconsequential.

In comparison, other persons who had received some schooling were more readily capable of performing abstract categorizations leading Luria to conclude that the processes that enable abstract thought are not invariably present but are a product of socioeconomic and cultural development. He eloquently states: “Education, which radically alters the nature of cognitive activity greatly facilitates the transition from practical to theoretical operations. Once people acquire education, they make increasingly greater use of categorization to express ideas that objectively reflect reality” (pg 99).

It can be surmised therefore that populations in societies that have a developing status (like the Caribbean) or are in a greater state of flux may exhibit variations in their ability to utilise abstraction or perform taxonomic thinking which may be reflected in performance on tasks that measure this skill.

2.5 FACTORS INFLUENCING MEASUREMENT IN NEUROPSYCHOLOGICAL ASSESSMENT OF DEMENTIA

In addition to individual and environmental factors, cognitive performance may also be influenced by measurement related factors (Graves, Larson, White, Teng & Homma, 1994). Cognitive impairment is critical to a diagnosis of dementia and in establishing a differential diagnosis of dementia. Niederehe & Oxman, (1994) point out that even in the presence of known brain lesions, a person who does not exhibit any cognitive impairment would not be considered for a diagnosis of dementia. Indeed, cognitive impairment is specified in both of the most commonly used diagnostic criteria for dementia: the DSM-IV TR and NINCDS-ADRDA. Specifically, memory impairment as well as impairment in one other cognitive function is indicated. Assessing cognitive impairment is thus critical in establishing the validity of a diagnosis of AD. The biggest challenge lies in extrapolating the cross-sectional assessment of cognitive functioning to a real-life indication of whether a person is experiencing a pathological decline ((Niederehe & Oxman, 1994).

As discussed in chapter one, assessment can be instrumental in the diagnosis or identification of persons with dementing illnesses and the discrimination between the different types of illness, in the measurement of change in performance and in the analysis of levels of functioning in order to facilitate decisions about management or treatment (Miller and Morris, 1993). Furthermore, Miller (2004) recognised two sets of factors that may influence assessment of persons: individual factors that pose a challenge to testing and limitations of the tests and instruments

themselves. Thus, before an assessment is carried out, consideration must be given to these factors.

2.4.1 INDIVIDUAL FACTORS

2.4.1.1 Sensory deficits

Persons suspected of AD are usually older or beyond retirement age and as such may be vulnerable to a number of other disorders or conditions that have implications for psychological testing (Miller, 2004). One of the most common handicaps affecting older persons' test performance is poor vision and hearing. Indeed, Lindenberger and Baltes (1994) found that among the elderly, visual and auditory skills account for 49% of total variance and 93% of the age-related variance in cognitive performance and concluded that performance and sensory acuity were indicative of brain capabilities. Crawford, Venneri and O'Carroll (1998) offer a further note of caution in interpreting scores suggesting that sensory deficit can place a further demand on processing resulting in lower scores.

2.4.1.2 Illness

Chronic illnesses like cardiovascular disease and diabetes may also affect cognitive performance (Worrall & Moulton, 1993). Mental confusion arising from relatively common chest infection and urinary tract infections or as a side effect of medication and drug interaction can lead to poor test performance that is not attributable to dementia (Miller, 2004). The presence of depression or pseudodementia and its implications has already been addressed (see section 1.4.5.7). These co-existing physical and psychological impairments can mask impairment due to cognitive decline. As previously discussed, these impairments

may be more prevalent in developing countries and as such prove a greater challenger for differential diagnosis (Chandra et al, 1994).

2.4.1.3 Premorbid ability

A person's premorbid intellectual ability may also complicate testing scores (Bucks and Loewenstein, 1999) as a person with high levels of ability may still perform within the normal range during early stages and escape detection while someone with below average ability may yield test results that are difficult to establish as typical or reflective of impairment (Miller, 2004). Crawford, Venneri and O'Carroll (1998) advised interpreting scores not only by using standardised norms but also by taking the individual's premorbid level of functioning into consideration.

2.4.1.4 Education

Educational attainment may also have a significant impact on test scores. Ardila, Roselli and Puente (1994) compared brain damaged and non brain damaged patients and found that non brain damaged illiterate patients performed very similarly to brain damaged literate patients, thus concluding that illiteracy can appear like brain damage. As previously discussed, higher education is thought to act as a cognitive reserve; delaying onset and compensating for neuropathological changes in older age (Lezak, 2004, McCullagh et al, 2001).

2.4.2 FACTORS RELATING TO INSTRUMENTS

Evans, Wilson and Emslie (1996) advise that the central processes involved in cognitive assessment include the correct test selection, administration and interpretation of standardized tests. They give guidelines for the standardisation of a test. These points are summarised below:

1. Establishing a procedure for administration- Administration must be consistent in order to enable comparison of test subject with population
2. Collecting norms from a representative population- Norms are the average scores of the reference group. In order to interpret test scores, they must be compared with the norms, Miller (2004) notes that many tests used in the assessment of Alzheimer's disease lack normative data for older age ranges or beyond age 80 but he also acknowledges that this may not be a critical problem for many of the screening instruments that have been developed specifically for dementia.
3. Developing a scoring procedure- Raw scores may need to be standardised in order to facilitate comparison
4. Determining the reliability of a test- Tests should have good inter-rater, test-retest and parallel-form reliability. Reliability is critical for ascertaining whether differences in scores are due to measurement error or changes in functioning (Crawford, Venneri and O'Carroll, 1998). Reliability is also dependent on having appropriate normative data.
5. Determining the validity of test- Tests should exhibit sound construct, content, criterion and ecological validity.

Where selecting the appropriate test is concerned, Evans, Wilson and Emslie (1996) advise that:

the right test for an assessment will be the one that adequately captures the particular cognitive function or functions you are aiming to assess (i.e. is valid and reliable), and the test will have normative data from a reference group suitable for comparison with the person being assessed. It should be suitable for the level of competence, physical status and cultural background of the subject (pg 154).

Miller (2004) noted a specific challenge in finding tests that can measure change in severely impaired patients. He stated that while low scores on cognitive tests may be useful in identifying dementia, assessing change or deterioration is much more challenging and that this remains a major problem in assessment. Crawford, Venneri and O'Carroll (1998) provided guidelines for monitoring change, suggesting information be gathered from test-retest studies, including correlations, means and standard deviations from which a regression equation can be constructed to predict scores. Interpretation of test scores is a critical component of test usage and it is recommended that scores be interpreted within a context of performance on a range of tests and that no one test result is used to support or rule out a diagnosis (Evans, Wilson and Emslie, 1996).

2.6 CROSS-CULTURAL NEUROPSYCHOLOGICAL ASSESSMENT OF DEMENTIA

The need for appropriate cross-cultural neuropsychological assessment has been instigated by two factors: the research trend towards epidemiological studies and comparisons across countries and also as a result of demographic changes within countries resulting in increased ethnic diversity (Mungas, 2000; Wolfe, 2002). Historically, test performance in cross-cultural groups has been interpreted using norms derived from the country that the test was developed in. However, this procedure has proven fallible given the differential impact of factors (such as education) on test scores. Irvine and Berry, (1988) comment:

The evidence from 20 years of sustained research into the study of test behaviour across cultures is conclusive. The abilities of mankind may be captured in Western tests, but they are not fully expressed in them, nor are

the causes of their growth and expression apparent in the use of groups to account for some of the variation in test scores. By far the largest source of variation that can be attributed to performance within groups is between subjects. The most critical between-group source is the amount of exposure to western education, a finding that is so widespread that it needs no separate reference (p 29).

Wolfe (2000) suggests that cross-cultural advances in neuropsychology may involve three approaches:

1. Modification of existing tests- tests are translated and adapted for different linguistic and socio-cultural groups
2. *De novo* test construction- creation of new tests specifically designed for use with cultural groups that take into consideration item selection and analysis, normative studies, reliability and validity analyses.
3. Development of norms- that also takes into consideration age and education for different ethnic groups

Many neuropsychological tests have been translated for use among linguistically diverse groups; for example, the MMSE has been translated into over 55 languages. Also, a number of instruments have been devised specifically for cross-cultural use. These include the Cognitive Abilities Screening Instrument (CASI) (Teng et al, 1994); Cross Cultural Cognitive Exam (CCCE) (Glosser et al, 1993) and the Community Screening Interview for Dementia (CSI 'D'), (Hall, Gao, Emsley et al, 2000).

Cross-cultural normative data have also been developed for some of the most frequent and popularly used instruments in dementia assessment (e.g. the MMSE in Brazil (Castro-Costa, Fuzikawa, Ochoa et al, 2008). These norms provide an

appropriate frame of reference for interpreting test scores in specific cultural populations. The popularity and accessibility as well as the established use of many screening and measurement instruments in dementia assessment in cross-cultural settings provides a convincing argument for the third approach in which normative data is developed while taking into consideration influential demographic variables. This dissertation deals with this last approach to cross-cultural assessment specifically as it relates to Caribbean populations.

2.6 DESCRIPTION OF CARIBBEAN POPULATION OF TRINIDAD AND TOBAGO

African-Caribbeans comprise the second largest ethnic minority in the United Kingdom. While there is a well-established history of a Caribbean presence in the UK prior to World War I, it was not until post World War II that there was an influx of immigrants to the UK from the Caribbean. Many of these Caribbean immigrants are now reaching the age where diseases like dementia pose a greater risk. A few UK studies who have included African-Caribbeans in their samples have acknowledged a consistent pattern of lower performance when compared to white British persons. Reasons for this disparity have been largely speculative. There is a paucity of information on the cognitive performance of native Caribbeans. Few if any studies exist that examine the performance on Caribbean populations on neuropsychological measures.

The Caribbean sample for this study will be drawn from Trinidad and Tobago: one of the largest English speaking countries that belong to the Caribbean region. It has a population of approximately 1.31 million persons who are largely the descendants of African slaves and indentured labourers. Trinidad and Tobago

experienced 160 years of colonisation under British rule until it achieved independence in 1962 and became a republic state in 1976. Its existing legal, political and educational systems are all modelled after British systems.

CHAPTER 3

AIMS AND OBJECTIVES

3.0 INTRODUCTION

The preceding background review outlines a case for cross-cultural assessment that is appropriate for the target population and which takes into consideration the demographic characteristics that exert an influence on neuropsychological performance. The validity of assessment among diverse populations is contingent on such practice.

Caribbean populations like many other developing countries are facing unprecedented ageing. A greater demand will be placed on health care resources to tailor to the needs of the growing elderly populations. At present, there exists no standard protocol for the screening and assessment of dementia in the Caribbean. Given the prohibitive costs of brain imaging and biomarker analyses, neuropsychological assessment will remain a critical tool for facilitating accurate and valid screening and diagnosis. The assessment will need to be valid, easily available and suitable for use with Caribbean persons. Furthermore, sites in developing countries are increasingly being of interest as possible centres for large trials of new treatments for dementia.

The main aim of this dissertation is to standardise a number of instruments for the assessment of dementia for use with Caribbean populations. The first instrument is the most popular screening instrument for cognitive impairment worldwide:

- The Mini Mental State Examination (MMSE)

The MMSE is usually the first screening instrument used in assessment and an abnormal score is usually an indicator for further testing. It is currently widely used in the Caribbean but its use has not been standardised or validated. The MMSE can be used in conjunction with a short neuropsychological battery which assesses areas of cognitive functioning that are known to be impaired in dementia including: memory, language, attention, executive functioning and abstract reasoning. This battery will consist of the following popularly used and widely available neuropsychological tests:

- Digit span (forward and backward)
- Digit Cancellation
- Logical Memory (immediate and delayed)
- Verbal Fluency: Semantic- Animal, Cities, Fruits

Phonemic- P, L, F

- Raven's Coloured Progressive Matrices

The use of these instruments will allow a more detailed evaluation that can result in the profiling of patients in terms of specific patterns of cognitive strengths and weakness which can aid assessment and differential diagnosis of dementia.

As clinical drug trials expand globally to include more developing countries, the validity of the use of neuropsychological instruments used in such trials becomes more significant. This dissertation will also include in its analysis the gold standard instrument used for assessing cognitive function in clinical anti-dementia drug trials:

- The Alzheimer's Disease Assessment Scale- cognitive section

The ADAS-cog is used to assess treatment efficacy and to monitor change in performance in dementia patients. While the ADAS-cog is thought to be culture free, the accuracy of that perception has not been tested with Caribbean populations.

Normative data will be collected from a Caribbean population from Trinidad and Tobago and compared with a British sample for each instrument. The effects of socio-demographic variables such as age, gender, education and ethnicity will be explored. Following this, a correction formula will be determined to adjust for the effects of each variable on performance scores which can be used to make adjustments to individual scores. Cut-off scores indicating limits for abnormal performance will be determined for each instrument and validated for the two main screening instruments using a clinical population.

The objectives of this study are to:

- 1. COLLECT NORMATIVE DATA TO DETERMINE THE EFFECTS OF AGE, GENDER, EDUCATION AND ETHNICITY ON TEST PERFORMANCE ON A NUMBER OF NEUROPSYCHOLOGICAL INSTRUMENTS**
- 2. GENERATE A CORRECTION FORMULA AND CUT-SCORES BASED ON STANDARDISED DATA FOR EACH INSTRUMENT**
- 3. VALIDATE THE DERIVED CUT-OFF SCORES FOR THE MMSE AND ADAS-COG USING A COMMUNITY AND CLINICAL SAMPLE FROM TRINIDAD AND TOBAGO AND BRITAIN**

Chapter 4 will focus on the two main screening instruments- the MMSE and the ADAS-cog. Chapter 5 will address the tests of memory and attention- digit span,

digit cancellation and Logical Memory and Chapter 6 will focus on the tests of executive functioning and abstract reasoning- verbal fluency and the Raven's Coloured Progressive Matrices. Each chapter will address objectives 1 and 2 as outlined above while Chapter 4 will also address objective 3.

CHAPTER 4

SCREENING TESTS FOR DEMENTIA

4.0 SCREENING TESTS FOR DEMENTIA

It is thought that dementia is under detected and this may be addressed by the use of more frequent and more accurate screening (Glosser et al, 1985). Screening tests for dementia are critical in assessment and diagnosis and assist the practitioner in detecting signs of cognitive decline that may warrant further evaluation. Screening tests may involve direct cognitive tests or functional assessments using patients or informants. A number of cognitive tests have emerged that are widely and popularly used for this purpose. The Mini Mental State Examination (MMSE) is the most frequently used cognitive screening instrument and the Alzheimer's Disease Assessment Scale- cognitive section is the most frequently used cognitive measure in global clinical trials. This chapter addresses the effects of demographic variables on performance, determines cut-off scores for normal performance based on standardised data and finally assesses the validity of the proposed cut-off scores for these two instruments.

4.1 THE MINI MENTAL STATE EXAMINATION (MMSE)

In 1975, Folstein, Folstein and McHugh developed the Mini Mental State Examination (MMSE) as a brief screen for cognitive functioning. Previous formal testing of elderly psychiatric patients (e.g. using the Wechsler Adult Intelligence Scale (Wechsler, 1939), Wechsler Memory Scale (Wechsler, 1945), Clinical tests of the Sensorium (Withers and Hinton, 1971)) was a lengthy process and regarded as too time consuming. The process was also criticised for being excessively steeped in

theory at the expense of practical utility (Folstein et al, 1975; Folstein, Anthony, Parhad et al, 1985). The MMSE represented a practical solution to these limitations and has irrevocably impacted the assessment of cognitive impairment since. Brayne (1998) remarked that popularity and the impact of the MMSE may be based on its appearance at a time when clinically oriented measurement rather than theoretically or research oriented measurement was gaining stride. The MMSE is now regarded as the most widely used cognitive screening instrument globally and has been translated in over 50 different languages (Boustani, Peterson, Hansen et al, 2003; Tombaugh and McIntyre, 1992).

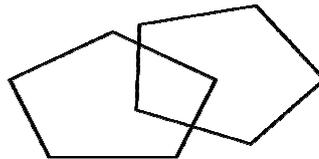
The MMSE consists of 11 items comprising 21 questions which assess different areas of functioning including orientation for time and place, attention and calculation, memory, language, visual and construction skills (Cossa, Sala, Musicco et al, 1997; Lezak, 2004). Examples of the items are listed in Table 4.1. The MMSE is an untimed test and administration usually takes 5-10 minutes (Folstein et al, 1975). Scores on the MMSE range from 0 to a maximum of 30 with the original study recommending a cut-off of 24, and scores below this indicating impairment (Folstein et al, 1975). However, the impact of education and culture on performance has resulted in a variety of cut-off scores being recommended for use. These will be discussed in more detail in later sections. The cut off score may also be contingent on the aim or priorities of testing. Kukull et al (1994) suggest the traditional cut-off score of 24 in instances that require few false positives (which warrant the need for further evaluation) and the higher cut-off score of 27 in cases in which obtaining few false negatives is a priority.

Sensitivity on the MMSE ranges from 61% to 87% while specificity ranges from 64% to 85% (Dick et al, 1984; Galasko et al, 1990; Anthony et al, 1982,

Table 4.0

Description of items used in the Mini Mental State Examination

Item	Points	Example
Orientation	10	1. What is the year we are in? 2. What season is it? 3. What is today's date? 4. What day of the week is it today? 5. What month are we in/ 6. What county are we in? 7. What country are we in? 8. What town are we in? 9. Can you tell me the name of this place? 10. What floor of the building are we on?
Registration	3	11. Immediate Recall of three objects "lemon, key, ball"
Attention and Calculation	5	12. Serial 7s backwards 13. Spell 'world' backwards
Recall	3	14. Delayed Recall of three objects "lemon, key, ball"
Naming	2	15. Can you tell me what this is? (wristwatch) 16. Can you tell me what this is? (pencil)
Repetition	1	17. "No ifs, ands or buts"
3-Stage Command	3	18. Take a sheet of paper in right hand, fold in half, and place on floor
Reacting	1	19. Perform action printed on paper "CLOSE YOUR EYES"
Writing	1	20. Write spontaneous sentence
Copying	1	21. Copy intersecting pentagons



Mazzoni et al, 1992; Tombaugh et al, 1996) with figures depending on the type and severity of dementia being assessed. Tierney et al (2000) studied a group of persons who later developed dementia over a two year period and found that MMSE scores at baseline, when using the traditional cut-off of 23 or less resulted in low sensitivity of 21% and high specificity of 98%. Rates may also depend on demographic variables such as education. Using a highly educated group (>16 years of education)

and the traditional cut off score of 23 and less, O'Bryant et al (2008) found sensitivity and specificity rates of 66% and 99% respectively. The sensitivity was increased (sensitivity = 89% and specificity = 91%) when a higher cut-off score of 27 when used.

Kochhann, Camozzato, Godinho et al, (2008) examined the MMSE performance of patients who had been referred to a geriatric clinic for the first time on the basis of cognitive complaints. Of these, only 38% of persons had MMSE scores which fell below suggested cut off values. No significant association was found between cognitive complaint and MMSE performance emphasizing the need for cognitive screening to detect clinically significant cognitive impairment.

In addition to screening for cognitive impairment, the MMSE can also be used to assess cognitive performance, estimate severity of impairment, monitor changes in cognitive performance over time and in response to treatment (Crum et al, 1993). Tombaugh and McIntyre (1992) and Folstein et al (2001) both provide suggested ranges to classify severity of cognitive impairment. These are illustrated in Figure 4.1 below.

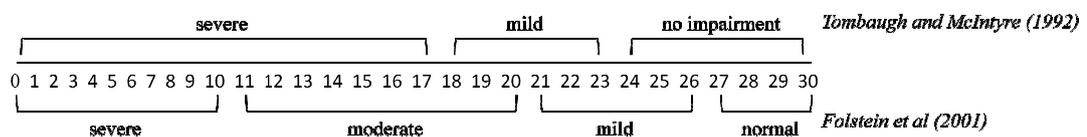


Figure 4.1 Suggested ranges for classifying severity of cognitive impairment using MMSE scores

4.1.1 ADMINISTRATION OF THE MMSE

Variations in the administration and scoring of items on the MMSE exist widely (Tombaugh and McIntyre, 1992). In the original publication, questions on orientation for place referred to a hospital setting. Subsequent revisions have modified these to suit a community setting.

The original instructions also gave the examiner the choice of any three words to use in the registration task. Various sets of words are now used for this registration/recall item including: 'honesty, brown, shirt', 'tree, clock, boat', 'apple, table, penny' 'rose, ball, key' and 'ball, flag, shirt' (Lopez et al, 2005; Brayne, 1998; Cullum et al, 1993). In South Asian groups, Rait, Morley, Lambat & Burns (1997) suggest the use of the words: 'car, rupee, carrot'. Examples of items used for repetition and spelling backwards may also vary from the original administration of 'No ifs, ands, or buts' and WORLD respectively. Caffarra, Dieci, Copelli and Vezzadini (2002) note the use of different variants of the spelling backwards and repetition tasks in Italy, citing the use of 'mondo' (world) and 'tigre contro tigre' (tiger against tiger) as well as the existence of 'carne' (meat) and 'sopra la panca la capra campa' (above the bench the goat gets by). The phrase 'If no reason there is no consequence' has been used in Chinese populations (Chiu et al, 1994) while the phrase 'Not this one, not that one, nothing at all' has been used with Gujrati populations (Rait et al, 1997).

The administration and scoring of items under attention and concentration (the serial sevens and the spelling backwards) have also attracted considerable scrutiny. The original instructions (Folstein et al, 1975) suggest that the serial sevens task should be administered and if the patient refuses or is unable to perform, they are then given the spelling backwards task. This variant of the administration is used

in some studies (Klein et al, 1985). However, Davey and Jamieson (2004) report considerable inconsistencies in the use of either or both items by practitioners as some use the items interchangeably, use only the serial seven subtraction, use only the world backwards (Morris et al, 1989) or use the higher of the two scores (Holzer et al, 1984; Escobar et al, 1986).

This issue is of clinical and psychometric significance as comparisons of performance on the two items reveal the serial sevens to be a significantly harder task than the spelling backwards, a finding which Folstein himself acknowledges (Folstein, 1998). This finding has been described qualitatively (Anthony et al 1982) but has also been substantiated quantitatively (Watkins, Gouvier, Gallon and Barkemeyer, 1989). Ganguli et al (1990) investigated performance on both items and found 1) a lower mean score for serial sevens than spelling world backwards, 2) more persons gained the maximum score (5/5) on spelling backwards than on serial sevens, 3) 25% of persons scored 0/5 on serial sevens and 5/5 on world backwards while no one scored 0/0 on spelling backwards and 5/5 on serial sevens and 4) more persons showed better performance on spelling backwards vs. serial sevens than better performance on serial sevens vs. spelling backwards.

Differences in administration of serial sevens and spelling backwards may also yield different overall MMSE scores as found in a study by Lopez et al, (2005). The authors examined MMSE scores in a large sample of elderly patients. The administration variant involved administering the serial sevens item and if the patient refused or couldn't complete the task, then he or she was asked to spell WORLD backwards. Results showed a difference in overall means of 21.27 (sd=6.21) for the group administered the serial sevens and 20.86 (sd=6.45) for the performing the spelling backwards. The authors however did not test the significance level of the

difference in the means. Davey and Jamieson (2004) emphasise caution in the comparison of scores and many researchers advocate for the specification of the attention and concentration task which has been used or which item has contributed to the MMSE total score (Ganguli et al, 1990; Watkins et al, 1989).

The issue is further complicated by the finding that some authors suggest that both tasks are too difficult and pose challenges in populations with low literacy or wide ranges of educational attainment and as such, they replace the task entirely, substituting a simpler subtraction task such as subtracting threes repeatedly from 20 (Parker et al, 2007). Rait et al (2000) also suggested cultural modifications of the MMSE for use in African-Caribbean populations in the UK which included replacing spelling backwards with saying the days of the week backwards and replacing serial sevens subtraction with counting backwards from 10 to 1.

Brayne (1998) in a commentary on the MMSE suggests that such differences in administration and scoring as seen in the recall and attention and concentration items do not impact performance. However, she did cite the work of Cullum et al (1993) as an exception to this. These authors used two different combinations of three word recall: 'rose, ball, key' and 'brown, tulip, honesty' and found great differences in scores with the percentage of persons recalling none of the words equal to 14% and 60% respectively. They suggest the option of letting examiners choose words changes the standardisation of the test and comparability of the results. This view is also endorsed by Caffarra et al (2003) who further caution against the use of normative data for items that are qualitatively different.

The difficulty of other items in the MMSE may also vary. Using established criteria for item difficulty, Lopez et al (2005) regarded any item as too easy if more

than 80% of persons got this item correct. In their assessment of an elderly American sample, they found the following MMSE items too easy: What place is this?, What city is this?, What state is this?, immediate recall for 'ball, flag, tree', naming of watch and pencil, 3-stage command and reading and performing of 'close your eyes'. There is no comparison in the literature of whether these findings apply to different ethnicities or countries.

4.1.2 RELIABILITY AND VALIDITY

Baseline and repeat scores over 24 hours and 28 days later show correlations of 0.9 in both normal and clinical samples illustrating good test-retest reliability (Folstein et al, 1975; Tombaugh and McIntyre, 1992). After a two year period, correlation between scores falls slightly to 0.8 in normal persons (Hopp et al, 1997).

High inter-rater reliability has been reported at 0.8 (Folstein et al, 1975) although lower rates have been reported due in part to differences in administration and scoring criteria as previously described (Bowie et al, 1999; Davey and Jamieson, 2004).

When using a cut-score of below 24 to indicate impairment, the MMSE has shown 87% sensitivity and 82% specificity in detecting dementia on medical wards (Anthony et al, 1982). While higher cut-off scores may increase sensitivity for less severe or mild cases of dementia especially in persons with higher education, Ridha and Rossor (2005) caution that higher cut-off scores practice may increase the rate of false positive screens in older uneducated groups and among ethnic minorities.

Different approaches have been taken to counter this limitation and improve the validity of the MMSE. Xu et al, (2003) propose cultural modifications. However a drawback of this approach involves comparison across items for which equivalence

has not been established. Crum et al (1993) suggest the generation of population based normative data which provide different cut-off scores and are stratified for age and education.

4.1.3 MMSE AND AGE

MMSE scores have been found to decrease with increasing age, especially after age 65 (Crum et al, 1993) with persons from older age groups (55 to 74 years) having lower scores than younger adults (35 to 54 years), (George, Landerman, Blazer et al, 1991). Some authors suggest different median scores for older age groups. For example, population norms derived from a large community sample in the United States suggested a median MMSE score of 29 for persons aged 18-24 and 25 for those over 80 years of age (Crum et al, 1993). The authors also acknowledged the role of education and suggested that median scores would vary not only with age but also as a function of education. For instance a median score of 20 would apply to an 85year old with 0 to 4 years of schooling whereas the median of 28 would apply to an 85 year old with a college education of higher.

4.1.4 MMSE AND EDUCATION

Although widely used in many countries, the MMSE has been criticized for its educational bias which may render it unsuitable for use in many underdeveloped and developing countries since formal education may be limited for large population groups (de Brito-Marques & Cabral-Filho, 2005). Jones and Gallo (2002) note that persons with low education were more likely to make errors on naming the season, serial sevens, spelling WORLD backwards, repetition, writing, and copying intersecting pentagons. Ganguli et al (1990) and Escobar et al (1986) suggest that low educated persons may find the serial sevens task harder than the spelling backwards.

de Brito-Marques & Cabral-Filho (2005) found a differential effect of age on MMSE scores according to education levels in a sample of Brazilians. Among illiterate persons, the correlation between age and scores was insignificant while among persons with more than 8 years of education, there was a significant negative correlation with increasing age associated with lower scores. One explanation put forward by the authors is that education confers a protection against reduction in cognitive functioning while low educated persons especially when evaluated by tests which contain 'sophisticated mathematical language' as in the serial seven task could display signs of aging even when young.

Kukull et al (1994) recommend a higher cut-off score of 27 in well educated persons. Median scores were also suggested for various levels of education; 29 for those with more than 9 years of schooling, 26 for those with 5 to 8 years and 22 for those with fewer than 5 years of schooling (Crum et al, 1993).

4.1.5 MMSE AND GENDER

Gender does not appear to have a significant impact on MMSE scores (Folstein et al, 1975; Tombaugh and McIntyre, 1992) and generally few gender differences are reported in the literature. Some exceptions are Huppert et al (2005) who report a modest effect of gender with women gaining lower MMSE scores especially in eldest age groups. In a study of Canadian elderly with an average of 10 years of education, Tombaugh et al (1996) found women had higher scores than men. Roselli, Ardila, Rosas et al (2000) studied Columbian elders with more than four years of education and found no gender differences. However in a low educated group (fewer than 3 years), males performed better than females.

Roselli, Ardila, Araujo (2007) examined performance in Spanish speaking Hispanics on the attention and concentration items (serial sevens and spelling

backwards) and found women had lower scores on the serial sevens item and although gender differences were greater in the lower education groups, these differences were not significant. Jones and Gallo (2002) reported women in the United States having more difficulties with serial sevens while men had more difficulties with spelling backwards. It appears gender differences may be mixed and vary with item, culture and education.

4.1.6 MMSE AND ETHNICITY

Parker and Philp (2004) note that it is often likely that screening tests which are sensitive enough to detect impairment may also classify some cases as impaired when they are in fact disease free. Fillenbaum et al (2001) note that this is especially the case for elderly black community residents in the United States in which the MMSE wrongly classified 6% of non-impaired whites, and 42% of non-impaired blacks.

Manly et al (1998) compared MMSE orientation performance among a sample of non-demented black and whites in the United States and also compared performance using a stratified sample matched for education. In both analyses, African Americans had lower scores than whites. However Manly et al reported these differences as not significant. This was due to the conservative level ($p < 0.01$) of significance used by the authors. If a less conservative level were used (e.g. $p < 0.05$), the findings in both analyses ($p = 0.01$ for the entire sample and $p = 0.038$ for the stratified sample) could be interpreted as being significantly different. Escobar et al (1986) observed an effect for ethnicity in both spelling backwards and serial sevens items in which Hispanics performed worse than their Caucasian American counterparts.

In the UK, Stewart et al (2002) examined MMSE scores in 248 adults aged 55-75 years and compared the performance of Caribbean-born African Caribbeans to a Medical Research Council Cognitive Function and Ageing Study (CFAS) sample. Median scores for Caribbean born persons were found to be 25 (IQ= 22-27), two points lower than that obtained for the CFAS sample (median =27, IQ= 25-29). Errors made by African Caribbeans were specific to certain items: naming the season, serial seven subtraction, phrase repetition, 3-stage command, and copying intersecting pentagons (Stewart et al, 2002). In addition, when the conventional cut off score of 23/24 was used, 31% of the African-Caribbean sample fell below this level as compared to 9% of the CFAS sample. A disproportionate number of persons from low education backgrounds had scores below the cut-off level and this was noticeably worse in the African-Caribbean sample. See Figure 4.2 below. The authors note however that in their sample, African-Caribbeans were more likely to have reading difficulties and less likely to have completed statutory education.

Richards et al (2000) also compared cognitive performance in African Caribbean and white elderly in the UK and found lower MMSE scores among African Caribbeans on two occasions of testing (screening interview and clinical interview). Scores on two items: registration and recall however, were not significantly different. The authors conducted a multiple regression which yielded a significant effect of ethnicity on MMSE scores (unadjusted $B=3.4$, $p<0.001$, adjusted $B=2.2$, $p=0.005$).

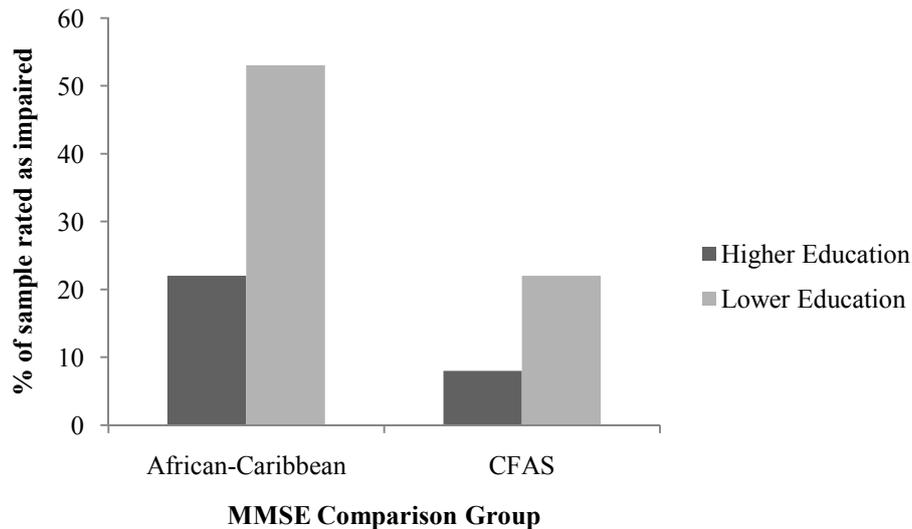


Figure 4.2 Comparison of education in African-Caribbean and CFAS elderly with impaired MMSE scores. Table adapted from Stewart et al. (2002).

In other countries, Dodge, Meguro, Ishii et al (2009) compared MMSE scores of Japanese and Americans and found similar median scores. However, analysis of individual items revealed a difference in the relative difficulty of certain items. The American group performed better on the reacting and copying items whereas the Japanese cohort found the recall and 3-stage command items easier. The authors emphasized the need for careful validation and appropriate cut-off scores for each cohort.

Among AD patients, significant effects for ethnicity have also been observed. Welsh et al (1995) compared black and white AD patients in the United States and found significantly lower performance on the MMSE among blacks after controlling for age, education, disease severity and activities of daily living. They attributed the disparity in scores to cultural differences and recommended a consideration of cultural differences in addition to age and education when interpreting performance among elderly black patients. The black patient group was older, had fewer years of education and more severe impairments in activities of daily living which the authors

controlled for statistically. However they also state that statistically adjusting for differences in education may not adequately capture differences in quality or experiences of education and express the need for normative information for minority ethnic groups.

4.1.7 MMSE AND DEMENTIA

Specific items on the MMSE can distinguish normal persons from mild AD patients as well as distinguish between patients at different stages of AD (Fillenbaum et al, 1994). Among AD patients, MMSE scores have been found to decline over time, with performance especially poor on recall and copying items (Teng, Chui, Schneider, Metzger, 1987). These authors also found scores to be worse in early onset than late-onset patients. Scores on the MMSE have also been found to be associated with macrostructural differences in brain volume in patients with mild to moderate AD (Fjell et al, 2009).

Performance on specific items can also help distinguish between types of dementia: patients with AD perform poorly on recall and orientation to time (Galasko et al, 1990; Jefferson, Cosentino, Ball et al, 2002) while performance on attention, 3-stage command, writing and copying are worse in vascular dementia, Parkinson's disease and DLB (Jefferson et al, 2002; Ala et al, 2002). MMSE scores in FTD may also be higher than in AD and show slower rates of annual decline (Ridha and Rossor, 2005).

4.1.8 STUDY 1

INVESTIGATING THE EFFECTS OF AGE, GENDER, EDUCATION AND ETHNICITY ON PERFORMANCE ON THE MMSE

4.1.8.1 AIM

The objectives of this study are to:

1. Assess the difference in performance on the MMSE based on age, gender, education and ethnicity in a community sample
2. Assess the difference in performance on individual MMSE items based on age, gender, education and ethnicity in a community sample
3. Compare within group performance on serial sevens and spelling backwards
4. Compare differences in total MMSE scores with either serial sevens, spelling backwards or higher of the two scores

4.1.8.2 METHOD

4.1.8.2.1 Participants

In this study, 124 participants (female= 70, male=54) from Trinidad and Tobago (n=62) and England (n=62) were assessed. The overall sample ranged in age from 18 to 89 years (m=47.37, sd=19.20) and years of education ranged from 3 to 30 years (m=14.49, sd=5.55). In the British sample, age ranged from 18 to 87 years (m=47.53, sd=20.22) and years of education ranged from 7 to 25 years (m=14.39, sd=4.32). In the Caribbean sample, age ranged from 19 to 89 years (m=47.21, sd=18.28) and years of education ranged from 3 to 30 years (m=14.58, sd=6.57). All participants were functionally independent, and those with any neurological or psychiatric impairment were excluded. See Tables 4.1a and 4.1b for a breakdown of the sample by ethnicity, gender and education.

4.1.8.2.2 Materials

The Mini Mental State Examination (Folstein et al, 1975) was administered to all participants. A list of the items used is provided in Table 4.0.

Table 4.1a

Breakdown of sample by age, ethnicity and gender

Age /years	Ethnicity			
	British		Caribbean	
	Male	Female	Male	Female
18-30	6	8	7	8
31-40	4	6	4	5
41-50	3	7	5	5
51-60	4	6	4	6
61-70	4	6	5	5
>70	4	4	4	4
Total	25	37	29	33

Table 4.1b

Breakdown of sample by age, ethnicity and education

Age /years		Ethnicity					
		British			Caribbean		
		Level of Education					
		Low	Average	High	Low	Average	High
18-30	Frequency	0	8	6	0	8	7
	Avg(range)	-	14(13-16)	20(17-23)	-	14(13-16)	21(17-25)
31-40	Frequency	0	3	7	0	4	5
	Avg(range)	-	13(13-15)	22(19-25)	-	14(13-16)	24(19-30)
41-50	Frequency	1	5	4	1	6	3
	Avg(range)	9(-)	15(14-16)	19(17-20)	5(-)	15(13-16)	19(17-22)
51-60	Frequency	3	4	3	3	3	4
	Avg(range)	11(9-12)	15(13-16)	21(18-25)	9(6-12)	15(14-16)	23(19-25)
61-70	Frequency	1	6	3	3	5	2
	Avg(range)	9(-)	14(13-16)	17(16-18)	8(5-12)	14(13-16)	18(17-18)
>70	Frequency	8	0	0	8	0	0
	Avg(range)	8(7-10)	-	-	5(3-9)	-	-
Total	Frequency	13	26	23	15	25	22

4.1.8.2.3 Procedure

The MMSE was administered to each participant in the listed order. There was one variation in the administration of the attention and concentration items. In

the Caribbean group, both serial sevens and spelling backwards items were administered and the higher score contributed to the overall MMSE score. In the British group, the serial sevens item was administered. If the participant failed to achieve a maximum score of 5, the spelling backwards item was then administered and the higher of the two scores contributed to the overall MMSE score. The variation in procedure did not affect the overall scores of participants, but it prevented a comparison of spelling backwards scores across the British and Caribbean group.

4.1.8.3 DESIGN AND STATISTICAL ANALYSIS

Univariate ANOVAs were performed on each of the 12 dependent variables (MMSE total and 11 item scores) comparing the effects of age, gender, ethnicity and education on performance.

Age was categorized into 6 levels corresponding to 18-30, 31-40, 41-50, 51-60, 61-70 and >70 years of age. Education was categorized into three levels- low, average and high education. The inclusion for each group was determined as follows: low education- 25th percentile (equivalent to a cut off of 10 years or fewer), above the 25th and below the 75th percentile comprised the average education category (equivalent to 11 to 16 years inclusive) and above the 75th comprised the high education category (equivalent to 17 or more years of education). A Bonferroni correction was employed in the post hoc analyses of the effects of education and age.

Enter and stepwise multiple regression analyses were also performed to determine the contribution of age, gender, education and ethnicity to MMSE total and item scores.

4.1.8.4 RESULTS

4.1.8.4.1 MMSE total

ANOVA Analysis

Mean overall score on the MMSE was 28.17 (sd=2.18) and scores ranged from 16 to 30. The mean performance on all MMSE items is shown in Tables 4.2.

Table 4.2

Mean performance, standard deviations and range for all MMSE items

Item	Mean	Minimum	Maximum	Std. Dev
Orientation	9.28	6	10	0.80
Registration	3.00	3	3	0.00
Serial sevens	4.10	0	5	1.51
Spelling backwards	4.45	0	5	1.19
Recall	2.55	0	3	0.80
Naming	2.00	2	2	0.00
Repetition	0.77	0	1	0.43
3-Stage Command	2.90	2	3	0.31
Reacting	1.00	1	1	0.00
Writing	0.98	0	1	0.13
Copying	0.93	0	1	0.26
MMSE Total Score	28.17	16	30	2.18

Results from the ANOVA analysis showed no significant effects of age, or gender with older participants performing similarly to younger and women performing similarly to men.

However, significant main effects for ethnicity $F(1,77)=29.33$, $p<0.001$) and education $F(2,77)=12.56$, $p<0.001$) were found. Post hoc analysis using a Bonferroni correction showed significant differences between education groups. The low

education group had a significantly lower mean performance ($m=25.93$, $se=.29$) than the average ($m=28.76$, $se=.20$) and high ($m=29.27$, $se=.24$) education groups. The difference between the average and high groups was not significant. The Caribbean group also had a significantly lower mean performance ($m=27.76$, $se=.19$) than the British group ($m=28.77$, $se=0.19$).

There was a significant interaction effect between ethnicity and education. As can be seen in Figure 3.1, whereas both Caribbeans and British persons with average and high education perform similarly, there is a larger disparity between the ethnic groups with low education in which Caribbean persons with low education perform much worse than their British counterparts.

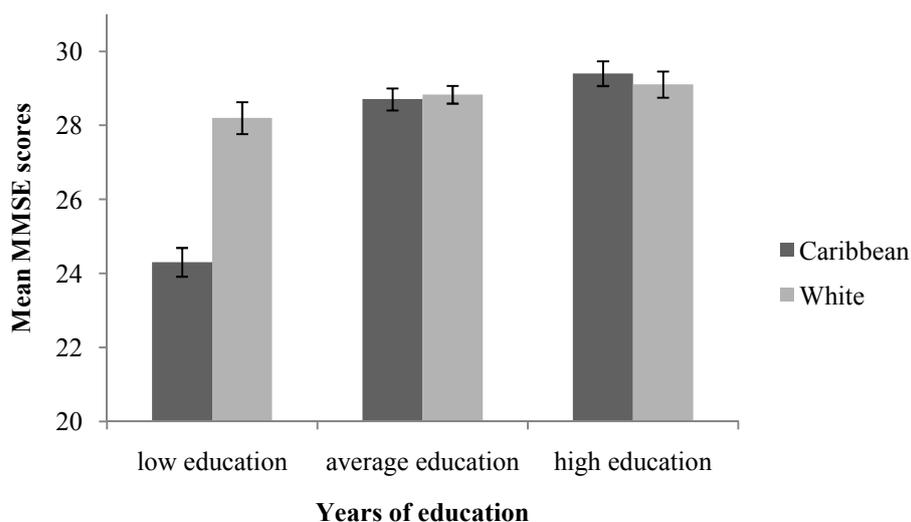


Figure 4.3 Mean scores on MMSE by ethnicity and years of education

Regression Analysis

The correlation between MMSE items are shown in Table 4.3 and the correlation between MMSE items and predictors are shown in Table 4.4. Total

MMSE score was significantly correlated with all other individual items. However, correlation coefficients were not calculated for three items: registration, naming and reacting due to the lack of variability in scores on these items. Total MMSE scores were significantly correlated with age, ethnicity and education but not gender.

Increasing age, fewer years of education and Caribbean ethnicity was associated with lower scores.

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 118)=21.12, p<0.001$). Of the four predictors, age, ethnicity and education made significant contributions to the overall model. The regression analysis was repeated with age, ethnicity and education as the only predictors and a significant model emerged ($F(3, 119)=31.05, p<0.001$) which accounted for 44% ($R^2=.44$), of the variance in performance. Education significantly predicted MMSE scores, $\beta=.49, t(119) = 6.16, p<0.001$ and accounted for 33%, $R^2 = .33$ of the variance in scores,. Ethnicity accounted for a further 9% of the variance, $R^2 = .09, \beta=.30, t(119) = 4.42, p<0.001$ and age contributed to 2% of the variance in scores, $R^2 = .02, \beta=-.16, t(119) = -2.02, p=0.046$.

4.1.8.4.2 Orientation

ANOVA Analysis

As seen in table 3.2, mean performance on orientation was 9.28 (s.d. = .80).

Performance ranged from a minimum of 6 to the maximum of 10.

Table 4.3

Table showing correlations between MMSE items

	Registration	Serial Sevens	Spelling Backwards	Recall	Naming	Repetition	3-Stage Command	Reacting	Writing	Copying	MMSE Total Score
Orientation	§	.19*	.48**	.20*	§	.10	-0.02	§	.45**	.33**	.63**
Registration		§	§	§	§	§	§	§	§	§	§
Serial sevens			.27*	.42**	§	.30**	0.00	§	.18*	.40**	.51**
Spelling backwards				.46**	§	.32**	-0.09	§	.64**	.51**	.73**
Recall					§	.40**	0.12	§	.26**	.41**	.75**
Naming						§	§	§	§	§	§
Repetition							0.14	§	0.08	0.14	.55**
3-Stage Command								§	-0.04	0.01	.201*
Reacting									§	§	§
Writing										.21*	.52*
Copying											.59**

* $p < 0.01$, ** $p < 0.001$, § not computed because 1 variable constant

Table 4.4

Table showing correlations between MMSE items and predictors

	Orientation	Registration	Serial Sevens	Spelling Backwards	Recall	Naming	Repetition	3-Stage Command	Reacting	Writing	Copying	MMSE Total Score
Age	-.04	§	-.13	-.49*	-.41**	§	-.35**	-.06	§	-.25**	-.25**	-.42**
Gender	-.06	§	.08	.21~	-.01	§	-.06	.04	§	.15	-.12	-.01
Ethnicity	.11	§	.44**	.11	.39**	§	.06	.00	§	.13	.16	.30**
Education	.35	§	.33**	.54**	.48*	§	.35**	-.04	§	.23*	.43**	.57**

* $p < 0.01$, ** $p < 0.001$, § not computed because 1 variable constant

Results from the ANOVA analysis showed no significant effects of gender, education or ethnicity on orientation. However, a significant main effect for age was found, $F(5,77)=3.86$, $p=0.004$) and post hoc analysis using a Bonferroni correction showed significant differences between groups. With the exception of the youngest age group (18-30 years) who had a mean score of 9.06 ($se=.14$), all other age groups had significantly higher orientation scores (31-40 years ($m=9.67$, $se=.23$), 41-50 years ($m=9.55$, $se=.19$), 51-60 years ($m=9.60$, $se=.17$), 61-70 years ($m=9.54$, $se=.20$) than the most elderly group (>70 years) with a mean of 8.69 ($se=.18$). No significant interaction effects were observed. The mean scores for each group are illustrated in Figure 3.3.

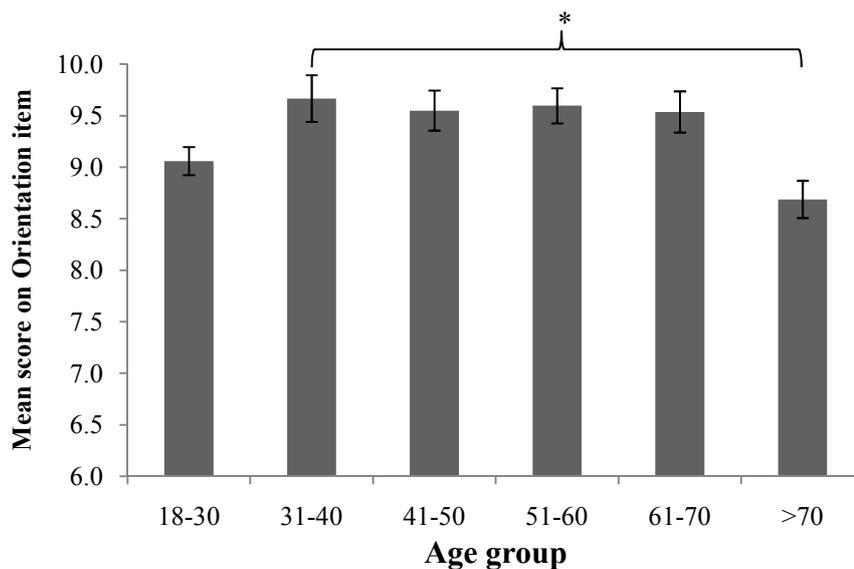


Figure 4.4 Graph showing mean orientation scores for each age group

Regression Analysis

Orientation scores were significantly correlated with some of the MMSE items: serial sevens, spelling backwards, recall, writing, copying and total MMSE score. Scores for repetition and 3-stage command were not significantly associated with orientation scores (See Table 3.3). Of the four predictors, fewer years of

education was significantly associated with lower scores. Neither age, gender, nor ethnicity was significantly associated with orientation scores (See Table 3.4).

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 118)=4.82, p=0.001$). Of the four predictors, only education made a significant contribution to the overall model ($\beta=.41, t(118) = 4.09, p<0.001$). The regression analysis was repeated with education as the only predictor and a significant model emerged ($F(1, 121)=16.32, p<0.001$). Education significantly predicted orientation scores, $\beta=.35, t(119) = 4.04, p<0.001$ and accounted for 12% ($R^2 = .12$) of the variance in scores.

4.1.8.4.3 REGISTRATION

ANOVA and Regression Analysis

As seen in table 3.2, mean performance on registration was 3.00 (s.d. =.00). All participants in the sample achieved the maximum score of 3 for this item. Due to the lack of variability of performance on this item, no ANOVA, correlation or regression analysis was possible.

4.1.8.4.4 SERIAL SEVENS

ANOVA Analysis

As seen in table 3.2, mean performance on serial sevens item was 4.10 (s.d. =1.51). Performance ranged from a minimum of 0 to the maximum of 5.

Results from the ANOVA analysis showed no significant effects of age, gender or education on serial sevens performance. However, a significant main effect for ethnicity was found, $F(1,77)=17.83, p<0.001$) and post hoc analysis using a

Bonferroni correction showed significant differences between groups. The Caribbean group had a significantly lower score ($m=3.53$, $se=.20$) than the British group ($m=4.78$, $se=.20$). See Figure 3.4. No significant interaction effects were observed.

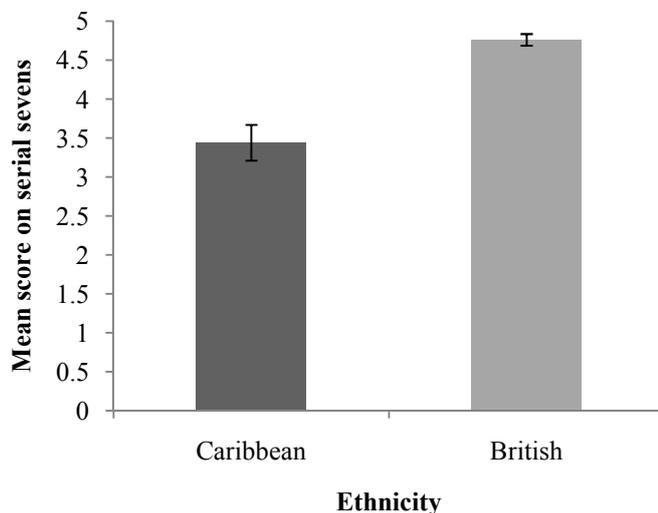


Figure 4.5 Comparison of serial sevens scores between Caribbean and British groups

The distribution of scores on the serial sevens task also showed a different pattern in Caribbeans than British. Whereas 84% of the British sample achieved a maximum score of 5, only 42% of Caribbeans achieved the same. More Caribbeans (11%) failed to score any points for this task whereas no British person fell into this category. The lowest score achieved in the British group was 3/5. The distribution of scores for each group is shown in Figure 4.5.

Regression Analysis

Serial sevens scores were significantly correlated with most MMSE items: orientation, serial sevens, spelling backwards, recall, repetition, writing, copying and total MMSE score. Scores for 3-stage command were not significantly associated with serial sevens scores (See Table 4.3). Of the four predictors, ethnicity and

education were significantly correlated with serial sevens performance, with

Caribbean ethnicity and fewer years of education associated with lower scores. Age

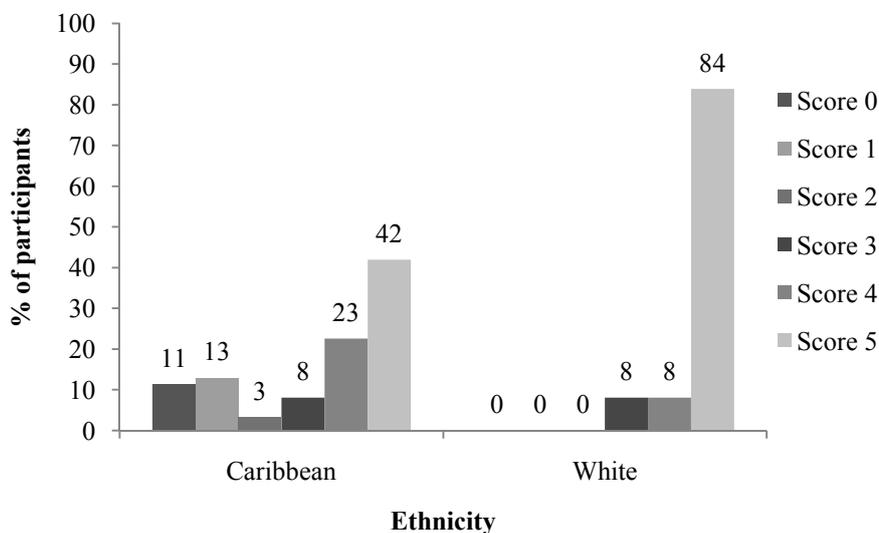


Figure 4.6 Distribution of scores on serial sevens task in Caribbeans and British.

and gender were not significantly associated with serial sevens scores (See Table 4.4).

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 119)=11.97, p=0.001$). Of the four predictors, education ($\beta=.30, t(119) = 3.24, p=0.002$) and ethnicity ($\beta=-.09, t(119) = -1.18, p<0.001$) made significant contributions to the overall model. A stepwise regression analysis was then performed with education and ethnicity as the only predictors and a significant model was produced ($F(2, 120)=26.50, p<0.001$) which accounted for 31% ($R^2=.31$) of the variance in serial sevens scores. Ethnicity ($\beta=.44, t(120) = 5.84, p<0.001$) accounted for 19% ($R^2 = .19$) of the variance while education ($\beta=.34, t(120) = 4.44, p<0.001$) accounted for a further 11% ($R^2 = .12$) of the variance in serial sevens scores.

4.1.8.4.5 SPELLING BACKWARDS

ANOVA Analysis

Mean performance on spelling backwards was 4.45 (s.d. =1.19) with scores ranging from 0 to 5 (See Table 3.2). There was a significant main effect of age ($F(5, 36) = 2.63, P=0.04$). A Bonferroni correction revealed the oldest age group (over 70 years) had significantly lower mean scores ($m=2.25, se=.29$) than all of the younger age groups whose mean scores ranged from 4.25 to 5.00. A comparison of groups based on ethnicity was not carried out due to the small number of scores available from the British sample. There were no other significant main effects or interaction effects.

Regression Analysis

Spelling backwards scores were significantly correlated with all MMSE items with the exception of repetition and 3-stage command (See Table 3.3). Scores were significantly correlated with age, education and gender (See Table 3.4). Increasing age, fewer years of education and male gender were associated with lower scores.

A stepwise regression analysis produced a significant model with age, gender or education predicting performance on spelling backwards ($F(3,67)=14.88, p<0.001$) and accounting for 40% of the variance in scores. Education ($\beta=.42, t(67) = 3.52, p=0.001$) accounted for 29% ($R^2 = .29$) of the variance, gender ($\beta=.26, t(67) = 2.68, p=0.009$) accounted for 7% ($R^2 = .07$) and age ($\beta=-.25, t(67) = -2.13, p=0.036$) explained a further 4% ($R^2 = .04$) of the variance in spelling backwards scores.

4.1.8.4.6 RECALL

ANOVA Analysis

Average performance for recall was 2.55 (s.d. =.80) with scores ranging from 0 to 3 (See Table 3.2). Results from the ANOVA analysis showed no significant effects of age, or gender with older participants performing similarly to younger and women performing similarly to men. However, significant main effects for ethnicity $F(1,77)=30.61, p<0.001$ and education $F(2,77)=8.08, p=0.001$ were found. Post hoc analysis using a Bonferroni correction showed significant differences between education groups. The low education group had a significantly lower mean performance ($m=1.79, se=.12$) than the average ($m=2.69, se=.08$) and high ($m=2.86, se=.10$) education groups. The difference between the average and high groups was not significant. The Caribbean group also had a significantly lower mean performance ($m=2.23, se=.08$) than the British group ($m=2.87, se=0.08$). There was a significant interaction effect between ethnicity and education. As can be seen in Figure 3.2, whereas both Caribbeans and British persons with average and high education perform similarly, there is a larger disparity between the ethnic groups with low education in which Caribbean persons with low education perform much worse than their British counterparts on recall.

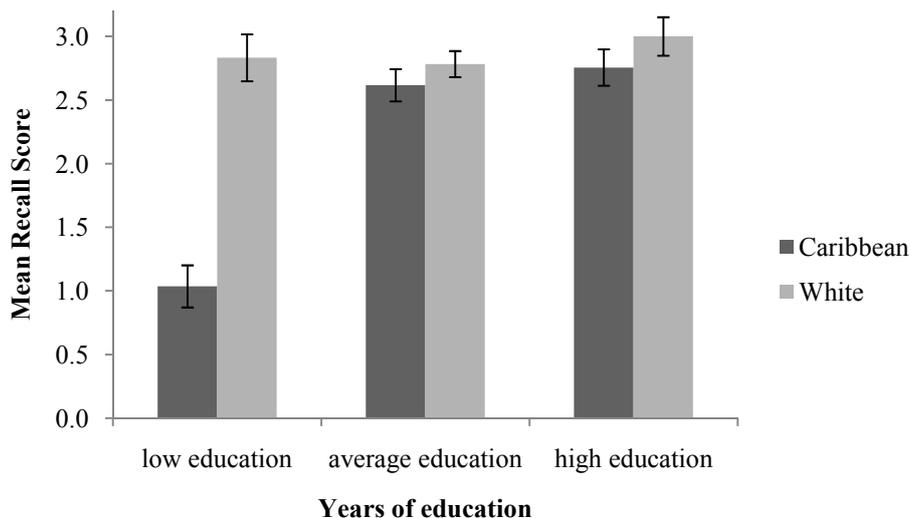


Figure 4.7 Mean scores for recall by ethnicity and years of education

Regression Analysis

Recall scores were significantly correlated with all other MMSE items with the exception of 3-Stage command (See Table 3.3). Of the four predictors, recall was significantly correlated with age, ethnicity and education but not gender. Increasing age, fewer years of education and Caribbean ethnicity was associated with lower scores.

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 118)=19.68, p<0.001$). Of the four predictors, age, ethnicity and education made significant contributions to the overall model. A stepwise regression analysis was then performed with age, ethnicity and education as the only predictors and a significant model emerged ($F(3, 119)=28.42, p<0.001$) which accounted for 42% ($R^2 = .42$), of the variance in performance. Education significantly predicted recall scores, $\beta=.37, t(119) = 4.55, p<0.001$ and accounted for 23% ($R^2 = .23$) of the variance in scores, ethnicity accounted for a

further 15% of the variance, $R^2 = .15$, $\beta = .39$, $t(119) = 5.58$, $p < 0.001$ and age contributed 4% of the variance, $R^2 = .04$, $\beta = -.22$, $t(119) = -2.69$, $p = 0.008$.

4.1.8.4.7 REPETITION

ANOVA Analysis

As seen in table 3.2, mean performance on repetition was 0.77 (s.d. = .43) with scores ranging from 0 to 1. No significant effects of gender, age, education or ethnicity were found for this item.

Regression Analysis

Repetition scores were significantly correlated with certain items: serial sevens, spelling backwards, recall and MMSE total score, but not orientation, 3-stage command, writing or copying (See Table 3.3). Of the four predictors, correlations for age and education were significant with increasing age and fewer years of education being associated with lower scores for repetition (See Table 3.4).

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 118) = 6.13$, $p < 0.001$). Of the four predictors, age and education made significant contributions to the overall model. A stepwise regression analysis was performed with age and education as the only predictors and a significant model emerged ($F(2, 120) = 11.54$, $p < 0.001$) which accounted for 16% ($R^2 = .16$) of the variance in performance. Education significantly predicted repetition scores ($\beta = .23$, $t(120) = 2.37$, $p = 0.019$) and accounted for 12% ($R^2 = .12$) of the variance in scores while age ($\beta = -.23$, $t(120) = -2.35$, $p = 0.020$) accounted for a further 4% of the variance in scores.

4.1.8.4.8 NAMING*ANOVA and Regression Analysis*

Mean performance on the naming item was 2.00 (sd=0.00) with all participants gaining the maximum score of 2 (See Table 3.2). Due to the lack of variability of performance on this item, no ANOVA, correlation or regression analysis was possible.

4.1.8.4.9 3-STAGE COMMAND*ANOVA Analysis*

As seen in table 3.2, mean performance on 3-stage command was 2.90 (s.d. =.31) with scores ranging from 2 to 3. No significant effects of gender, age, education or ethnicity were found for this item.

Regression Analysis

Scores for 3-stage command failed to show significant correlations with any of the other MMSE items with the exception of the total score (See Table 3.3). This item also failed to correlate significantly with any of the predictors (See Table 3.4). A forced entry regression analysis with age, gender, ethnicity and education failed to produce a significant model.

4.1.8.4.10 REACTING*ANOVA and Regression Analysis*

As seen in table 3.2, mean performance on reacting was 1.00 (s.d. =.00). All participants in the sample achieved the maximum score of 1 for this item. Due to the

lack of variability in performance for this item, no ANOVA, correlation or regression analysis was possible.

4.1.8.4.11 WRITING

ANOVA Analysis

Mean performance on writing was 0.98 (s.d. =.13) with scores ranging from 0 to 1 (See Table 3.2). No significant effects of gender, age, education or ethnicity were found for this item.

Regression Analysis

Scores for writing were significantly correlated with certain items: orientation, serial sevens, spelling backwards, recall, copying and total MMSE scores. Writing was not significantly correlated with repetition, 3-stage command or reacting (See Table 3.3). Of the four predictors, correlations for age and education were significant, with increasing age and fewer years of education being associated with lower scores for writing (See Table 3.4). A forced entry regression analysis with age, gender, ethnicity and education failed to produce a significant model.

4.1.8.4.12 COPYING

ANOVA Analysis

As seen in table 3.2, mean performance on copying was 0.93 (s.d. =.26) with scores ranging from 0 to 1. No significant effects of gender, age, education or ethnicity were found for this item.

Regression Analysis

Scores for copying were significantly correlated with certain items: orientation, serial sevens, spelling backwards, recall, writing and total MMSE scores.

Writing was not significantly correlated with repetition, 3-stage command or reacting (See Table 3.3). Of the four predictors, correlations for age and education were significant, with increasing age and fewer years of education being associated with lower scores for copying (See Table 3.4). A forced entry regression analysis with age, gender, ethnicity and education failed to produce a significant model.

The results from the multiple regression analyses for all MMSE items are presented below in Table 4.5. The significant predictors for each item are also summarised in Table 4.6.

Table 4.5

Multiple Regression Analysis- unstandardised and standardized coefficients for MMSE items

Item			B	SE B	β	R²	
MMSE total	Model(Enter)	(Constant)	25.44	.91			
		Age	-.02	.01	-.17		
		Gender	.04	.31	.01		
		Ethnicity	1.33	.31	.31		
		Years of Education	1.44	.26	.47	.44*	
	Model(Stepwise)	(Constant)	25.56	.80			
		Years of Education	.20	.03	.49	.33*	
		Ethnicity	1.32	.30	.30	.09*	
		Age	-.02	.01	-.16	.02*	
	Orientation	Model (Enter)	(Constant)	7.91	.41		
Age			.01	.00	.18		
Gender			-.05	.14	-.03		
Ethnicity			.20	.14	.12		
Years of Education			.47	.11	.41	.14*	
Model (Stepwise)		(Constant)	8.56	.19			
		Years of Education	.05	.01	.35	.12*	
Registration		--	--	--	--	--	--
Serial sevens		Model(Enter)	(Constant)	2.22	.69		
			Age	.00	.01	.02	
	Gender		-.28	.24	-.09		
	Ethnicity		1.35	.23	.45		
	Years of Education		.63	.20	.30	.29*	
	Model (Stepwise)	(Constant)	2.10	.34			
		Ethnicity	1.34	.23	.44	.19*	
		Years of Education	.09	.02	.34	.11*	

Table 4.5 continued

Multiple Regression Analysis- unstandardised and standardized coefficients for MMSE items

Item			B	SE B	β	R ²
Spelling backwards	Model(Stepwise)	(Constant)	3.76	.65		
		Years of Education	.08	.02	.42	.29*
		Gender	.61	.23	.26	.07*
		Age	-.02	.01	-.25	.04*
Recall	Model(Enter)	(Constant)	1.91	.34		
		Age	-.01	.00	-.23	
		Gender	-.01	.12	-.01	
		Ethnicity	.63	.11	.39	
	Years of Education	.39	.10	.34	.40*	
	Model (Stepwise)	(Constant)	1.22	.17		
		Years of Education	.07	.01	.49	.23*
		Ethnicity	.62	.12	.39	.15*
Age					.04*	
Naming	--	--	--	--	--	--
Repetition	Model(Enter)	(Constant)	.69	.21		
		Age	-.01	.00	-.22	
		Gender	-.04	.07	-.05	
		Ethnicity	.05	.07	.06	
	Years of Education	.15	.06	.24	.17*	
	Model (Stepwise)	(Constant)	.75	.19		
		Years of Education	.02	.01	.23	.12*
		Age	-.01	.00	-.23	.04*
3-stage command	Model(Enter)	(Constant)	3.01	.16		
		Age	-.00	.00	-.09	
		Gender	.02	.06	.04	
		Ethnicity	-.00	.06	-.01	
Years of Education	-.03	.05	-.06	.01		
Reacting	--	--	--	--	--	--
Writing	Model(Enter)	(Constant)	-2.46	6.49		
		Age	.13	.07		
		Gender	2.69	2.22	.11	
		Ethnicity	-.19	2.20	-.01	
Years of Education	-1.27	1.83	-.07	.08		
Copying	Model(Enter)	(Constant)	-3.08	6.65		
		Age	.14	.07	.21	
		Gender	2.66	2.25	.11	
		Ethnicity	-.08	2.22	-.00	
Years of Education	-1.11	1.86	-.06	.07		

Table 4.6

Significant predictors from regression analyses for MMSE items

Item	Age	Gender	Education	Ethnicity
MMSE Total	√	-	√	√
Orientation	-	-	√	-
Registration	*	*	*	*
Serial Sevens	-	-	√	√
Spelling Backwards	-	-	√	*
Recall	√	-	√	√
Naming	*	*	*	*
Repetition	√	-	√	-
3-Stage Command	-	-	-	-
Reacting	*	*	*	*
Writing	-	-	-	-
Copying	-	-	-	-

*=not computed, - = p=NS, √= p<0.05

4.1.8.4.13 SERIAL SEVENS VS SPELLING BACKWARDS IN CARIBBEANS

Spelling backwards scores were only available for 9 participants in the British sample and as such the analysis was limited to the Caribbean group. The mean score for serial sevens was 3.44 (se=.23), while the mean score for spelling backwards was higher at 4.40 (se=0.16). A repeated measures ANOVA found this difference to be statistically significant ($F(1,61) = 614.15, p < 0.001$). The distribution of scores also differs for each item. For example, in spelling backwards, 74% of participants achieved the maximum score compared to 42% for serial sevens. In addition whereas 15 persons scored 0 or 1 on the serial sevens task, only 3 persons had those scores (3 received 0 points and none received 1 point) for the spelling backwards. The distribution of scores for each item is shown in Figure 3.7

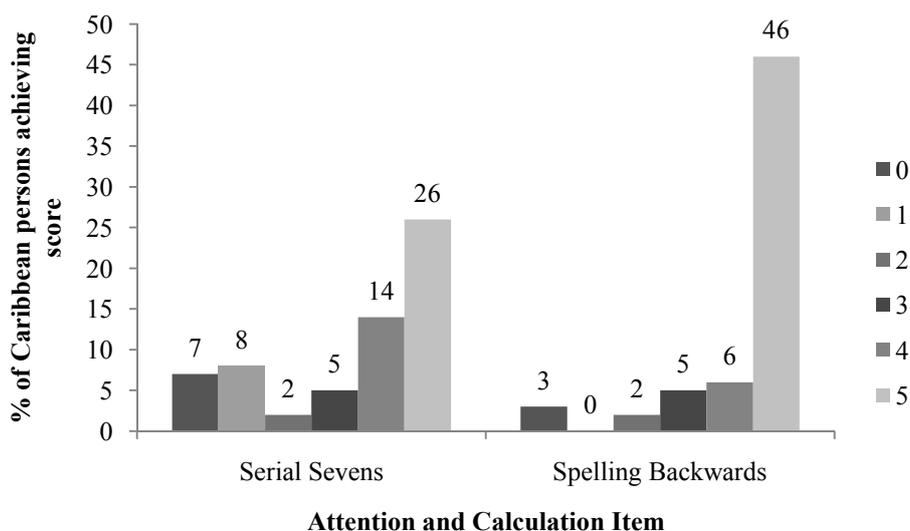


Figure 4.8 Distribution of serial sevens and spelling backwards scores in Caribbeans

4.1.8.4.14 MMSE TOTAL SCORES USING EITHER SERIAL SEVENS, SPELLING BACKWARDS, OR HIGHER OF THE TWO SCORES IN CARIBBEANS

Two sets of total scores were calculated for Caribbean persons based on 1) inclusion of the serial seven item score only and 2) inclusion of the spelling backwards score only and 3) using the higher of both scores. Total MMSE scores calculated using the higher of the two measures yielded the highest mean scores ($m=27.55$, $se=.35$) followed by scores using the spelling backwards item ($m= 27.35$, $se=0.39$), and MMSE scores using the serial sevens item had the lowest mean of 26.43 ($se=0.43$). A repeated measure ANOVA found this difference to be statistically significant ($F(2, 58)= 18.62$, $p<0.001$) and post hoc analyses revealed significant differences between MMSE scores using the spelling backwards item yielding significantly higher scores than those using the serial sevens item, MMSE scores using the higher of the two scores yielded significantly higher means than scores calculated using the serial sevens. The means using the higher of the two

scores was not significantly different from the mean obtained from using the spelling backwards score.

4.1.8.5 DISCUSSION

Age, education and ethnicity were significant predictors of performance on many MMSE items. This study found no effect of gender on total MMSE scores and gender failed to predict MMSE performance. This finding coincides with the literature which consistently reports no effect of gender on MMSE scores. Gender differences were observed however on one item: spelling backwards in which Caribbean females performed better than Caribbean males. This finding concurs in part with the findings of Jones and Gallo (2002) but these authors, along with Roselli et al (2007) also found gender differences in the serial sevens task and this study did not confirm this finding. This disparity may be explained by the use of different ethnicities across the studies. This interpretation is supported by Roselli et al (2007) who stated the contradictory effect of gender may be the result of differences in cultures across studies.

Age significantly predicted overall MMSE scores as well as recall and repetition, but only accounted for a small percentage (2-4%) of the variance in the scores. This finding endorses that of other studies which report decreasing scores with increasing age (Crum et al, 1993; George et al, 1991). The small effect for age may be explained by the relatively high levels of education in this sample. Crum et al (1993) noted that there was great variability in MMSE scores with increasing age in the lowest educational groups, and as education increased, the range of scores narrowed. This sample had an average of 14.49 years of education and 75% of the sample had over 10 years of education. The cognitive reserve hypothesis may also

lend credence to these findings. Since highly educated individuals are thought to be less likely to manifest cognitive impairment, education may serve as a protective factor against decline in cognitive performance in older persons.

The most influential factor on MMSE performance was education which significantly predicted scores on total MMSE scores and five individual items: orientation, serial sevens, spelling backwards, recall and repetition. In all items, increasing education was associated with higher scores. Education explained 11% to 23% of the variance in individual items and 33% of variance in total MMSE scores. These findings concur with the literature which state the MMSE is highly influenced by education (Prince et al, 2003; de Brito-Marques & Cabral-Filho, 2005; Jones and Gallo, 2002).

Ethnicity also significantly predicted scores for total MMSE, serial sevens and recall in which Caribbean ethnicity was associated with lower scores. In two of these items (total MMSE and recall) however, the presence of a significant interaction effect modifies the interpretation. The interaction in both scores showed that while performance between the two ethnic groups was similar in the average and high education groups, there was a divergence in the low education group with Caribbeans performing much worse than their British counterparts. Thus, the differences due to ethnicity may be restricted to persons with low educational attainment. This explanation coincides with the findings of Stewart et al (2001) who reported that African Caribbeans had lower median scores and a greater proportion of persons with scores below the cut-off. However they also go on to note that a disproportionate number of persons with low scores had low levels of education and this was especially so in the African Caribbean group in which low educated African Caribbeans performed much worse than low educated British.

These findings suggest that low performance attributed to ethnicity may also be masking disproportionately low levels of education in these groups. Participants in this study were matched for education and the matching criterion used was years of education. However, as Manly et al (1998) highlight, years of education may suffice in analyses within group but may be inadequate for analyses that compare different ethnic groups as it may not sufficiently capture variability in quality or experiences of schooling. This is a valid criticism, however, the results of this study illustrate that this caveat may apply specifically for groups with low levels of education. In persons with higher levels of education, a comparison based on years may be adequate.

Caribbean persons showed significant differences in performance on the items for attention and concentration (serial sevens and spelling backwards). They performed significantly worse on the serial sevens, confirming widely reported findings that these performance on the two items are different, the two items are not equivalent and that the serial sevens task is more difficult (Folstein, 1998; Anthony et al, 1982; Hamby, 1994; Watkins et al, 1989; Ganguli et al, 1990, Lopez et al, 2005). The distribution of scores across ethnic groups also indicate that Caribbeans found the task more difficult than the British and as such were less likely to score maximum points and more likely to score zero points on this item. This task is the only MMSE item that requires arithmetic ability and as such, worse performance on this task may be explained by poorer arithmetic ability in Caribbeans or if arithmetic ability is not responsible, there may be a feature of this task that is uniquely influenced by ethnicity. This hypothesis was tested in Study 2 and will be further addressed in later sections of this chapter.

Brayne (1998) remarked that differences in the versions of MMSE used (different words for recall, different administrations of serial sevens vs. spelling backwards) do not have an impact on performance however this opinion may be due to the lack of published studies which compare the effect of variations in administration on scores.

This study confirmed that variations in the administration and scoring procedure for items under attention and concentration (serial sevens and spelling backwards) produced significantly different total MMSE scores, and showed that use of the serial seven item only results in lower MMSE scores in Caribbean persons. As such, variations in administration can cause significantly different MMSE scores and have both clinical and psychometric implications for the use of the MMSE in Caribbean populations.

4.1.9 STUDY 2

DISCOVERING THE SOURCE OF THE ETHNICITY EFFECT ON SERIAL SEVENS

4.1.9.1 AIM

The objectives of this study are to:

1. Clarify the source of ethnicity driven difference in performance on the serial sevens item in a student sample matched for age, gender and education.
2. Investigate whether differences due to ethnicity are due to differences in arithmetic achievements in people of different ethnic origin.

4.1.9.2 METHOD

4.1.9.2.1 Participants

In this study, 60 participants (female= 30, male=30) from Trinidad and Tobago (n=30) and England (n=30) were assessed. The mean age of participants was 20.78 years (sd=2.57) while the mean number of years of education was 16.45 (sd=2.11). All participants were functionally independent, with no neurological or psychiatric impairment.

4.1.9.2.2 Materials

The Mini Mental State Examination (Folstein et al, 1975) was administered to all participants. A list of the items used is provided in Table 3.1. The blue form of the Wide Range Achievement Test III (Arithmetic subtest) was also administered to each participant.

4.1.9.2.3 Procedure

The MMSE was administered to each participant in the listed order. For the attention and concentration section, both serial sevens and spelling backwards items were administered and the higher score contributed to the overall MMSE score.

4.1.9.3 DESIGN AND STATISTICAL ANALYSIS

One-way ANOVAs were performed on each of the 12 dependent variables (MMSE total and 11 item scores) comparing the effects of ethnicity on performance.

4.1.9.4 RESULTS

Significant differences were observed in performance on the orientation, serial sevens and MMSE total scores.

Closer examination of the orientation score revealed 75% of the Caribbean sample made errors on the county question as compared to 10% of the British sample and 3% of the Caribbean sample made errors on the season question as compared to 27% of the British sample. When these two questions were excluded from the analysis, the difference between the groups on orientation and MMSE total scores failed to reach significance.

In the serial sevens item, Caribbean students had a lower mean score ($m=4.10$, $se=1.16$) than British students ($m=4.67$, $se=0.61$) and this difference was found to be statistically significant ($F(1,58)= 5.66$, $p=0.021$).

Significant differences were also observed in arithmetic performance with the Caribbean students ($m=28.30$, $se=0.75$) achieving significantly higher scores than the British students ($m=24.10$, $se=0.54$), $F(1,58)=20.66$, $p<0.001$. The performance of both groups on serial sevens and WRAT-Arithmetic are illustrated in Figure 3.8.

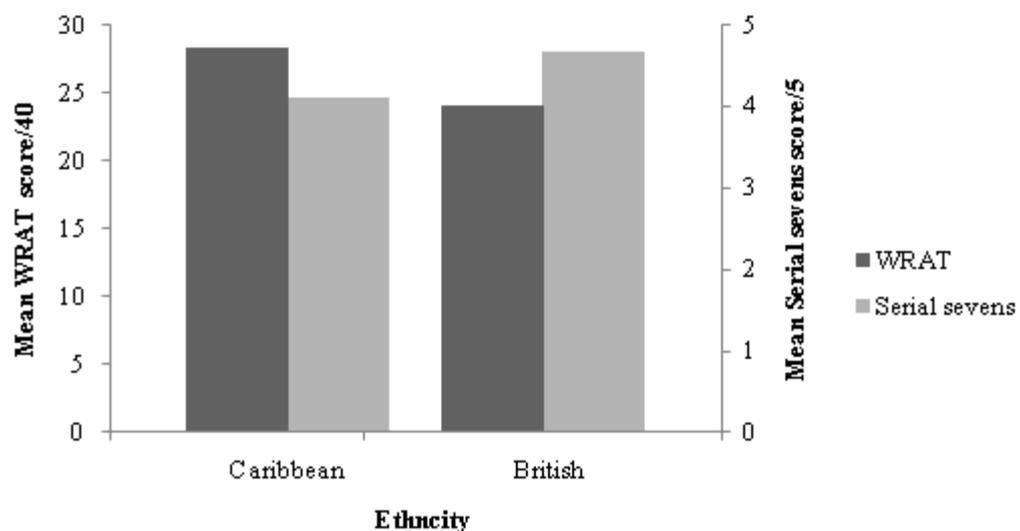


Figure 4.9 Comparison of WRAT and serial sevens scores among Caribbean and British students

4.1.9.5 DISCUSSION

This study found a significant difference in scores on the orientation item whereas Stewart et al (2002) failed to do so. This may be attributed to cultural and measurement factors. More Caribbean students made errors on the county item and this may be due to the discontinuation in the 1990s of the use of counties for designating geographical areas in Trinidad and Tobago. Whereas older Caribbean persons would have grown up using the term counties, younger persons would probably be less familiar with these now outdated county designations. In the UK, county designations have been around for centuries with the most recently established taking place over 30 years ago, thus the use of counties would be familiar and entrenched in most normal, healthy persons.

In the season item, the opposite pattern was shown in which British students made more errors than Caribbean. There are two Caribbean seasons (wet and dry) and four British seasons (spring, summer, autumn and winter) and as such the chances for error are increased in the British setting. This risk of error is also exacerbated as boundary dates between seasons are not clear cut and based on the solstices and equinoxes of the sun which may vary slightly from year to year. This study was conducted over the months of April and May in the UK and many British students who made errors did so by answering summer instead of spring when prompted for the season. Whereas some instruments make allowances for potentially vague boundaries, (for e.g. the ADAS-Cog allows a two week margin of error for the season), the MMSE does not. Also, the perceived meaningfulness or utility of the item measuring temporal orientation may impact on the motivation to respond

accurately. Arguably, knowing the correct day or month is more important in terms of remembering schedules or appointments as compared to knowing the correct season.

This difference which was found in both younger age groups but not in studies using community samples suggests that in addition to cultural differences in items, there may exist changes in responses over time and generation. Whereas items are sometimes scored on the basis of the culture being assessed (e.g. seasons, states, counties may vary), it may also be useful to see how error rates vary in items in the same population over different generations.

One finding however was consistent with the first study and that of Stewart et al (2002). This was the significant difference in performance on the serial seven subtraction item. Caribbean students performed significantly worse on this item than British students. The worse performance by Caribbean students could not be attributed to arithmetic ability as scores on the WRAT Arithmetic subtest show significantly higher arithmetic achievement scores in Caribbean than British students.

Apart from being a verbal, arithmetic calculation task, the serial sevens item is an attention and concentration task. Thus the difference in performance could be attributed to worse attention and concentration in Caribbean persons. However, there was no difference in performance on the other attention and concentration item- spelling WORLD backwards, a finding which replicates that of the community study (Study 1). The difference in performance, however, may also be interpreted as a function of difficulty with an interaction of ethnicity in which there are no differences for easier items but when the task becomes harder, Caribbeans respond

differently than British persons. The digit span task can also be regarded a task of attention and concentration and the backwards version of the task is regarded as more difficult than the forwards version. Similar patterns of performance on the digit span task may corroborate the argument for an interaction of ethnicity and difficulty of the item.

Campbell and Xue (2001) have noted cross cultural differences in cognitive strategies employed in arithmetic across cultures. University students who performed worse on arithmetic tasks employed more procedural than retrieval skills and superior performance was attributed not to difference in formal education among Chinese, Chinese Canadian and non-Chinese Canadian students but to informal culture-specific factors. These factors include attitude to mathematics, belief that effort mediates success, pursuing extra-curricular instruction, and positive attitudes to achievement. Thus informal, cultural factors may explain the differences in performance on the serial seven subtraction task in which Caribbean students endorse different attitudes to the task.

Unlike the WRAT which is a written task in which the students complete all items and then submit the form for scoring, the serial sevens requires five consecutive verbal responses. One qualitative difference noticed during administration was the greater use of qualifying and self-deprecating comments by Caribbeans in the serial sevens task (e.g. 'I'm no good with numbers', 'I think I did stupidness' or 'I don't think I'm too good at Math'). These comments may infer a greater level of anxiety experienced by Caribbeans which may interfere with performance.

The findings of this study show that controlling for education removes the effect of ethnicity on certain items that were found to have an interaction with education: total MMSE scores and recall scores. The difference, however, persists in measures of serial sevens in which Caribbean persons consistently show lower scores than British persons. Since lower scores are generally interpreted as indicating greater levels of impairment, the difference between the ethnic groups suggests that lower scores may be partially independent of impairment and that performance on the serial sevens items and scores which use the serial sevens item warrant careful interpretation among Caribbean populations.

4.1.10 STUDY 3

MMSE PERFORMANCE IN ELDERLY AD PATIENTS AND NON-PATIENTS

4.1.10.1 AIM

The objectives of this study are to:

1. Assess the difference in performance on the MMSE in a community and clinical sample of Caribbean and British elderly matched for age, gender and education.
2. Verify if current scoring and cut-off correctly differentiate normal from abnormal performance.

4.1.10.2 METHOD

4.1.10.2.1 Participants

In this study, 40 participants (female= 20, male=20) from Trinidad and Tobago (n=20) and England (n=20) were assessed. Half of the sample consisted of healthy adults from a community setting and half consisted of persons who had received a diagnosis of probable AD. The mean age of participants was 75.76 years (sd=9.33) while the mean number of years of education was 9.73 (sd=4.72).

Diagnosis of probable AD in Trinidad was based on clinical assessment and laboratory analyses. The use of brain imaging is not a feature of routine diagnostic practice in Trinidad due to cost and availability constraints. Patients from Britain were diagnosed based on clinical assessment, laboratory analyses and neuroimaging (MRI scans). Severity of the condition for both groups was not ascertained. The Mini Mental State Examination (Folstein et al, 1975) was administered as a screening instrument in both samples and comprised part of the screening/diagnostic procedure.

4.1.10.2.2 Materials

The Mini Mental State Examination (Folstein et al, 1975) was administered to all participants. A list of the items used is provided in Table 3.1.

4.1.10.2.3 Procedure

The MMSE was administered to each participant in the listed order. For the attention and concentration section, both serial sevens and spelling backwards items were administered and the higher score contributed to the overall MMSE score.

4.1.10.3 DESIGN AND STATISTICAL ANALYSIS

Univariate ANOVAs (2x2) were performed on each of the 12 dependent variables (MMSE total and 11 item scores) comparing the effects of ethnicity and AD status on performance.

One way ANOVAs (1x4) were also conducted to compare the performance between the four groups, Caribbean control, British control, Caribbean AD, British AD.

4.1.10.4 RESULTS

4.1.10.4.1 2 x 2 ANOVA analysis

MMSE Total

Significant main effects were observed for AD status ($F(1,37) = 21.23$, $p < 0.001$) in which AD patients had lower mean scores ($m = 19.57$, $se = .98$) than the non-AD adults ($m = 26.08$, $sd = 1.02$). A significant main effect for ethnicity ($F(1,37) = 15.60$, $p < 0.001$) was also observed in which Caribbean persons had lower scores (20.00 , $se = .98$) than British persons ($m = 25.65$, $se = 1.02$). The interaction between ethnicity and AD status was not significant.

Orientation

Significant main effects were observed for both ethnicity and AD status. AD patients had significantly lower mean scores for orientation ($m = 6.02$, $se = .40$) than the non-AD adults ($m = 9.14$, $se = .41$), ($F(1,37) = 29.67$, $p < 0.001$). Caribbean persons also had significantly lower orientation scores ($m = 6.37$, $se = .40$) than British persons ($m = 8.79$, $se = .41$), ($F(1,37) = 17.85$, $p < 0.001$). The interaction between ethnicity and AD status was not significant.

Serial Sevens

A significant main effect of AD status was found for performance on serial sevens scores, ($F(1,37) = 13.98, p=0.001$). AD patients performed significantly worse ($m=1.00, se=.49$) than non-patients ($m=3.40, se=.42$). While British persons scored higher on serial sevens than Caribbean persons, this difference was not significant and neither was the interaction between ethnicity and AD status.

Spelling Backwards

A significant main effect of ethnicity was found for spelling backwards performance, ($F(1,37) = 13.98, p=0.001$). Caribbeans performed significantly worse ($m=2.83, se=.40$) than British ($m=4.34, se=.42$). While the healthy controls had higher spelling backwards scores than AD patients, this difference was not significant and neither was the interaction between ethnicity and AD status.

Recall

Significant main effects were observed for both ethnicity ($F(1,37)=6.88, p=0.013$) and AD status ($F(1,37)=29.55, p<0.001$) and the interaction between these two factors was also significant. AD patients performed significantly worse than non-patients as did Caribbean persons compared to British. The interaction showed a larger disparity between British controls and British AD groups while Caribbean controls had scores that were more similar to the Caribbean AD group. See Figure 4.10.

Writing

A significant main effect of ethnicity was found for scores on the writing item ($F(1,37)=4.912, p=0.034$). Caribbean persons had significantly lower scores ($m=.67, se=.09$) than their British counterparts ($m=.95, se=.09$). While controls had higher

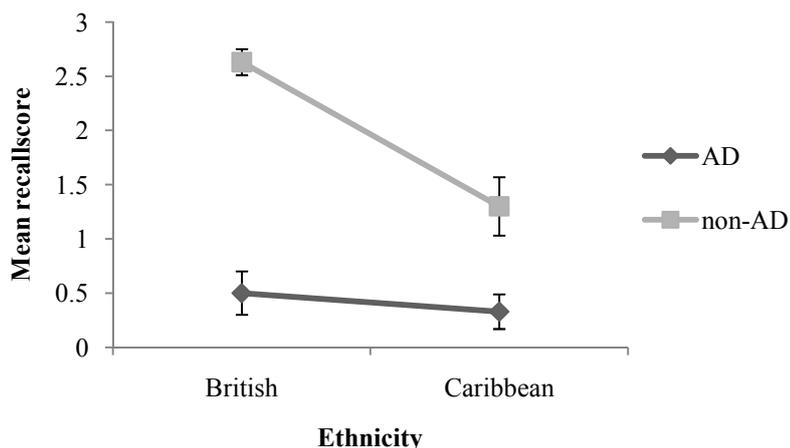


Figure 4.9 Mean recall scores by ethnicity and AD status

scores than AD patients, the difference was not significant and the interaction between the two factors was also insignificant.

Registration, Naming, Repetition, 3-stage command, Reacting, Copying

In the registration, naming, repetition and 3-stage command, reacting and copying items, no significant main effects or interaction effect were observed. In all these items, scores by AD patients were lower than in controls and scores by Caribbeans were lower than in the British group, however these differences were not significant.

4.1.10.4.2 One way ANOVA

Significant group differences were noticed in total MMSE scores ($F(3,37)=15.92$, $p<0.001$), orientation ($F(3,37)=6.76$, $p=0.001$), serial sevens ($F(3,37)=12.52$, $p<0.001$), and recall scores ($F(3,37)=11.70$, $p<0.001$). Post hoc analyses revealed significant differences between groups. No significant differences

were observed for performance on registration, spelling backwards, naming, repetition, 3-stage command, reacting writing and copying.

Orientation

In the orientation item, the Caribbean AD group ($m=4.33$, $se=.88$) had the lowest mean scores followed by the British AD group ($m=7.70$, $se=.56$), Caribbean control ($m=8.40$, $se=.40$) and British control ($m=9.88$, $se=.13$). Significant group differences were observed between both control groups and Caribbean AD and also between British AD and Caribbean AD groups.

Serial sevens

In serial sevens, the Caribbean AD ($m=1.00$, $se=.41$), and British AD group ($m=1.00$, $se=1.00$) performed the worst, followed by the Caribbean control ($m=2.30$, $se=.67$) and British control ($m=4.50$, $se=.50$). Significant group differences were observed between the British control and both AD groups.

Recall

In recall, the Caribbean AD group performed the worst ($m=.33$, $se=.24$), followed by the British AD group ($m=.50$, $se=.27$), Caribbean control ($m=1.30$, $se=.37$) and British control ($m=2.63$, $se=.18$). Significant group differences were observed between the British control and both AD groups as well as between the British control and Caribbean control. The comparison of group scores for all four measures is illustrated in Figure 4.11.

MMSE total

For total MMSE, the Caribbean AD group had the lowest mean scores ($m=16.33$, $se=2.24$), followed by the British AD group ($m=22.80$, $se=1.08$), Caribbean control ($m=23.66$, $se=1.22$) and British control ($m=28.50$, $se=.33$) who

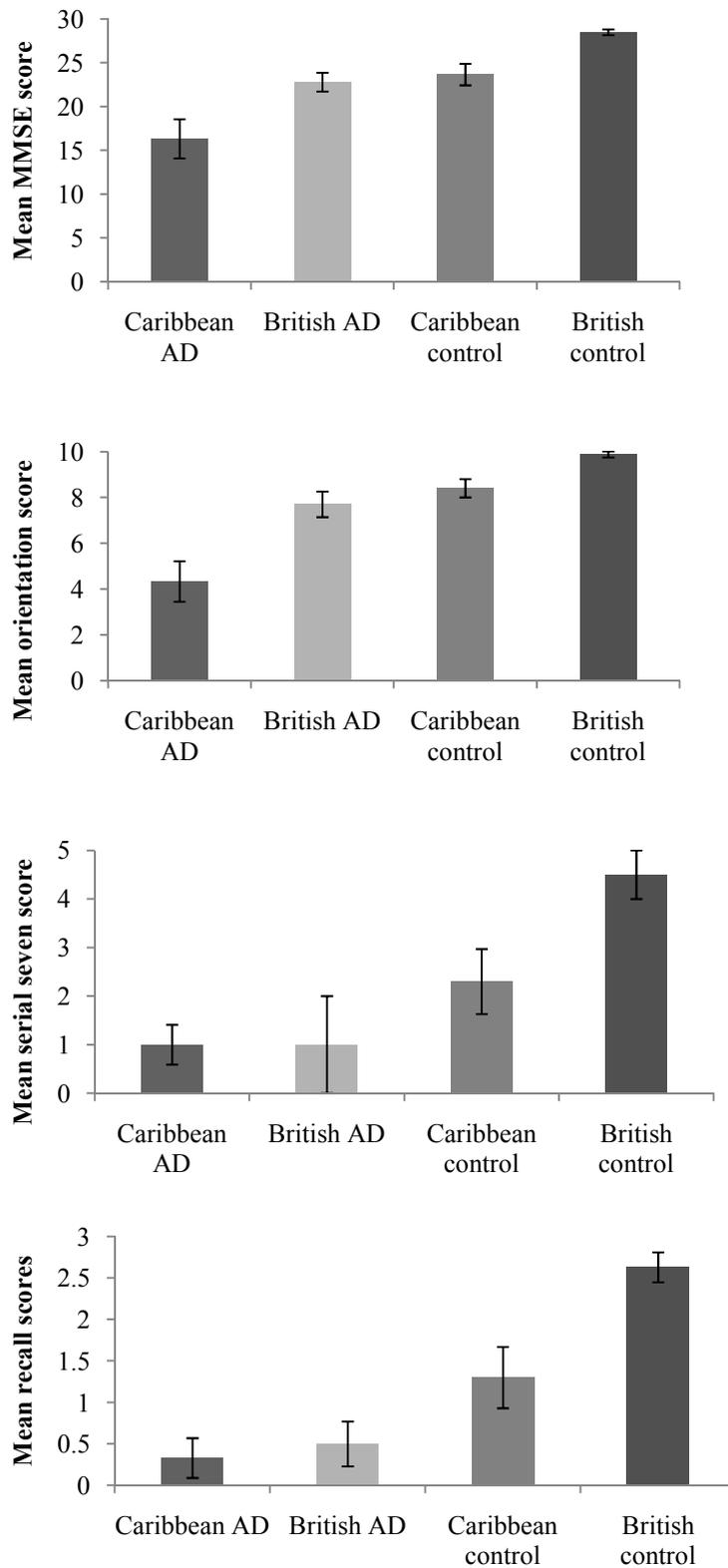


Figure 4.11 Graphs comparing groups for MMSE score, orientation, serial sevens and recall scores

had the highest mean. Significant group differences were observed between the British control and both AD groups, between the British AD and Caribbean AD groups, between the Caribbean control and Caribbean AD groups, but not the Caribbean control and British AD.

4.1.10.5 DISCUSSION

Total MMSE distinguished groups based on AD status in which patients had lower scores than controls. Three items: orientation, serial sevens and recall were successful in distinguishing the patient group from the healthy group while other items: registration, naming, repetition, 3-stage command, reacting and copying failed to do so. This suggests that some items on the MMSE may be more sensitive at detecting impairment than others. This has long been noted in the literature as some researchers point out that shortened versions of the MMSE can be just as accurate as the long form (Schult-Larsen et al, 2007). Comparison of group performance also shows that of the two AD groups, the Caribbean group performed significantly worse on total MMSE and orientation. One explanation for this may pertain to the lack of information on onset or severity of disease. Caribbean persons tend to seek treatment at later stages of the disease and as such, the patients in this sample may have a greater disease burden implying greater impact on cognitive performance.

Ethnicity had an effect on total MMSE scores as well as orientation, spelling backwards, recall and writing in which Caribbean persons had lower scores. The findings for an ethnicity effect for total MMSE scores and recall are similar to those found in study 1 and as such a similar explanation may be advanced by examining the educational level of the sample. This elderly sample had an average of less than 10 years of education and as previously discussed, ethnicity effects are more prominent in groups with low education. As previously discussed, years of education

may not capture the quality or experience of the type of education received. Given the mean age of the participants (75.76 years), it is also reasonable to assume that during the period when these adults were receiving education (the 1930s, 1940s and 1950s), the standards across the two countries would have been very different. While the Trinidad and Tobago education system largely mirrors the British system due to the colonial past, it only achieved universal primary education in the 1960s after gaining national independence from the United Kingdom and as such elderly persons may have had limited educational opportunities prior to this time.

This explanation may also account for the performance of the Caribbean control group. Whereas scores of the British control group were significantly better than the British AD group and Caribbean AD group for total MMSE, serial sevens and recall items, the Caribbean control groups showed similar scores to the British AD group. Thus the MMSE failed to distinguish between healthy Caribbeans and British AD patients. One explanation for the poorer performance among Caribbean elderly may relate to cultural differences in attitudes to ageing. As discussed in Chapter 2, in societies where the elderly assume less functional responsibility, changes in performance may be harder to detect. This finding emphasizes the need for norms and cut-off scores that are appropriate for elderly Caribbean populations.

4.1.11 STUDY 4

ACCOUNTING FOR AGE, EDUCATION, GENDER AND ETHNICITY EFFECTS ON PERFORMANCE ON THE MMSE: A STANDARDIZATION STUDY

4.1.11.1 AIM

The objectives of this study are to:

1. Establish standardised scores for the MMSE based on age, gender, years of education and ethnicity.

4.1.11.2 METHOD

4.1.11.2.1 Participants

The participants are the same as described in Section 4.1.10.2.1

4.1.11.2.2 Materials

The MMSE was administered to all participants.

4.1.11.2.3 Procedure

The procedure is the same as that described in Study 1, Section 4.1.10.2.3

4.1.11.3 STATISTICAL ANALYSIS

The adjustment of scores was based on the procedure described by Capitani (1997) in which a linear regression model was applied to the MMSE scores to adjust for the effects of the significant predictors. This approach has been adopted in a number of normative studies (Rizzo et al, 2002; Anselmetti et al, 2008; Caffara et al,

2002; Caffara et al, 2003; Caffara et al, 2004). The demographic variables need not have a linear relationship to the model and may prove to be better predictors after either a logarithmic transformation or a square root transformation. The predictors in this analysis included age in years, gender, education (years of education) and ethnicity. Preliminary processing involved different transformations of the demographic variables, using the raw score, logarithmic score or square root. The final variables entered into the model were the ones that best approximated a linear distribution.

An adjusted score was calculated by adding or subtracting the contribution of each significant predictor to account for the influence of each. Correction grids were then generated to provide correction factors to adjust the scores for new persons performing the task.

Tolerance limits were calculated to determine a cut-off score to establish the range of normal performance. The cut-off indicates the score below which the probability that the person belongs to the normal population is less than 0.05 with a confidence level of 95%.

Equivalent scores were calculated by transforming adjusted scores into a 5-point interval scale from 0 to 4 with 0 corresponding to the cut-off score and 4 to the median score. The equivalent scores allow comparison across different tests.

4.1.11.4 RESULTS

The overall adjusted mean score for the MMSE was 28.25 (sd=2.34) with scores ranging from 18.00 to 30. The variables selected for entry into the regression model were the logarithm of age, logarithm of gender, education and ethnicity. Significant predictors were identified as education and ethnicity. The logarithmic

transformation of age and a logarithmic transformation of gender failed to significantly influence performance.

A formula for correction was obtained as follows:

$$\begin{aligned} \text{Corrected MMSE score} = & \text{Raw score} + [-(0.593) (\text{Education}^* - 14.12)] \\ & + [-(0.312) (\text{Ethnicity}^{**} - 1.53)] \end{aligned}$$

*Years of education **Caribbean ethnicity coded as 1, British coded as 2

The formula above allows for calculation of individual scores. Tolerance limits defined a cut-off score of 23.13. A frequency distribution of the adjusted MMSE scores shows a negatively skewed pattern with a median of 29.31 (interquartile range=27.3-30) (See Figure 4.12).

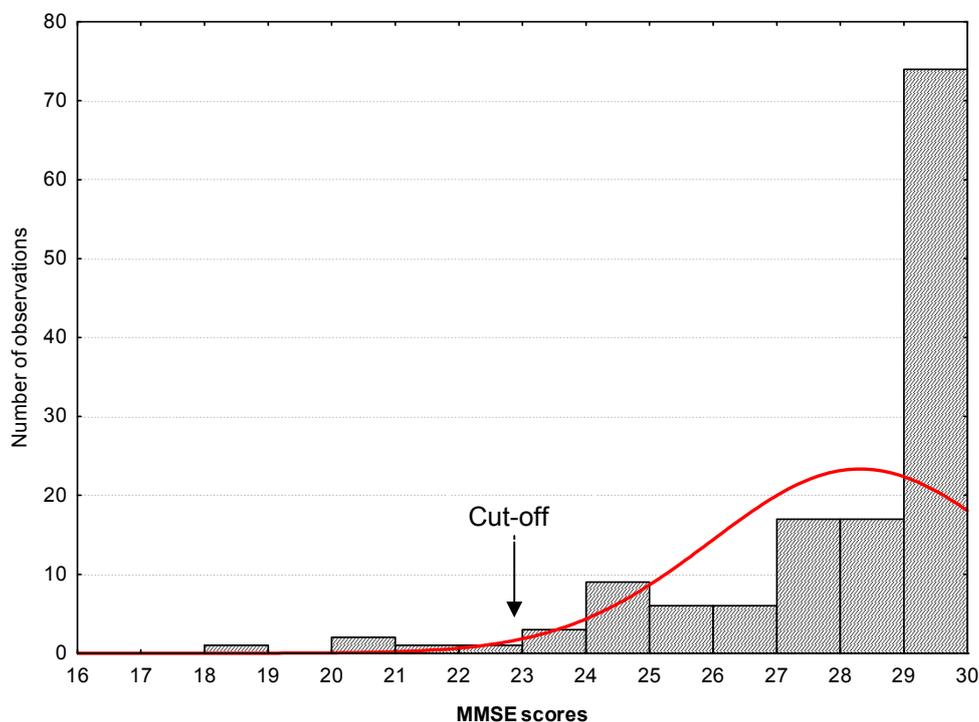


Figure 4.12 Frequency distribution of adjusted MMSE scores

A correction grid with pre-calculated values for the combined effect of the variables is shown below based on the education groups derived from the sample. See Table 4.7a. The median value of each education category was used to generate the correction grid. Equivalent scores are presented in Table 4.7b.

Table 4.7a

Correction grids for MMSE scores with adjustments based on education and ethnicity

Ethnicity	Years of Education		
	<10years	11-16 years	17-30 years
Caribbean	3.20	0.83	-3.02
British	2.89	0.52	-3.34

Table 4.7b

Equivalent scores for MMSE

Test	Equivalent Scores				
	0	1	2	3	4
MMSE	<23.13	23.14-24.67	24.68-26.22	26.23-27.76	27.76-29.31

4.1.11.5 DISCUSSION

These findings clearly indicate that MMSE scores are affected by demographic variables of education and ethnicity. The derived formula provides a means whereby the effects of education and ethnicity can be accounted for. The obtained median score of 29 is consistent with that reported by Crum who recommended that cut-off score for persons with more than 9 years of education. Given that 75% of the sample used in this study had more than 10 years of education, it seems that a median of 29 is a reliable finding. The obtained cut-off score of 23 or less is also consistent with the original cut-off of less than 24 suggested by Folstein et al (1975). The replication of this cut-off in this study also lends credence to its validity. Given the impact of education and ethnicity on score

however, it should be noted that the recommended individual scores should be adjusted to account for the relative effects of these variables before interpretation of an individual's performance is made. Adjusted scores will also enable more accurate comparisons across different groups.

4.1.12 STUDY 5

VALIDATION OF STANDARDISED MMSE SCORES

4.1.12.1 AIM

The objectives of this study are to:

1. Validate standardised scores for the MMSE in a sample of AD patients and controls.

4.1.12.2 METHOD

4.1.12.2.1 Participants

The participants are the same as described in Section 3.2.2.1

4.1.12.2.2 Materials

The MMSE was administered to all participants.

4.1.12.2.3 Procedure

The procedure is the same as that described in Study 1, Section 3.2.2.3

4.1.12.3 STATISTICAL ANALYSIS

Corrections to MMSE scores were calculated using the formula derived in Study 4. Patients and controls were classified according to AD status based on their

raw MMSE scores and corrected MMSE scores and classified as impaired or non-impaired using a cut-off scores of 23 or less. Specificity and sensitivity rates were calculated for raw MMSE scores and the corrected MMSE scores.

4.1.12.4 RESULTS

Raw scores on the MMSE successfully identified 65% of patients and 60% of non-patients with a false positive rate of 40%. Corrected MMSE scores successfully identified 50% of patients and 95% of non-patients with a false positive rate of 5%. This represents a 15% decrease in sensitivity, but a 35% increase in specificity with an accompanying 35% decrease in false positive rates. The sensitivity, specificity and false positive rates for both sets of scores are shown in the graph below.

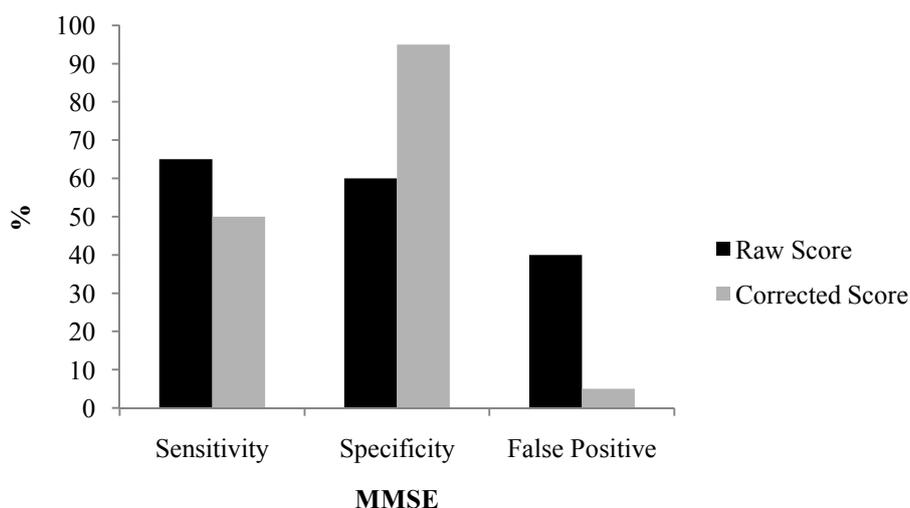


Figure 4.13 Sensitivity, specificity and false positive rates for raw and corrected MMSE scores.

4.1.12.5 DISCUSSION

Sensitivity and specificity rates for the raw MMSE were quite moderate with a high false positive rate of 40%. The adjustment of the MMSE scores resulted in a decrease in sensitivity; however these rates are still comparable to those observed in the literature in which there is a great amount of variability due to education and

severity of disease. As noted by O'Bryant et al (2008) the use of the traditional cut-off in highly educated persons results in lowered sensitivity which can be rectified by using a higher cut-off score. As such, the development of cut-off scores stratified for years of education may prove useful.

The corrected scores had a considerable impact on specificity rates, with a 35% increase in specificity to 95% which is slightly higher than that reported in the literature (e.g. 85% by Tombaugh et al, 1996). The adjusted scores thus greatly improve the test's ability to correctly rule out persons without impairment. The very low false positive rate of 5% suggests that the corrected MMSE scores will result in far fewer persons being subjected to unnecessary and costly further assessment procedures.

4.2 THE ALZHEIMER'S DISEASE ASSESSMENT SCALE- COGNITIVE SECTION (ADAS-COG)

4.2.1 THE ALZHEIMER'S DISEASE ASSESSMENT SCALE (ADAS-COG)

The MMSE and the Alzheimer's Disease Assessment Scale- cognitive section (ADAS-cog) are two of the most widely used instruments globally in the screening of dementia. It is thought that the MMSE is not sensitive enough to detect small changes in cognitive performance that may occur during the course of dementia (Tombaugh and McIntyre, 1992). The Alzheimer's disease Assessment Scale (ADAS) was published in 1984 by Rosen, Mohs and Davis and was designed specifically for use in evaluating the cognitive and non-cognitive behavioural symptoms associated with AD. Rockwood et al (2007, pg 1) describe the ADAS-cog as the '*de facto* standard primary outcome neuropsychological measure for AD trials'. By 2009, Cano et al (2010) reported that the ADAS-cog had been used in over 127 clinical trials for AD but its use has also been extended to other conditions including mild cognitive impairment (Farlow et al, 2004), vascular dementia (Malouf and Birks, 2004) and Parkinson's disease (Emre et al, 2004). The ADAS-cog is widely regarded as the standard for evaluating cognitive performance in clinical drug trials (e.g tacrine, donepezil, rivastigmine, ginkgo, memantine, galantamine and metrifonate) worldwide (Rogers et al, 1996; Rogers et al, 1998; Burns et al, 1999; Corey-Bloom et al, 1998; Forette et al, 1999; Rosler et al, 1999; .Rockwood et al, 2001).

The ADAS consists of two sections: a cognitive subscale (ADAS-cog) and a non-cognitive subscale. The non-cognitive component includes an assessment of tearfulness, depressed mood, psychosis, concentration, cooperation, gait, agitation,

Table 4.8

Description of Items on ADAS-Cog

Item	Score	Description
Word Recall	10	3 trials of 10-word list learning task. Score is average number of words not recalled
Naming Objects and Fingers	5	Subject shown and asked to name 12 objects: flower, bed, whistle, pencil, rattle, mask, scissors, comb, wallet, harmonica, stethoscope, tweezers Subject then asked to name fingers on dominant hand
Commands	5	Subject asked to perform five commands. E.g. point to the ceiling and then to the floor
Constructional Praxis	5	Reproduction of circle, two overlapping rectangles, diamond and cube
Ideational Praxis	5	Subject instructed to fold letter, insert into envelope, seal and address envelope and indicate position of stamp.
Orientation	8	Subject asked to indicate full name, day, month, year, season, time of day, place
Word Recognition	12	3 trials of 12-word recognition task
Word recognition reminders	5	Number of reminders needed for word recognition
Spoken language ability	5	Rating of quality of speech, e.g. clarity
Word finding difficulty	5	Rating of difficulty in finding desired words e.g. circumlocutions
Comprehension	5	Rating of ability to understand speech
Concentration/Distractibility	5	Rating of frequency of distraction by irrelevant stimuli and/or need to be re-oriented to task

motor activity, tremors and change in appetite (Davis et al, 1992; Mohs, 1996; Rosen et al, 1984). The ADAS-cog consists of 7 items that are administered and 5 items that are assessed by the examiner based on observation of the patient. These items assess memory (word recall and word recognition, rating ability to remember test instructions), constructional and ideational praxis, expressive and receptive language (including word finding difficulty and naming) and orientation (Mohs, 1996; Pena-Cassanova, 1997). A description of all the items is listed in Table 4.8.

Administration time may range from 30 to 45 minutes depending on the severity of dementia (Zec et al, 1992). Scores on the ADAS-cog range from 0 to 75 and are based on errors with a higher score indicating worse performance. Graham et al (2004) found a mean ADAS-cog score of 5.0 in a sample of healthy elderly aged 55 to 89 while Zec et al (1992) report mean scores of 5.5. Scores equal to or exceeding 18 are usually interpreted as indicating cognitive impairment (Rosen et al, 1984; Rockwood et al, 2007). Wouters et al (2009) attempted a comparison of the MMSE and ADAS-cog and using an estimated common dimension of global impairment, they suggested that a mean level of global cognitive impairment would correspond to a score of 22.5 on the MMSE and 11.4 on the ADAS-cog. After making adjustments for age and education, Monllau et al (2007) report sensitivity and specificity values for the ADAS-cog, using a cut-off score of greater than or equal to 12, as 89.19% and 88.53% respectively.

The ADAS-cog is normally used in elderly and clinical populations and is primarily used as measurement of drug efficacy and to assess change over time ((Rogers et al, 1996; Rogers et al, 1998; Burns et al, 1999; Corey-Bloom et al, 1998; Forette et al, 1999; Rosler et al, 1999; .Rockwood et al, 2001; Wilkinson et al, 2001). Few studies examine ADAS-cog performance in normal persons and even fewer examine performance on individual items. Zec et al (1992).

4.2.2 ADAS-COG AND AGE

Studies using the ADAS-cog tend to involve older samples. There are mixed findings on the effects on age which seem to depend on whether the sample comprises healthy adults or clinical patients. For example, Fioravanti et al (1994) found no effect of age in an Italian sample of 95 volunteers aged 50 to 79 years, whereas Doraiswamy et al (2001) reported a significant but small effect of age ($r=-$

.09) in a sample of 536 AD patients with a mean age of 71.6 years ranging from 45 to 80 years. Pena-Cassanova (1997) reports a significant effect of age with an increase by 1 point in ADAS-cog score for every 10 years of age starting at age 40.

4.2.3 ADAS-COG AND EDUCATION

The ADAS-cog appears to be less influenced by education than the MMSE but an effect may still exist in which lower levels of education are associated with worse ADAS-cog performance (Weyer et al, 1997). Zec et al (1992) found no effects of education on ADAS-cog scores in both normal and clinical samples however they explained that it may have been due to the narrow range of education found in their sample. Kolibas et al (2000) investigated a sample of elderly Slovaks and found the ADS-cog to be less influenced by education than the standardised MMSE (SMMSE) (Molloy and Standish, 1997). While patients with higher levels of education had higher scores than those with fewer years of education, the difference was not found to be significant. This however may be the result of the low range of education (6 to 8 years) found among the patients in that sample.

Other studies report significant effects of education. In a retrospective study, Doraiswamy et al (1995) found a significant impact of education on ADAS-cog scores in 444 patients with AD. They also examined the scores of a subset of the 138 placebo AD patients 12 weeks later and found that the effect of education was still significant. A significant effect of years of education was also found in an Italian sample of healthy adults aged 50 to 79 years (Fioravanti et al, 1994). Pena-Cassanova (1997) also reports a significant effect of education on ADAS-cog scores with an average decrease of 1 point for every 5 years of formal education.

There may also be an interaction between AD status and education in which there may be an overlap of scores between high education demented patients and low educated non-demented patients (Schultz et al, 2001). The authors also examine ADAS-cog item scores and note differences in performance according to education level (0-4 years, 5-11 years, over 12 years). In a control group, scores differed by educational levels for naming objects and fingers, commands, constructional praxis, ideational praxis, remembering test instructions and total ADAS-cog score.

4.2.4 ADAS-COG AND GENDER

Significant effects of gender on ADAS-cog scores are not usually found although Doraiswamy et al (1997) report better performance among males. However the majority of studies report no gender differences (Fioravanti et al, 1994; Weyer et al, 1997; Doraiswamy et al, 1997; Stern et al, 1994; Schultz et al, 2001; Graham et al, 2004).

4.2.5 ADAS-COG AND ETHNICITY

The ADAS-cog is generally regarded as being culture-free as ethnicity is thought to have little impact on ADAS-cog scores (Graham et al, 2004; Wicherts et al, 2009). Graham et al. obtained mean scores of 5.0 in a sample of white Americans. They compared their results with two other studies: one comprising an entirely Chinese sample (Liu et al 2002) and another comprising a sample of mixed ethnicities including white, African American, Hispanic, Asian American and American Indian (Grundman et al, 2004) and found no significant differences between the groups.

However, Chiu and Lam (2007) advocate for more studies to assess the role of ethnicity in assessment. They emphasize the difficulties faced in conducting

clinical trials in developing countries and highlight challenges such as linguistic and cultural diversity, high illiteracy, few human resources and time constraints. They also suggest that due to the prohibitive costs of neuroimaging and the use of other biological markers, the use of functional outcome measures like the ADAS-cog becomes increasingly useful in developing countries. Most assessment instruments for dementia (like the ADAS-cog) were designed in developed countries and their use in developing countries is under-researched. However, the increasing prevalence of dementia in developing countries necessitates more global studies which recruit patients from wide range of populations. Schindler (2010) acknowledges however that as more global clinical trials take place in countries which have not previously been included in studies, the challenges associated with cross cultural assessment will become more apparent.

4.2.6 ADAS-COG AND DEMENTIA

Scores on the ADAS-cog can differentiate between healthy persons and clinically diagnosed AD patients and can also be used to track changes in across time (Rosen et al, 1984; Kramer-Ginsberg et al, 1988; Zec et al, 1992). The ADAS-cog may also be used to stage AD with four suggested levels of dementia with mean scores as follows: very mild = 23.1, (sd= 7.7), mild = 22.9, (sd= 8.9), moderate = 38.6 (sd= 9.8) and severe = 54.8 (sd= 7.6) (Zec et al, 1992).

Longitudinal analyses show AD patients deteriorating on average at a rate of 9.55 points on the ADAS-cog per year, AD patients on placebo at a rate of 8 points while non-demented persons gain an average of 0.23 points per year (Stern et al, 1994). Ito et al (2010) conducted a meta-analysis of clinical trials and used the change in baseline ADAS-cog scores in mild and moderate AD patients to estimate the progression of the disease. Progression was thought to occur at a rate of 5.5

points per year and the rate did not differ between placebo and acetylcholinesterase inhibitor treatment groups. They noted that baseline ADAS-cog was a significant covariate in which affected disease progression and this has also been reported by other authors. Zec et al (1992) stated rate of change in ADAS-cog scores may vary with disease severity and patients with more severe impairment at initial measurement show slower rates of change in scores than patients with less impairment. Changes in ADAS-cog scores in clinical trials have also been proposed as surrogate markers for long-term prognosis in which fast decliners who experienced a change in score of 7 or more points in 6 months had an increased risk of severe dementia or death within two years (Helmer et al, 2007).

The ADAS-cog is considered more precise in detecting mild cognitive impairment than the MMSE and the Blessed IMC (Information, Memory, Concentration) test (Burch and Andrews, 1987; Mohs, 1996; Wouters et al, 2010). Zec et al (1992) found the orientation item and total score to be the best indicators of severity of dementia. ADAS-cog scores may also differentiate AD from other disorders. Kolibas et al (2000) found significantly higher scores among AD patients than depressed patients.

4.2.7 STUDY 6

INVESTIGATING THE EFFECTS OF AGE, GENDER, EDUCATION AND ETHNICITY ON PERFORMANCE ON THE ADAS-COG

4.2.7.1 AIM

The objectives of this study are to:

1. Identify the influence of age, gender, education and ethnicity on performance on ADAS-cog and individual items.

4.2.7.2 METHOD

4.2.7.2.1 Participants

In this study, 82 participants (female= 47, male=35) from Trinidad and Tobago (n=41) and England (n=41) were assessed. The sample ranged in age from 19 to 87 years (m=46.83, sd=19.14) and years of education ranged from 3 to 30 years (m=14.63, sd=5.92). All participants were functionally independent, and those with any neurological or psychiatric impairment were excluded.

4.2.7.2.2 Materials

The ADAS-cog (Rosen et al, 1984) was administered to all participants. A list of the items is described in Table 4.8

4.2.7.2.3 Procedure

The ADAS-cog was administered to all participants in the listed order. See Table 4.8

4.2.7.3 DESIGN AND STATISTICAL ANALYSIS

Regression analyses were also performed to determine the contribution of age, gender, education and ethnicity to total ADAS-cog and item scores.

4.2.7.4 RESULTS

4.2.7.4.1 ADAS-cog total

Scores on the ADAS-cog had a mean of 3.98 (sd=3.28), and ranged from 0 to 18. See Table 4.9 for the means and standard deviations of all ADAS-cog items. The correlations between individual items are shown below in Table 4.10 and the correlations between ADAS-cog items and the predictors are shown in Table 4.11.

Table 4.9

Means, standard deviation and range for performance on all ADAS-cog items

	Minimum	Maximum	Mean	Std. Dev
Word Recall	0	7	2.51	1.709
Naming Objects and Fingers	0	2	.30	.489
Commands	0	1	.05	.217
Constructional Praxis	0	3	.34	.613
Ideational praxis	0	2	.07	.306
Orientation	0	3	.11	.416
Word Recognition Task	0	4	.57	.903
Word Recognition Reminders	0	3	.04	.331
Spoken Language Ability	0	0	.00	.000
Word-Finding Difficulty	0	0	.00	.000
Comprehension	0	0	.00	.000
Concentration/Distractibility	0	0	.00	.000
ADASCOG total score	0	18	3.98	3.281

Total ADAS-cog scores were significantly correlated with all individual items with the exception of commands. Of the four predictors, significant correlations were observed for age and education but not gender or ethnicity. Increasing age and fewer years of education were associated with worse ADAS-cog performance.

A forced entry regression analysis with predictors: age, gender, education and ethnicity produced a significant model ($F(4, 77)=18.06, p<0.001$). Of the four predictors, age, and education made significant contributions to the overall model. Gender and ethnicity were not significant predictors. A stepwise regression analysis was then performed with age and education as the only predictors and a significant model emerged ($F(2,79)=36.99, p<0.001$) which accounted for 48% ($R^2=.48$), of the variance in performance. Age significantly predicted total ADAS-cog scores, $\beta=.48, t(79) = 5.05, p<0.001$ and accounted for 41%, of the variance in scores. Education accounted for a further 7% of the variance, $R^2 = .07, \beta=-.31, t(79) = -3.27, p=0.002$. The regression model is shown in Table 4.13.

Table 4.10

Table showing correlations between ADAS-cog items

	Naming	Commands	Constructional Praxis	Ideational Praxis	Orientation	Word Recognition	Word Recognition Reminders	ADAS-cog Total
Word Recall	.259*	.067	.394**	.382**	.293**	.387**	.107	.819**
Naming		.012	.400**	.436**	.326**	.445**	.162	.580**
Commands			.101	-.049	.104	-.052	-.022	.106
Constructional Praxis				.390**	.381**	.345**	.302**	.653**
Ideational Praxis					.323**	.438**	-.028	.581**
Orientation						.399**	-.031	.549**
Word Recognition							.307**	.732**
Word Recognition Reminders								.314*

** $p < 0.01$ *Spoken Language ability, Word-finding difficulty, Comprehension, Concentration/ Distractibility* values not computed because of low variability

Table 4.11

Table showing correlations between ADAS-cog items and predictors

	Recall	Naming	Commands	Constructional Praxis	Ideational Praxis	Orientation	Word Recognition	Word Recognition Reminders	ADAS-cog Total
Age	.639**	.333**	.210	.438**	.436**	.329**	.283*	.185	.645**
Gender	-.123	.017	.039	.209	.048	-.129	-.104	.098	-.055
Ethnicity	.176	-.156	.024	-.082	-.061	.100	-.080	-.07	.034
Education	-.432**	-.559**	-.108	-.476**	-.436**	-.319**	-.319**	-.106	-.567**

* $p < 0.05$, ** $p < 0.01$

Spoken Language ability, Word-finding difficulty, Comprehension, Concentration/ Distractibility values not computed because of low variability

4.7.4.2 Word Recall

The mean score for word recall was 2.51 (sd=1.71), and ranged from 0 to 7. Word recall scores were significantly correlated with all individual items with the exception of commands, word recognition reminders and remembering test instructions. Of the four predictors, significant correlations were observed for age and education but not gender or ethnicity. Increasing age and fewer years of education were associated with worse word recall performance.

A forced entry regression analysis with predictors: age, gender, education and ethnicity produced a significant model ($F(4, 77)=14.96, p<0.001$). Of the four predictors, age made a significant contribution to the overall model. Gender, ethnicity and education were not significant predictors. A stepwise regression analysis was then performed with age as the only predictor and a significant model emerged ($F(1, 80)=50.90, p<0.001$) which accounted for 38% ($R^2=.38$), of the variance in performance. Age significantly predicted word recall scores, $\beta=.62, t(80) = 7.14, p<0.001$. The regression model is shown in Table 4.13.

4.2.7.4.3 Naming Objects and Fingers

The mean score for naming was 0.3 (sd=0.49), and ranged from 0 to 2. Naming objects and fingers were significantly correlated with all individual items with the exception of commands and word recognition reminders. Of the four predictors, significant correlations were observed for education but not age, gender or ethnicity. Fewer years of education were associated with worse performance on naming.

A forced entry regression analysis with predictors: age, gender, education and ethnicity produced a significant model ($F(4, 77)=10.25, p<0.001$). Of the four

predictors, education made a significant contribution to the overall model. Age, gender and ethnicity were not significant predictors. A stepwise regression analysis was then performed with education as the only predictor and a significant model emerged ($F(1,80)=36.89$, $p<0.001$) which accounted for 32% ($R^2=.32$), of the variance in performance, ($\beta=-.56$, $t(80) = -6.07$, $p<0.001$). The regression model is shown in Table 4.13.

4.2.7.4.4 Commands

The mean score for commands was 0.05 ($sd=0.22$), and ranged from 0 to 1. Command scores were not significantly correlated with any of the ADAS-cog items or any of the predictors. A forced entry regression analysis with predictors: age, gender, education and ethnicity failed to produce a significant model. The regression model is shown in Table 4.13 below.

4.2.7.4.5 Constructional Praxis

Scores on constructional praxis had a mean of .34 ($sd=.61$), and ranged from 0 to 3 (see Table 4.9). Constructional praxis performance was significantly correlated with all individual items with the exception of commands. Of the four predictors, significant correlations were observed for age and education but not gender or ethnicity. Increasing age and fewer years of education were associated with worse performance on constructional praxis (see Table 4.10 and Table 4.11).

A forced entry regression analysis with predictors: age, gender, education and ethnicity produced a significant model ($F(4, 77)=10.12$, $p<0.001$). Of the four predictors, age, education and gender made significant contributions to the overall model. Ethnicity was not a significant predictor. A stepwise regression analysis was then performed with age, education and gender as predictors and a significant model

emerged ($F(3,78)=12.13$, $p<0.001$) which accounted for 32% ($R^2=.32$), of the variance in performance. Education significantly predicted constructional praxis scores, $\beta=-.32$, $t(78)=-2.92$, $p=0.005$ and accounted for 23%, of the variance in scores. Age accounted for a further 4% of the variance, $R^2=.04$, $\beta=.28$, $t(78)=2.53$, $p=0.013$ and gender accounted for 5% of the variance in constructional praxis scores $R^2=.05$, $\beta=.22$, $t(78)=2.36$, $p=0.02$. The regression model is shown in Table 4.13.

4.2.7.4.6 Ideational Praxis

Scores on ideational praxis had a mean of 0.07 ($sd=.61$), and ranged from 0 to 2 (see Table 4.9). Ideational praxis performance was significantly correlated with all individual items with the exception of commands and word recognition reminders. Of the four predictors, significant correlations were observed for age and education but not gender or ethnicity. Increasing age and fewer years of education were associated with worse performance on constructional praxis (see Table 4.10 and Table 4.11).

A forced entry regression analysis with predictors: age, gender, education and ethnicity produced a significant model ($F(4, 77)=6.80$, $p<0.001$). Of the four predictors, age and education made significant contributions to the overall model. Gender and ethnicity were not significant predictors. A stepwise regression analysis was then performed with age and education as predictors and a significant model emerged ($F(2, 79)=12.78$, $p<0.001$) which accounted for 24% ($R^2=.24$), of the variance in performance. Education significantly predicted ideational praxis scores, $\beta=-.29$, $t(79)=-2.52$, $p=0.014$ and accounted for 19%, of the variance in scores. Age accounted for a further 5% of the variance, $R^2=.05$, $\beta=.28$, $t(79)=2.40$, $p=0.019$. The regression model is shown in Table 4.13.

4.2.7.4.7 Orientation

Orientation scores had a mean of 0.11 ($sd=.42$), and ranged from 0 to 3 (see Table 4.9). Orientation performance was significantly correlated with all individual items with the exception of commands and word recognition reminders. Of the four predictors, significant correlations were observed for age and education but not gender or ethnicity. Increasing age and fewer years of education were associated with worse performance on orientation (see Table 4.10 and Table 4.11).

A forced entry regression analysis with predictors: age, gender, education and ethnicity produced a significant model ($F(4, 77)=3.47, p=0.012$). However, none of the four predictors, age and education made individual significant contributions to the overall model.

4.2.7.4.8 Word Recognition

Word recognition scores had a mean of 0.57 ($sd=.90$), and ranged from 0 to 4 (see Table 4.9). Performance on word recognition was significantly correlated with all individual items with the exception of commands. Of the four predictors, significant correlations were observed for age and education but not gender or ethnicity. Increasing age and fewer years of education were associated with worse performance on word recognition (see Table 4.10 and Table 4.11).

A forced entry regression analysis with predictors: age, gender, education and ethnicity produced a significant model ($F(4, 77)=3.12, p=0.02$). However, none of the four predictors, age and education made individual significant contributions to the overall model.

4.2.7.4.9 *Word recognition reminders*

Word recognition reminders had a mean of 0.04 (sd=.33), and ranged from 0 to 3 (see Table 4.7.1. Performance on word recognition reminders was significantly correlated with two items: constructional praxis and word recognition. There were no significant correlations with any of the predictors (see Table 4.7.2 and Table 4.7.3). A forced entry regression analysis with predictors: age, gender, education and ethnicity failed to produce a significant model. The regression model is shown in Table 4.13.

4.2.7.4.10 *Spoken Language ability, Word finding difficulty, Comprehension, Concentration/Distractibility*

All participants in the sample scored 0 for the items: performance on spoken language ability, word finding difficulty, comprehension and concentration/distractibility. Due to the lack of variability in scores, no correlation coefficients or regression analyses could be computed. See Table 4.13.

A summary of the significant predictors for the ADAS-cog are shown in Table 4.12.

Table 4.12

Significant predictors from regression analyses for MMSE items

Item	Age	Gender	Education	Ethnicity
ADAS-cog total	√	-	√	-
Word Recall	√	-	√	-
Naming Objects and Fingers	-	-	√	-
Commands	-	-	-	-
Constructional Praxis	√	√	√	-
Ideational Praxis	√	-	√	-
Orientation	-	-	-	-
Word Recognition	-	-	-	-
Word Recognition Reminders	-	-	-	-
Spoken Language Ability	*	*	*	*
Word Finding Difficulty	*	*	*	*
Comprehension	*	*	*	*
Concentration/Difficulty	*	*	*	*

*=not computed, - = p=NS, √= p<0.05

Table 4.13 continued

Multiple Regression Analysis- unstandardised and standardized coefficients for the ADAS-cog

Item			B	SE B	β	R ²
Ideational Praxis	Model(Enter)	(Constant)	.13	.18		
		Age	.01	.00	.30	
		Gender	.05	.06	-.11	
		Ethnicity	-.07	.07	-.11	
		Years of Education	-.02	.01	-.28	.26*
	Model (Stepwise)	(Constant)	.09	.15		
		Years of Education	-.02	.01	-.29	.19*
Orientation	Model(Enter)	(Constant)	.11	.26		
		Age	.00	.00	.19	
		Gender	-.10	.09	-.12	
		Ethnicity	.06	.10	.07	
		Years of Education	-.02	.01	-.22	.15*
Word Recognition	Model(Enter)	(Constant)	.99	.57		
		Age	.01	.01	.18	
		Gender	-.21	.20	-.12	
		Ethnicity	-.15	.21	-.08	
		Years of Education	-.03	.02	-.22	.14*
Word Recognition reminders	Model(Enter)	(Constant)	-.01	.24		
		Age	.01	.00	.24	
		Gender	.08	.08	.11	
		Ethnicity	-.11	.09	-.14	
		Years of Education	-.00	.01	-.05	.09*
Spoken Language Ability	-	-	-	-	-	-
Word Finding Difficulty	-	-	-	-	-	-
Comprehension	-	-	-	-	-	-
Concentration Distractibility	-	-	-	-	-	-

*p<0.05, - analysis unable to be computed

4.2.7.5 DISCUSSION

Mean scores on the ADAS-cog for this sample were 3.98. This is smaller than the reported figures of 5.0 in other healthy samples (Graham et al, 2004). While both samples had a similar mean level of education, this study employed a wider age range and a younger sample. Since increasing age may be associated with worse performance (Doraisawamy et al, 2001; Pena-Cassanova, 1997), this may account for the fewer number of errors reported in this study. This interpretation is also corroborated by the finding that age was the most influential of the predictors of ADAS-cog scores and explained 41% of variance in performance.

Gender differences were not found on the total ADAS-cog scores or on most of the individual tests with the exception of one- constructional practice. This lack of a gender effect is consistent with the majority of the literature (Fioravanti et al, 1994; Pascual et al, 1997; Weyer et al, 1997; Doraiswamy et al, 1997; Stern et al, 1994; Schultz et al, 2001; Graham et al, 2004)

The inverse effect of education on ADAS-cog scores is also consistent with other findings (Doraiswamy et al, 1995; Pena-Cassanova, 1997; Fioravanti et al, 1994) in which fewer years of education is associated with worse performance.

There was no effect of ethnicity on total ADAS-cog scores or any of the individual items. This finding is consistent with widespread views that the ADAS-cog is culture-free, however the findings of this study have established that this assertion is also valid in a comparison of performance between British and Caribbean persons.

4.2.8 STUDY 7

ADAS-COG PERFORMANCE IN ELDERLY AD PATIENTS AND NON-PATIENTS

4.2.8.1 AIM

The objectives of this study are to:

1. Assess the difference in performance on the ADAS-cog in a community and clinical sample of Caribbean and British elderly matched for age, gender and education.
2. Verify current scoring and cut-off correctly differentiate normal from abnormal performance.

4.2.8.2 METHOD

4.2.8.2.1 Participants

The participants are the same as described in section 4.2.7.2.1

4.2.8.2.2 Materials

The ADAS-cog (Rosen et al, 1984) was administered to all participants. A list of the items used is provided in Table 4.8.

4.2.8.2.3 Procedure

The ADAS-cog was administered to each participant in the listed order.

4.2.8.3 DESIGN AND STATISTICAL ANALYSIS

Univariate ANOVAs (2x2) were performed on each of the 12 dependent variables (ADAS-cog total and 11 item scores) comparing the effects of ethnicity and AD status on performance.

One way ANOVAs (1x4) were also conducted to compare the performance between the four groups, Caribbean control, British control, Caribbean AD, British AD.

4.2.8.4 RESULTS

4.2.8.4.1 2 x 2 ANOVA analysis

4.2.8.4.1.1 ADAS-cog Total

Significant main effects were observed for AD status ($F(1,37)= 35.62$, $p<0.001$ in which AD patients had higher mean scores ($m=27.51$, $se=2.33$) than the non-AD adults ($m=7.87$, $se=2.33$) There was no significant main effect of ethnicity and no significant interaction effect.

4.2.8.4.1.2 Word Recall

A significant main effect was observed for AD status ($F(1,37)= 38.57$, $p<0.001$ in which AD patients had higher mean scores ($m=7.28$, $se=.38$) than the non-AD adults ($m=4.01$, $se=.37$). There was no significant main effect of ethnicity and there was no significant interaction effect.

4.2.8.4.1.3 Naming Objects and Fingers

A significant main effect was observed for ethnicity ($F(1,37)= 14.17$, $p=0.001$ in which Caribbeans had worse performance ($m=1.00$, $se=.15$) than the British ($m=.21$, $se=.15$). There was no significant main effect of AD status and there was no significant interaction effect.

4.2.8.4.1.4 Commands

A significant main effect of AD status ($F(1,37)= 6.63$, $p=0.014$) was found in which AD patients had higher mean scores ($m=1.14$, $se=.26$) than the control adults

($m=.20$, $se=.25$). There was no significant main effect of ethnicity and there was no significant interaction effect.

4.2.8.4.1.5 Constructional Praxis

A significant main effect was observed for ethnicity ($F(1,37)= 5.33$, $p=0.027$) in which Caribbeans had worse performance ($m=1.67$, $se=.30$) than the British ($m=.67$, $se=.31$). There was no significant main effect of AD status and there was no significant interaction effect.

4.2.8.4.1.6 Ideational Praxis

There were no significant main or interaction effects of AD status or ethnicity.

4.2.8.4.1.7 Orientation

A significant main effect of AD status ($F(1,37)= 8.73$, $p=0.006$) was found in which AD patients had higher mean scores ($m=2.54$, $se=.45$) than the non-AD adults ($m=.70$, $se=.43$). There was no significant main effect of ethnicity and there was no significant interaction effect.

4.2.8.4.1.8 Word Recognition

Significant main effects were observed for AD status ($F(1,37)= 22.56$, $p<0.001$). AD patients had higher mean scores ($m=6.17$, $se=.72$) than the non-AD adults ($m=1.33$, $se=.72$). There was no significant main effect of ethnicity and there was no significant interaction effect.

4.2.8.4.1.9 Remembering Test Instructions, Spoken Language Ability, Word Finding Difficulty, Concentration, Concentration/Difficulty

Significant main effects were observed for AD status only for each of these measures in which AD patients performed worse than non-AD adults. There was no

effect of ethnicity and no significant interaction effects. The means for performance as well as the ANOVA results are listed in Table 4.14.

Table 4.14

Means and F-values for observed items of ADAS-cog

Item	AD		Non-AD		F	p-value
	Mean	SE	Mean	SE		
Word recognition reminders	2.94	.41	.22	.41	29.43	<.001
Spoken language ability	.94	.19	.00	.19	12.28	.001
Word finding difficulty	.99	.22	.00	.17	15.14	<.001
Comprehension	1.04	.22	.05	.22	8.82	.005
Concentration/Distractibility	1.18	.23	.00	.23	13.209	.001

4.2.8.4.2 Oneway ANOVA

Significant group differences were noticed in several ADAS-cog items: total ADAS-cog scores ($F(3,37)=12.97$, $p<0.001$), word recall ($F(3,37)=13.14$, $p<0.001$), naming objects and fingers ($F(3,37)=4.90$, $p=0.006$), orientation ($F(3,37)=4.02$, $p=.015$), word recognition ($F(3,37)=9.32$, $p<0.001$) and all of the observed items: word recognition reminders ($F(3,37)=7.57$, $p<0.001$), spoken language ability ($F(3,37)=4.41$, $p=.010$), word finding difficulty ($F(3,37)=6.01$, $p=.002$), comprehension ($F(3,37)=3.32$, $p=.031$), and concentration/distractibility ($F(3,37)=6.25$, $p=.002$). Post hoc analyses revealed significant differences between groups and the results for the administered tasks will be presented below. No significant differences were observed between groups for performance on commands, constructional praxis and ideational praxis.

4.2.8.4.2.1 ADAS-cog

The means for each group are presented in Table 4.15. Significant group differences were observed between the British control and both AD groups, between

Table 4.15

Means and standard deviations for ADAS-cog scores for AD and control groups for each ethnicity

Item	Caribbean				British			
	AD		Non-AD		AD		Non-AD	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
ADAS-cog Total	32.11	6.28	9.40	1.83	22.90	1.38	6.33	1.58
Word Recall	7.11	.59	3.80	.47	7.44	.50	4.22	.55
Naming Fingers and Objects	1.10	.31	.90	.18	.22	.15	.20	.13
Commands	1.50	.64	.20	.13	.78	.28	.20	.13
Constructional Praxis	2.00	.65	1.33	.41	.89	.20	.44	.24
Ideational Praxis	.60	.16	.60	.22	.67	.24	.11	.11
Orientation	3.30	.79	.70	.60	1.78	.64	.70	.40
Word Recognition	7.78	1.45	1.78	.72	4.56	1.14	.89	.46
Word recognition reminders	2.67	.78	.44	.34	3.22	.85	.00	.00
Spoken language ability	1.10	.46	.00	.00	.78	.28	.00	.00
Word finding difficulty	1.20	.44	.00	.00	.67	.50	.00	.00
Comprehension	1.20	.57	.00	.00	.78	.22	.10	.10
Concentration/Distractibility	1.70	.62	.00	.00	.67	.17	.00	.00

the British AD and Caribbean AD groups, between the Caribbean control and Caribbean AD groups, but not the Caribbean control and British AD.

4.2.8.4.2.2 Total ADAS-cog

Post-hoc analyses reveal the ADAS-cog successfully differentiated between both sets of AD groups and control groups.

4.2.8.4.2.3 Recall

Post-hoc analyses reveal the ADAS-cog successfully differentiated between both sets of AD groups and control groups.

4.2.8.4.2.4 Naming Objects and Fingers

AD status failed to distinguish groups in both ethnicities. As such, Caribbean AD performance was similar to Caribbean control and British AD performance was similar to British control. While the British control group had significantly better performance than the Caribbean AD group, the Caribbean control group was not distinguished from the British AD group. See Figure 4.14.

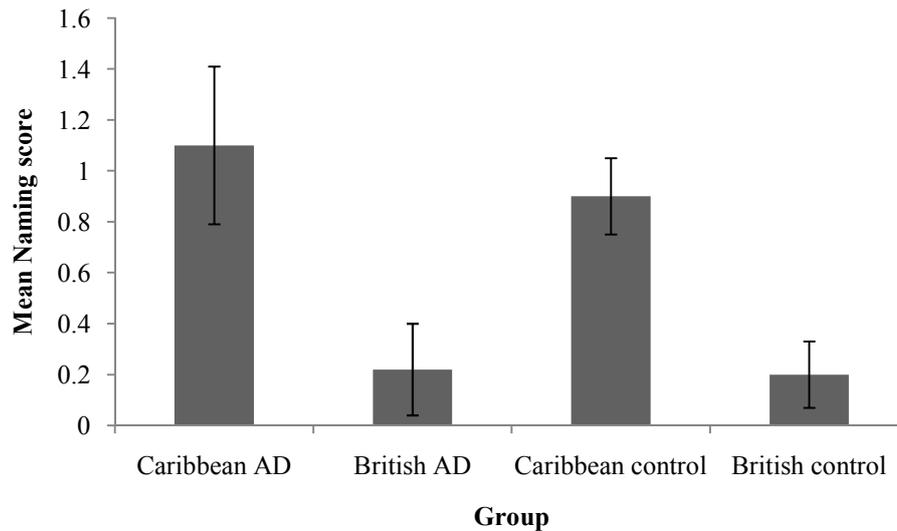


Figure 4.14 Mean naming scores for groups based on ethnicity and AD status

4.2.8.4.2.5 Orientation

The Caribbean AD group had significantly worse performance than all other groups. There was no difference between the British non-AD and Caribbean non-AD groups. There was also no difference between the British AD group and both non-AD groups.

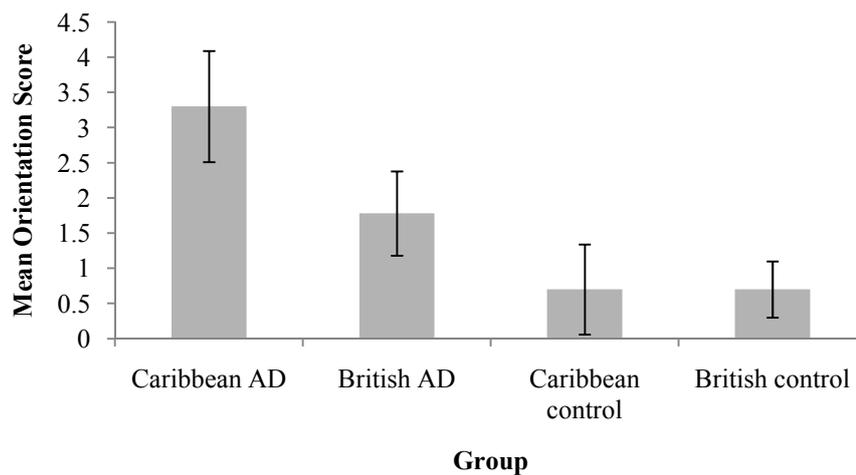


Figure 4.15 Mean orientation scores for groups based on ethnicity and AD status

4.2.8.3.2.6 Word Recognition

The Caribbean AD group had significantly worse performance than all other groups. There was no difference between the British non-AD and Caribbean non-AD groups. There was also no difference between the British AD group and both non-AD groups.

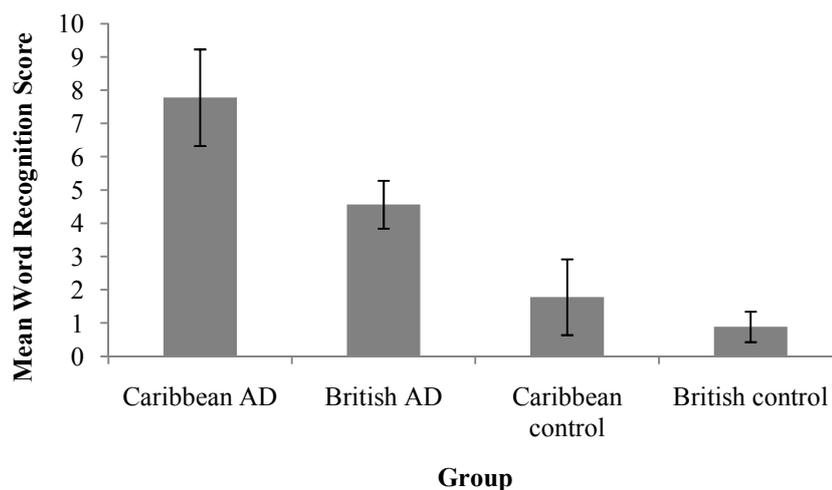


Figure 4.16 Mean word recognition scores for groups based on ethnicity and AD status

4.2.8.4 DISCUSSION

Total ADAS-cog scores distinguished groups based on AD status in which patients had lower scores than controls. Four items: word recall, commands, orientation, word recognition and all five of the observed items (remembering test instructions, spoken language ability, word finding difficulty, comprehension, concentration/distractibility) were successful in distinguishing the patient group from the healthy group while other items: naming objects and fingers, constructional praxis and ideational praxis failed to do so. There was no effect of either AD status or ethnicity on ideational praxis, but for the remaining two items, ethnicity had a

significant effect in which Caribbean persons made more errors on naming objects and fingers and more errors in copying geometric figures.

This finding on the naming and constructional praxis tasks may be explained in part by the low average education in the elderly sample. Education is a significant predictor of performance on both tasks; however, there may be another explanation since other tasks which are predicted by education did not also show effects of ethnicity in the elderly sample. The nature of the tasks may have an impact, in which certain items may have more salience or familiarity with British persons than Caribbean and so may be more likely to provoke errors in Caribbean persons.

One observation pertaining to naming of objects was the use of cultural variants for some items: e.g. 'mouth organ' for harmonica and 'chac chac' (a local musical instrument, usually consisting of a gourd filled with dried seeds) for rattle. These variants were scored as correct. However, while many older Caribbean persons were familiar with a stethoscope and knew its function, they could not give the actual name for it. In addition, when naming fingers, Caribbean persons were less likely to give the correct answer for the third finger as 'ring' finger. Culturally, in the Caribbean, the phrase 'ring' finger is used solely to refer to the third finger on the left hand. Since all but one of the Caribbean participants was right handed and the task is performed using the dominant hand, they were less likely to refer to the third finger on the right hand as 'ring' finger. More common but incorrect answers were 'fourth finger' and saying they did not have a name for that finger.

In constructional praxis, Caribbean elderly also performed worse on copying of geometric shapes. There was no effect of ethnicity for both these tasks in the younger sample (Study 5), however there was a significant impact of education. As

discussed previously, ethnicity effects are more prominent in groups with low education and this finding may be reflective of a difference in quality of education among the elderly in Britain and the Caribbean that are not accounted for by years of education. However, it may also relate to differences in functional abilities and lifestyles between the two ethnicities in which familiarity with pen and paper tasks, is less likely to be a characteristic of everyday life for the elderly in the Caribbean than in Britain.

Overall, the ADAS-cog and the majority of individual items are able to successfully distinguish healthy persons from AD patients in both British and Caribbean groups.

4.2.9 STUDY 8

ACCOUNTING FOR AGE, EDUCATION, GENDER AND ETHNICITY EFFECTS ON PERFORMANCE ON THE ADAS-COG: A STANDARDIZATION STUDY

4.2.9.1 AIM

The objectives of this study are to:

1. Establish standardised scores for the ADAS-cog based on age, gender, years of education and ethnicity.
2. Establish cut off scores to indicate abnormal performance

4.2.9.2 METHOD

4.2.9.2.1 Participants

The participants are the same as described in Section 4.2.7.2.1

4.2.9.2.2 *Materials*

The ADAS-cog was administered to all participants.

4.2.9.2.3 *Procedure*

The procedure is the same as that described in Section 4.2.7.2.3

4.2.9.3 *Statistical Analysis*

The procedure is the same as that described in Section 4.1.11.3

4.2.9.4 RESULTS

The overall adjusted mean score for the ADAS-cog was 3.91 (sd=2.76) with scores ranging from 0 to 14.28. The variables selected for entry into the regression model were the logarithm of age, gender, education and ethnicity. Significant predictors were identified as logarithm of age and education. Gender and ethnicity failed to significantly influence performance.

A formula for correction was obtained as follows:

$$\begin{aligned} \text{Corrected ADAS-cog score} = & \text{Raw score} + [-(0.409) (\text{Age } \log_{10}^* - 1.632)] \\ & + [(0.340) (\text{Education}^{**} - 14.634)] \end{aligned}$$

*logarithm of years of age **years of education

The formula above allows for calculation of individual scores. The formula above allows for calculation of individual scores. Tolerance limits defined a cut-off score of 10.16. A frequency distribution of the adjusted ADAS-cog scores shows a positively skewed pattern with a median of 3.55 (interquartile range=2.29-5.43) (See Figure 4.11).

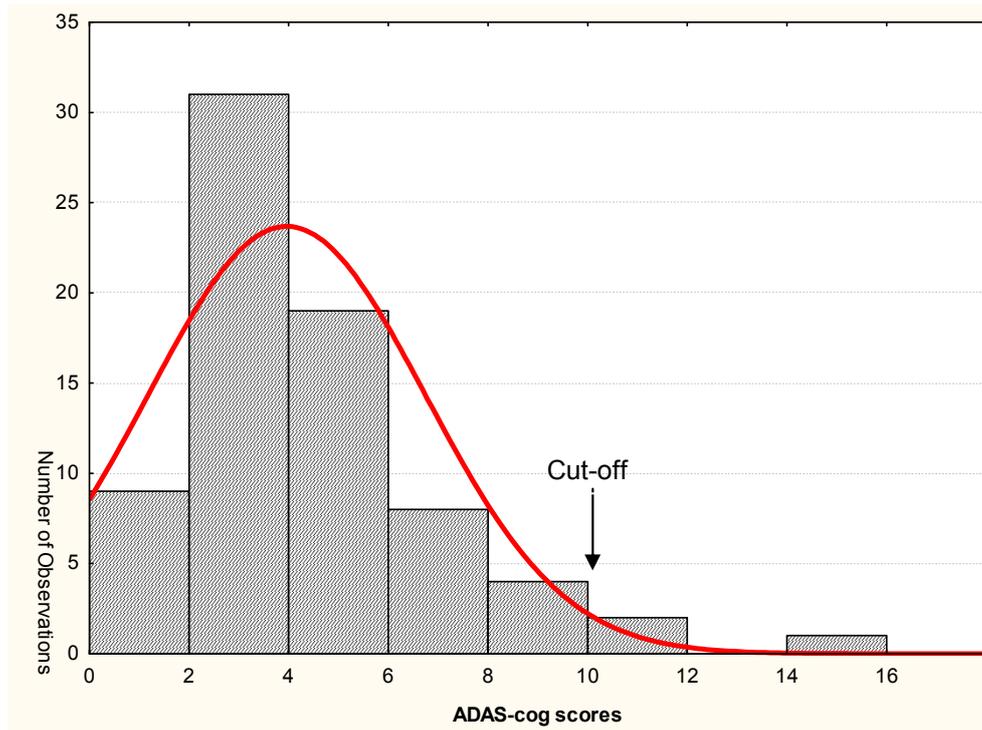


Figure 4.17 Frequency distribution of adjusted ADAS-cog scores

A correction grid with pre-calculated values for the combined effect of the variables is shown below based on the education groups derived from the sample. The median value of each education category was used to generate the correction grid. See correction grid and equivalent scores below in Tables 4.16 a and 4.16b.

Table 4.16a

Correction grids for ADAS-cog scores with adjustments based on age and education

Years of education	Years of age											
	20	25	30	35	40	45	50	55	60	65	70	75
<10	-1.78	-1.82	-1.85	-1.88	-1.90	-1.93	-1.94	-1.96	-1.98	-1.99	-2.00	-2.02
10-16	-0.42	-0.46	-0.49	-0.52	-0.54	-0.57	-0.58	-0.60	-0.62	-0.63	-0.64	-0.66
>17	1.79	1.75	1.72	1.69	1.67	1.64	1.63	1.61	1.59	1.58	1.57	1.55

Table 4.16b

Equivalent scores for ADAS-cog

Test	Equivalent Scores				
	0	1	2	3	4
ADAS-Cog	>10.16	10.15-8.51	8.50-6.85	6.84-5.20	5.19-3.55

4.2.9.5 DISCUSSION

These findings indicate that ADAS-cog scores are affected by demographic variables of education and age. This finding concurs with that of Fioravanti et al (1994) who also suggested correction scores for the ADAS-cog in an Italian sample based on age and education. Individual scores should be adjusted to account for the relative effects of these variables before interpretation of an individual's performance is made and the provision of the correction formula enables this to be done on an individual basis.

The recommended adjusted cut-off score of 10 exceeds the suggested cut-off of 18. However the sample used in this study consisted of a wider age range and younger average age than is normally used in studies of the ADAS-cog. Graham et al (2004) used a sample with a mean age of 71.2 which ranged from 55 to 89 and Fioravanti et al (1994) used a sample which ranged from 50 to 79 years. However the achieved cut-off score does approximate the value suggested by Wouters et al (2009) in which an ADAS-cog score of 11.4 corresponds to a estimate of global cognitive impairment and is also close to the cu-off of 12 suggested by Monllau et al (2007)

4.2.10 STUDY 9

VALIDATION OF STANDARDISED ADAS-COG SCORES

4.2.10.1 AIM

The objectives of this study are to:

1. Validate standardised scores for the ADAS-cog in a sample of AD patients and controls.

4.2.10.2 METHOD

4.2.10.2.1 Participants

The participants are the same as described in Section 4.2.7.2.1

4.2.10.2.2 Materials

The ADAS-cog was administered to all participants.

4.10.2.3 Procedure

The procedure is the same as that described in Study 1, Section 4.2.7.2.3

4.2.10.3 STATISTICAL ANALYSIS

Corrections to ADAS-cog scores were calculated using the formula derived in Study 6. Patients and controls were classified according to AD status based on their raw ADAS-cog scores and corrected ADAS-cog scores and classified as impaired or non-impaired using a cut-off scores of 10. Specificity and sensitivity rates were calculated for raw ADAS-cog scores and the corrected ADAS-cog scores.

4.2.10.4 RESULTS

Raw scores on the ADAS-cog successfully identified 84% of patients and 89% of non-patients with a false positive rate of 11%.

Corrected ADAS-cog scores successfully identified 89% of patients and 89% of non-patients with a false positive rate of 11%. This represents a 5% increase in sensitivity, while specificity and false positive rate remains unchanged. The sensitivity, specificity and false positive rates for both sets of scores are shown in the graph below.

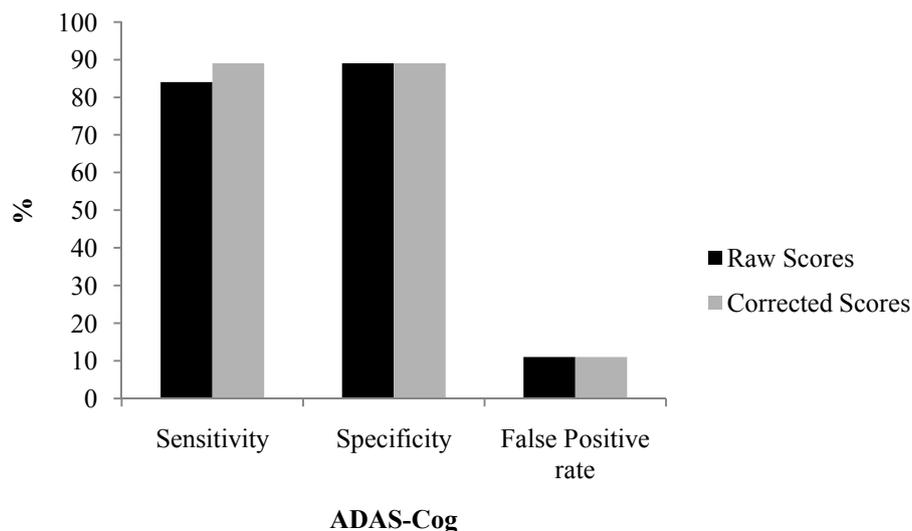


Figure 4.18 Sensitivity, specificity and false positive rates for raw and corrected ADAS-cog scores.

4.2.10.5 DISCUSSION

Sensitivity and specificity rates of 89% and 89% respectively for the ADAS-cog were quite high indicating its ability to successfully detect person with impairment and successfully rule out healthy persons. Adjustment of the ADAS-cog scores resulted in a slight increase in sensitivity and while specificity rates and false positive rates remain unchanged. These values obtained in this study correspond almost exactly with the sensitivity and specificity figures reported by Monllau et al (2007) of 89.19% and 88.53% respectively. These authors validated the ADAS-cog in a large sample of healthy controls and AD patients in Spain and the similar findings across both studies, conducted with different ethnic groups also reiterates the lack of an ethnicity effect for the ADAS-cog and endorses its use in ethnically diverse populations. Furthermore, Monllau et al (2007) also adjusted ADAS-cog scores for effects of age and education, thus emphasising the influence of these

factors on performance and the need to make corrections before interpretation is undertaken.

4.3 CONCLUSION

Performance on both the MMSE and the ADAS-cog are influenced by age and education, a finding that is consistent with the literature. Gender did not have an influence on scores for either instrument and this is also a reliable finding. Ethnicity had an impact on MMSE scores in both community and clinical elderly samples. However, this effect seems to be a function of education, namely low education. When interaction effects were investigated, the lower performance by Caribbean persons was restricted to those with the lowest level of education. This interpretation was also confirmed by the finding of no difference in MMSE scores among groups matched for education: Caribbean and British university students.

It would thus be expected that the effect of education on performance in Caribbean persons would be inflated in the elderly who tend to have fewer years of education. This assertion was confirmed by the finding of worse performance in the elderly sample by both Caribbean AD and non-AD groups when compared to British groups. As such, the factor of education is of critical importance in the interpretation of MMSE scores among Caribbean persons especially since the target population for most screening for dementia is the elderly, whose performance, as seen from this study are most susceptible to the effects of education.

The persistent finding of an effect of ethnicity on the serial sevens in both the community and student samples suggest that there may be underlying cultural factors affecting performance that are unrelated to mathematical ability or impairment. These could be related to differences in cultural attitudes or anxiety affecting

performance. However, given its significant impact on overall MMSE scores in the Caribbean sample, it is recommended that the scoring method of using the higher of the serial sevens or spelling backwards would be less biased and the recommended variant of administration for Caribbean populations.

Performance on the ADAS-cog proved resistant to the effects of ethnicity, a finding which has been suggested by other studies but which can now be applied to Caribbean populations. The ADAS-cog is also less influenced by years of education than the MMSE as seen in the lower regression coefficients for education (.07 for MMSE versus .44 for ADAS-cog) a finding which has been suggested in the literature (Weyer et al, 1997; Zec et al, 1992) and confirmed in this study.

Ongoing efforts are needed then to compile norms for these ethnic groups that take age and education into consideration and which can be used to facilitate more accurate screening of cognitive impairment and dementia in these populations. The adjusted scores presented in this study along with the recommended cut-off scores offer a practical aid to interpretation of MMSE and ADAS-cog scores in Caribbean populations and comparison of these scores with other ethnic groups. The adjusted ADAS-cog scores produced a small increase in sensitivity and maintained high specificity rates which are consistent with other reported rates (Monllau et al, 2007). This relatively small change is a reflection of the test's robustness against the effects of education, a finding which makes the ADAS-cog particularly useful in developing countries whose populations contain more persons with lower levels of education and who exhibit a greater range of educational experience.

The adjusted MMSE scores resulted in 30% reduction of the false positive rate, a finding which suggests that adjusting for the effects of education and ethnicity

using the correction formula provided, can greatly improve the effectiveness of the use of the MMSE in Caribbean persons. These findings reiterate the call by Parker and Philp (2004) for tests which accurately reflects the abilities of ethnic groups. It also underpins the ethos of cross cultural assessment which argues for tests to be normed for populations on which they are being used to avoid the pitfalls of false positives and invalid test results (Evans, Wilson and Emslie, 1996, Lezak et al, 2004). This is especially critical since health care in developing countries like Trinidad and Tobago face considerable constraints due to limited financial and human resources. As such, the use of these adjusted scores in screening may pre-empt further, unnecessary assessment.

The popularity of the MMSE and ADAS-cog ensures their future use in both clinical and research settings globally. The provision of standardised scores, correction formulas and revised cut-off scores as presented in these studies make a meaningful and practical contribution to the validity of the use of these instruments with Caribbean populations.

CHAPTER 5

MEMORY AND ATTENTION

5.0 INTRODUCTION

Attention and memory functions are often impaired in dementia, with deficits appearing at earlier stages in some forms than others. Tasks used to assess memory and function may differentiate patterns of impairment in dementia. For example, in the earlier stages of AD, performance on the digit span forward task may be spared while performance on the backward task may be impaired (Wilson and Kasniak, 1986). In a timed digit cancellation task, Della Sala et al (1992) found AD patients exhibited significantly slower scanning. Working memory has been found to be impaired in many mild to moderately affected AD patients. Delayed memory is also affected with AD patients and they tend to show greater impairments than VaD patients (Becker, 1988; Belleville et al, 1996; Larrabee, et al, 1993; Villardita, 1993). This chapter focuses on assessment using three commonly used tests of attention and memory: digit span, digit cancellation and Logical Memory.

5.1 DIGIT SPAN

The concept of memory span can be traced to the late nineteenth century where Oliver Holmes (1871) and Ebbinghaus (1885) recognized that there seemed to be a limit or fixed capacity for the number of verbal items a person could correctly repeat. Jacobs,(1886), Galton (1887) and Bolton (1892) later made the association between memory span and cognitive performance when they observed that memory span seemed to be shorter in persons of lower intelligence. Digit span tests were

included in intelligence tests for children (e.g. Stanford-Binet) on a wide scale in the early 1900s and were later included in Wechsler's Intelligence scales and Memory scales (1939, 1945).

Factor analysis showed that in addition to previous findings of digit span being related to verbal and performance IQ, it appeared to also load on a third factor of attention and concentration (also referred to as freedom from distractibility in some studies) (Crawford, Allan, Stephen, Parker, & Besson, 1989). In the third edition of the WAIS, it was also considered to be a measure of working memory (Golden, Espe-Pfeifer, & Wachsler-Felder, 2000). The digit span test is now one of the most commonly used neuropsychological instruments in the measurement of verbal recall, attention and working memory (Ostrosky-Solis & Lozano, 2006).

The digit span forwards (DSF) task involves a random sequence of numbers which is read out at the rate of one digit per second and the patient is asked to recall the digits in order immediately after. Digit span backwards (DSB) is a variation of the task in which the person is required to recall the sequence of digits in reverse order. Sequences usually start with a string of two to three digits in DSF and two in DSB and when correctly recalled, the examiner states the next number sequence which is increased by one digit up to a string of nine in the DSF and eight in the DSB.

A person's span is indicated by the number of digits correctly recalled. Studies have reported average DSF as seven plus or minus two (Miller, 1956), or six plus or minus one (Spitz, 1972). Wechsler (1945) reported 90% of adults achieving a span of 5 to 8 within a range of 4 digits. In another normative sample, 89% yielded spans between 5 and 8 digits (Kaplan, Fein et al, 1991). Lezak (2004) suggest an

interpretation of DSF scores as follows: 6 or more- normal, 5- marginal to normal, 4- borderline, 3- defective.

The number of digits recalled in DSB is usually fewer than on the DSF task, and the difference can range from a low of 0.59 (Mueller & Overcast, 1976), to 1.0, (Kaplan, et al, 1991) to a high of 2 (Black and Strub, 1978; Reynolds, 1997). Lezak (2004) suggest the following interpretation for DSB scores: 4 to 5- within normal limits, 3- borderline defective or defective (depending on educational background), 2- defective.

5.1.1 DIGIT SPAN FORWARD VERSUS BACKWARDS TASK

In the WAIS-III version of the digit span task, the forwards and backwards scores are combined to produce an overall score. However, researchers have long asserted that these two scores should not be combined; that the two tasks correspond to different memory processes and should be considered separately. Evidence for the two tasks involving different processes comes from many sources. In the original standardization of the WAIS, the authors report only a 0.6 correlation between the two tasks (Tulsky, et al., 2003). A later study reported a more modest correlation between the two tasks at $r=0.44$ (Reynolds, 1997). Neuroimaging also provides some evidence for this claim in which it was observed that while both forwards and backwards tasks involve activation of the mid-ventrolateral frontal cortex, the backwards task also involves activation of the mid-dorsolateral frontal cortex (Owen, Lee, & Williams, 2000). As such, performance on each task may be affected differentially by damage to cortical and subcortical structures.

The DSB is considered the more cognitively demanding task which involves an element of cognitive transformation not required in the forwards task (Jensen,

1980; Jensen and Figueroa, 1975). Some authors suggest DSF involves a more verbal (de Renzi & Nichelli, 1975) and stronger attentional element while DSB incorporates a visuospatial component that invokes the working memory system (Baddeley, 2000; Lezak, 2004; Rapport, Webster, & Dutra, 1994).

Baddeley and Hitch (1974) proposed the concept of working memory which refers to ‘a limited capacity system allowing the temporary storage and manipulation of information necessary for such complex tasks as comprehension, learning and reasoning’ (Baddeley, 2000, pg 418). The model comprises a control system called the central executive which is assisted by two accompanying slave systems- the phonological loop and the visuospatial sketchpad. Digit span forward is thought to engage the phonological loop which involves verbal and acoustic information. The backwards aspect of the task would implicate a greater involvement of the central executive system, visuospatial sketchpad and episodic buffer. (Baddeley, 2000; Ostrosky-Solis and Lozano, 2006).

Evidence for differing components in each task was also investigated by Li & Lewandowsky (1993, 1995) who presented participants with long sequences of visually presented letters and then immediately had them perform either an irrelevant verbal task (mental arithmetic) or an irrelevant spatial task (mental rotation). Forward span was affected by both tasks but backwards span was affected by the spatial task and not the verbal task.

5.1.2 DIGIT SPAN AND AGE

DSF is largely unaffected by age and usually any negative impact of age if present becomes noticeable only after age 65 (Craik, 1990; Jarvik, 1988). In a study of verbal and spatial memory span tests, involving the use of the digit span and Corsi

Block Tapping Test (Milner, 1971), Carlesimo et al (1998) found a progressively decreasing span with age: 5.4 for young adults ($m=29.4$, $sd=5.6$), 4.7 for elderly ($m=66.7$, $sd=4.6$), and 3.8 for the very old ($m=82.5$, $sd=3.9$). A meta-analysis by Babcock and Salthouse (1990) found that age-related decrease in performance was almost twice as much for DSB performance than for DSF (14% vs 8% respectively). Hester, Kinsella and Ong, (2004) also examined the hypothesis that the rate of decrease of DSB was greater than that for DSF. They re-examined the standardisation sample of the Wechsler Memory Scale- Third Edition and found similar age-related decline for both DSF and DSB suggesting that while some older persons may have lower DSB scores, not all elderly persons do.

5.1.3 DIGIT SPAN AND EDUCATION

The effects of education on digit span appear to interact with age. In participants with fewer years of education (less than 10), digit span backwards performance appears to remain stable across different ages, however in persons with more than 10 years of education, performance tends to decline slightly in older subjects (Ardila et al, 2000). Lezak (2004) suggest that DSB may decrease by one point after age 60 or later in better educated groups, however, this finding has not been substantiated by other studies (Howieson et al, 2003). Ostrosky-Solis and Lozano (2006) also highlight that the relationship between education and neuropsychological performance is not a linear one. Between 0, 1, 2, 3 and 4 years of education, differences are greater than between persons with 5 to 9 years of education and differences are even less between persons with more than 10 years of education (Ardila et al, 2000; Ostrosky-Solis, 1998).

One study on Mexican adults investigated the effects of age and education on digit span and found education to be the stronger predictor. While both age and education significantly predicted digit span forward, explaining 14% and 25% of variance respectively, only education proved to be a significant predictor of digit span backwards, explaining 31% of total variance (Ostrosky-Solis and Lozano, 2006). The authors also compared the findings with those from other countries and found significant differences that could not be fully explained by age or years of education. They acknowledged that digit span is larger in countries with languages possessing a faster speech rate (e.g. mean digit span for English is 7.2, mean digit span for Arabic is 5.77) (Naveh-Benjamin and Ayres, 1986). However this only partially explains the differences and this also applies only to the digit span forward condition and not the backward condition. Instead, Ostrosky-Solis and Lozano focus their explanation on the educational differences between countries. Citing the arguments of Ardila and colleagues (Ardila, 2000; Ardila et al, 2000), they view schooling as a subculture which may vary in the abilities and attitudes emphasised in the educational system. Thus differences in education systems can have a differential impact on the development of certain cognitive skills like verbal attention and working memory, thus affecting performance on digit span.

5.1.4 DIGIT SPAN AND ETHNICITY

Performance on digit span tasks also varies with ethnicity. An effect of ethnicity has been reported among children on the digit span task with the Black-White difference in performance twice as great in the DSB than that for the DSF (Jensen and Figueroa, 1975). Within groups difference (DSF-DSB) are also greater among Black children and while this discrepancy decreased with age from 5 to 12

years, it was less apparent in the ethnic minority group (Mayfield and Reynolds, 1995; Jensen and Figueroa, 1975). Among adults, significant differences among ethnicities also exist on digit span performance. Specifically, Caucasians had significantly higher digit span scores than African-Americans and Hispanics (Boone, Victor, Wen, Razani, & Pontan, 2007).

5.1.5 DIGIT SPAN AND DEMENTIA

Digit span performance in AD has been found to be impaired. The memory span of patients with AD was found to be significantly lower than those of normal young, elderly and very old adults (Carlesimo et al., 1998). An examination of the DSF-DSB difference was also found to be significant in the AD group but not in any of the normal groups. This finding reiterates that of Wilson and Kasniak, (1986) and Carlesimo et al's (1994) earlier study of dementia patients (18 AD and 18 VaD) which shows a differential pattern- normal performance on DSF but reduced performance on DSB when compared to controls. Among MCI patients, digit span performance was found to be worse than healthy controls for both the DSF and DSB tasks and DSB proved to be a significant predictor of MCI diagnosis (Muangpaisan, Intarapaporn, & Assantachai, 2007).

5.1.6 STUDY 1

EXPLORING THE EFFECT OF AGE, GENDER, EDUCATION AND ETHNICITY ON DIGIT SPAN FORWARD AND BACKWARD

5.1.6.1 AIM

The objectives of this study are to:

1. Assess the difference in performance on the digit span forward, backward and forward-backward based on age, gender, education and ethnicity.
2. Identify the contribution of each predictor to performance on each measure.

5.1.6.2 METHOD

5.1.6.2.1 Participants

In this study, 121 participants (female= 68, male=53) from Trinidad and Tobago (n=62) and England (n=59) were assessed. The sample ranged in age from 18 to 89 years (m=47.37, sd=19.20) and years of education ranged from 3 to 30 years (m=14.49, sd=5.55). All participants were functionally independent, and those with any neurological or psychiatric impairment were excluded.

5.1.6.2.2 Materials

The digits used in the DSF and DSB backward tasks are presented in Figures 5.1 and 5.2 below.

2	28	93
3	582	694
4	6439	7286
5	42731	75836
6	619472	392487
7	5917428	4179386
8	58192647	382957174
9	275862584	713942568

Figure 5.1 Digits used in Digit Span Forwards Task

2	28	93
3	629	415
4	3279	4968
5	15286	61843
6	539418	724856
7	8129365	4739128
8	94376258	72819652

Figure 5.2 Digits used in Digit Span Backwards Task

5.1.6.2.3 Procedure

The digit span task was administered with the DSF followed immediately by DSB. The strings of digits were read to participants at a rate of 1 per second after which the participant was required to recall them verbally in correct sequence in the DSF and in reverse order in the DSB. There are two trials for each span level.

However if the participant successfully recalls the first trial, the examiner moved on to the next span level. If a participant failed on the first trial, the second trial would be administered. The task ended when the participant failed to correctly recall both trials on a span level. The span recorded would be the last correct number of digits

recalled. A maximum score of 9 and 8 was possible in the DSF and DSB respectively.

5.1.6.3 DESIGN AND STATISTICAL ANALYSIS

Univariate ANOVAs were performed on each of the three dependent variables (DSF, DSB and DSF-DSB) comparing the effects of age, gender, ethnicity and education. Age was categorized as previously described. A Bonferroni correction was employed in the post hoc analyses of the effects of education and age. A stepwise regression analysis was also performed to determine the contribution of age, gender, education and ethnicity to DSF, DSB and DSF-DSB scores.

5.1.6.4 RESULTS

5.1.6.4.1 Digit Span Forwards (DSF)

Table 5.1 presents the mean performance on all three digit span measures.

Table 5.1

Mean performance on three measures of digit span

	Mean	Min	Max	Std. Dev.
Digit Span Forward	6.61	3	9	1.35
Digit Span Backwards	4.75	2	8	1.28
Digit Span forwards-backwards	1.86	-2	5	1.36

ANOVA Analysis

As seen in table 5.1, performance on digit span forward (DSF) ranged from 3 to 9 with a mean of 6.59 (sd=1.35). No significant main effects of age, gender, education or ethnicity were observed for DSF scores.

Regression Analysis

DSF scores were correlated significantly with age, education and ethnicity but not gender (See Table 5.2). Increasing age, fewer years of education was associated with lower DSF scores. Neither gender nor ethnicity was significantly associated with DSF scores.

*Table 5.2**Correlations between Digit Span Forward and Predictors*

	Age	Gender	Education	Ethnicity
DSF	-.18*	-.01	.26*	-.08
Age		-.03	-.43*	-.27*
Gender			-.11	.10
Education				.12

* $P < 0.001$

A forced entry regression analysis with predictors age, gender, education and ethnicity failed to produce a significant model ($F(4, 116) = 2.42, p = 0.052$). Of the four predictors, education made a significant contribution to the overall model ($\beta = .23, t(116) = 2.17, p = 0.032$). The regression analysis was repeated with education as the only predictor and a significant model was produced ($F(1, 119) = 9.26, p = 0.003$). Education significantly predicted DSF scores, $\beta = .27, t(119) = 3.04, p = .003$ and accounted for 7% ($R^2 = .07$) of the variance in DSF scores.

5.1.6.4.2. Digit Span Backwards (DSB)*ANOVA Analysis*

Performance on digit span backward ranged from 2 to 8 with a mean of 4.75 ($sd = 1.28$). Results from the ANOVA analysis showed a significant main effect for education ($F(2, 121) = 7.55, p = 0.001$). Post hoc analysis showed significant differences between groups: the low education group had a significantly lower DSB mean ($m = 3.56, se = 0.24$) than both the average ($m = 4.92, se = 0.26$) and high

($m=5.37$, $se=0.19$) groups. The difference between the average and high education groups was not significant. These differences are illustrated in Figure 5.3.

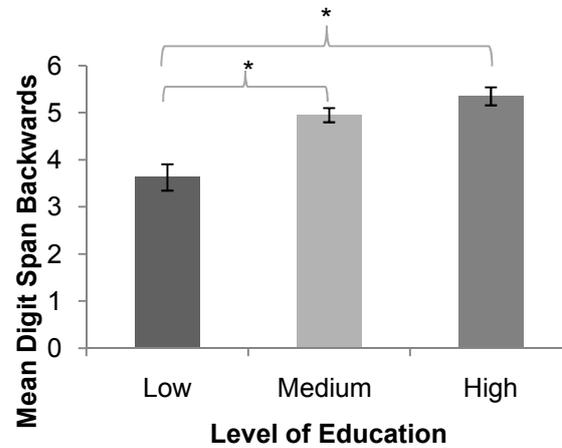


Figure 5.3. Bar chart showing mean digit span backwards as a function of education

A significant main effect was also observed for ethnicity ($F(1,121)=6.93$, $p=0.01$). Caribbean persons had a significantly lower mean DSB ($m=4.10$, $se=0.21$) than British persons ($m=4.88$, $se=0.20$). See Figure 5.4. No other significant main effects were found and there were no significant interaction effects.

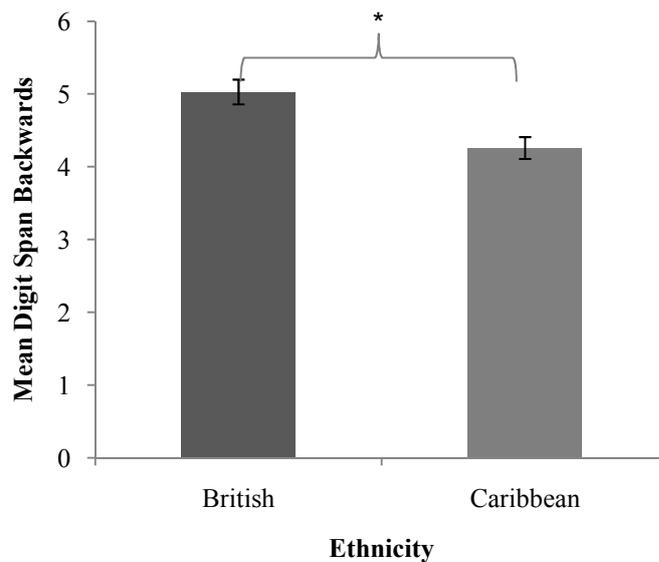


Figure 5.4 Bar chart showing mean digit span backwards as a function of ethnicity

Regression Analysis

DSB scores correlated significantly with age, education and ethnicity but not gender. Increasing age, fewer years of education and Caribbean ethnicity were associated with lower DSB scores. See Table 5.3 below.

*Table 5.3**Correlations between Digit Span Backwards and Predictors*

	Age	Gender	Education	Ethnicity
DSB	-.33*	-.10	.46*	.33*
Age		.01	-.52*	.01
Gender			-.13	.07
Education				-.02

* $p < 0.001$

The regression analysis with all four predictors (age, gender, education and ethnicity) revealed significant effects of education and ethnicity but no significant effect of gender or age on DSB performance. The regression analysis was then repeated with the two significant predictors- education and ethnicity. Using a stepwise method, a significant model emerged, $F(2, 118) = 28.04$, $p < 0.001$ which accounted for 33% of the variance in scores. Education significantly predicted DSB scores, $\beta = .46$, $t(119) = 6.14$, $p < 0.001$ and on its own accounted for 22% ($R^2 = .22$) of the variance in DSB scores. When included in the model, ethnicity also significantly predicted DSB scores, $\beta = .47$, $t(118) = 6.135$, $p < 0.001$ and accounted for a further 11% ($R^2 = .11$) of the variance in DSB scores.

5.1.6.4.3 DSF-DSB

The difference between DSF and DSB scores ranged from -2 to 5 with a mean of 1.86 ($sd = 1.36$). Three persons or 2.5% of the sample had a Digit Backwards span which exceeded their Digit Forwards span by 1 or 2. A further 18 persons or 14.8% of the sample had equal digit forwards and backwards spans.

ANOVA Analysis

The ANOVA analysis produced a significant main effect of ethnicity ($F(1,121)=6.59, p=0.01$). Caribbean persons ($m=2.93, se=0.19$) had a significantly higher difference between digit span forward and backwards scores than British persons ($m=1.52, se=0.19$). This difference is illustrated below in Figure 5.5 Other main and interaction effects failed to reach significance.

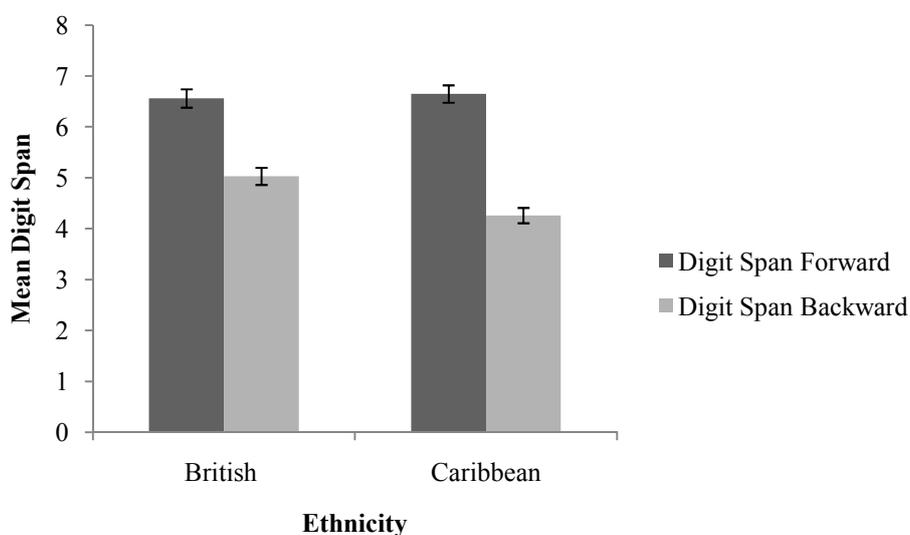


Figure 5.5 Mean Digit Span Forwards and Backwards by ethnic group

Regression Analysis

Differences correlated significantly with ethnicity but not with age, gender or education. Caribbean ethnicity was significantly associated with increasing difference between DSF and DSB scores. See Table 5.3 below. A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 116)=3.96, p=0.005$). Of the four predictors, only ethnicity made a significant contribution to the overall model ($\beta=-.80, t(116) = -3.40, p=0.001$).

Table 5.3

Correlations between Digit Span Difference and Predictors

	Age	Gender	Education	Ethnicity
DSB	.12	.07	-.17	-.28*
Age		.01	-.51*	.01
Gender			-.13	.07
Education				-.02

*P<0.001

The regression analysis was repeated with ethnicity as the only predictor and a significant model was produced ($F(1, 119)=9.80, p=0.002$). Ethnicity significantly predicted difference scores, $\beta = -.74, t(119) = -3.13, p=.002$ and accounted for 8% ($R^2 = .08$) of the variance in DSF scores. The results from the regression analyses for all digit span items is shown below in Table 5.4.

Table 5.4

Multiple Regression Analysis- unstandardised and standardized coefficients for digit span measures

Item			B	SE B	β	R^2
Digit Span Forward	Model (Enter)	(Constant)	6.03	.67		
		Age in years	-.01	.01	-.08	
		Gender	-.01	.24	-.01	
		Ethnicity	.05	.24	.02	
		Years of Education	.06	.03	.23	.08
Digit Span Forward	Model (Stepwise)	(Constant)	5.65	.33		
		Years of Education	.07	.02	.27	.07*
Digit Span Backward	Model (Enter)	(Constant)	3.52	.54		
		Age in years	-.01	.01	-.13	
		Ethnicity	.84	.19	.33	
		Gender	-.16	.20	-.06	
		Years of Education	.09	.02	.39	.34*
Digit Span Backward	Model (Stepwise)	(Constant)	2.78	.29		
		Years of Education	.107	.02	.47	.22*
		Ethnicity	.84	.19	.33	.11*
Digit Span Difference	Model (Enter)	(Constant)	3.52	.54		
		Age in years	-.01	.01	-.13	
		Migrant Status	.84	.19	.33	
		Gender	-.16	.20	-.06	
		Years of Education	.09	.02	.39	.12*
		Ethnicity	-.74	.24	-.28	.08*

*p<0.05

5.1.6.5 DISCUSSION

The overall average digit span for DSF and DSB obtained from this sample lie well within the ranges of normal performance reported in the literature (Lezak, 2004). The mean difference between the forward and backward condition is also similar to those previously reported (Kaplan, Fein et al, 1991; Black and Strub, 1978; Reynolds, 1997).

While age was significantly correlated with DSF and DSB, no significant age effects were observed. There were no significant between group differences and age did not contribute significantly to the regression model for either measure. This finding concurs with the literature which report a lack of age effects on digit span especially in younger adults (Craik, 1990) and the lack of an age-related decrease in DSB performance (Hester, Kinsella, Ong, 2004).

Education proved to be a significant predictor of DSF performance accounting for a modest 7.2% of the variance in scores. This figure is lower than that reported by Ostrosky-Solis & Lozano, (2006) in which education explained 25% of the variance in DSF scores in a Mexican sample. However this disparity may be explained by the difference in mean years of education between the two samples. The Mexican sample had a much lower mean (6.42, $sd=5.55$) when compared to this sample (14.49, $sd=5.55$). Given that differences are fewer between persons with more than 10 years of education as compared to less than 5 (Ardila, 2000; Ostrosky-Solis, 1998), this may account for the more modest contribution of education to DSF scores in this study.

DSB performance also differed significantly by educational level. Those with the lowest years of education had lower spans than both groups with higher

education while the two higher education groups performed similarly. This reiterates Ardila's (2000) assertion that differences in performance between lower levels of education are greater than those between higher levels of education and that education may contribute significantly to performance up until a certain point after which the gain to be expected is reduced. The proportion of variance explained by education in DSB was almost three times the proportion found for DSF suggesting that education plays a greater role in the backwards task as compared to the forward task. This finding contributes to the theoretical assertion that the DSF and DSB tasks are measuring different cognitive components.

A significant effect was found for ethnicity but only on the DSB task in which Caribbeans performed worse than British participants. This finding refutes that of Boone et al (2007), however this may be explained by the failure of those authors to compare DSF and DSB separately. While Jensen and Figueroa (1975) also found differences in performance between Whites and Blacks on both DSF and DSB, they note that the difference between ethnic groups is larger on the DSB task, a finding which is confirmed by this study.

The differences in performance on the DSF versus DSB tasks in Caribbean persons may be explained by examining the nature of the task. As described earlier, while digit span is regarded as an attentional task, the DSB component is thought to be more difficult and also invokes the working memory system. Thus, differences in performance may relate to differences in working memory and not attention, between British and Caribbean persons.

These findings have practical implications for interpreting digit span performance. Given the differences in performance on the DSF vs DSB tasks, it

advocates a scoring system that considers these two measures separately. Also it should be noted that the pattern of performance of the low education and Caribbean groups in both DSF and DSB conditions is comparable to that of dementia patients, in that both groups show similar performance to comparison groups on DSF but reduced performance on DSB (Carlesimo, et al., 1994). However, it must be clarified that unlike AD patients, the scores obtained in DSB by participants in this study were still within the range of normal performance.

5.1.7 STUDY 2

ACCOUNTING FOR AGE, EDUCATION, GENDER AND ETHNICITY EFFECTS ON PERFORMANCE ON DIGIT SPAN: A STANDARDIZATION STUDY

5.1.7.1 AIM

The objectives of this study are to:

1. Establish standardised scores for digit span tasks based on age, gender, years of education and ethnicity.

5.1.7.2 METHOD

5.1.7.2.1 Participants

The participants are the same as described in Section 5.1.6.2.1

5.1.7.2.2 Materials

The digit span task was administered to all participants.

5.1.7.2.3 Procedure

The procedure is the same as that described in section 5.1.6.2.3

5.1.7.3 STATISTICAL ANALYSIS

The procedure is the same as that described in Section 4.1.11.3

5.1.7.4 RESULTS**5.1.7.4.1 Digit Span Forward**

The overall adjusted mean score for digit span forward was 6.56 (sd=1.63) with scores ranging from 1.79 to 9. The variables selected for entry into the regression model were the square root of age, gender, ethnicity and education. Only education emerged as a significant predictor. A formula for correction was obtained as follows:

Corrected digit span forward score = Raw score + $[-(0.266) (\text{Education}^* - 14.21)]$

*Years of education

The formula above allows for calculation of individual scores. Tolerance limits defined a cut-off score of 2.99. The frequency distribution of scores on digit span forward shows a negatively skewed distribution with a median score of 6.92 (interquartile range: 5.52 – 7.59) (see Figure 5.6).

A correction grid with pre-calculated values is shown below for the different education groups. See Table 5.6a. The median value of each education category is used to generate the correction grid. Equivalent scores are also provided in Table 5.6b.

Table 5.6a

Correction grids for digit span forward scores with adjustments based on education

Years of Education		
3-10 years	11-16 years	>17 years
1.39	0.32	-1.41

Table 5.6b

Equivalent scores for digit span forward

Equivalent Scores					
Test	0	1	2	3	4
Digit Span Forwards	<2.99	3.00-3.97	3.98-4.95	4.96-5.94	5.95-6.92

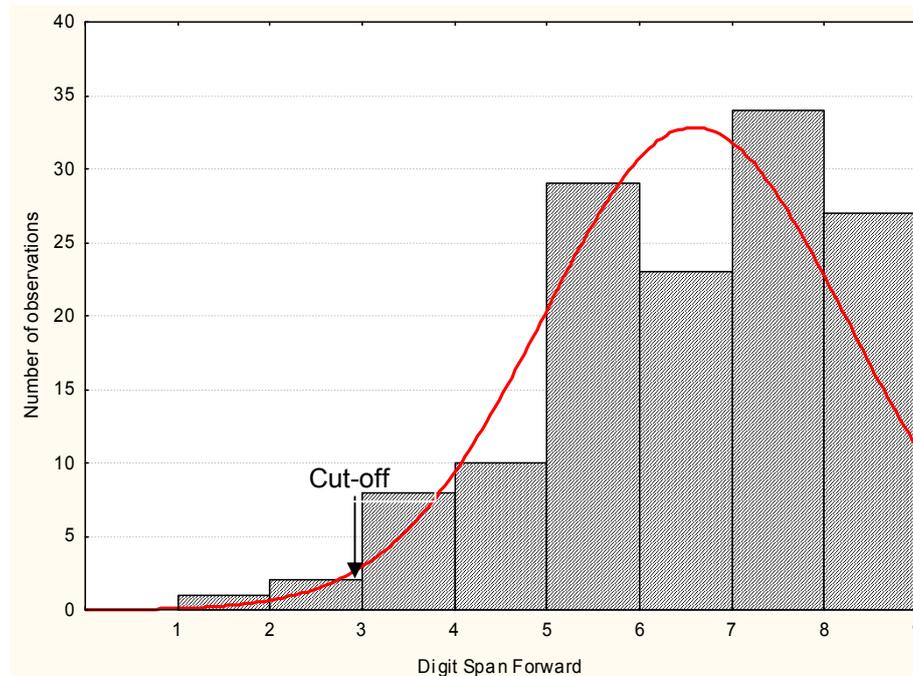


Figure 5.7 Frequency distribution for digit span forward scores

5.1.7.4.2 Digit Span Backward

The overall adjusted mean score for digit span backward was 4.88 (sd=1.71) with scores ranging from 0.46 to 8. The variables selected for entry into the regression model were square root of age, gender, ethnicity and education. Only

education emerged as a significant predictor. A formula for correction was obtained as follows:

$$\begin{aligned} \text{Corrected digit span backward score} = & \text{Raw score} + [-(0.400) (\text{Education}^* - 14.21)] \\ & + [-(0.352) (\text{Ethnicity}^{**} - 1.54)] \end{aligned}$$

*Years of education **Caribbean coded as 1, British coded as 2

The formula above allows for calculation of individual scores. Tolerance limits defined a cut-off of 1.13. The frequency distribution of scores on digit span backwards shows a negatively skewed distribution with a median score of 4.91 (interquartile range: 3.94 – 6.07) (see Figure 5.8).

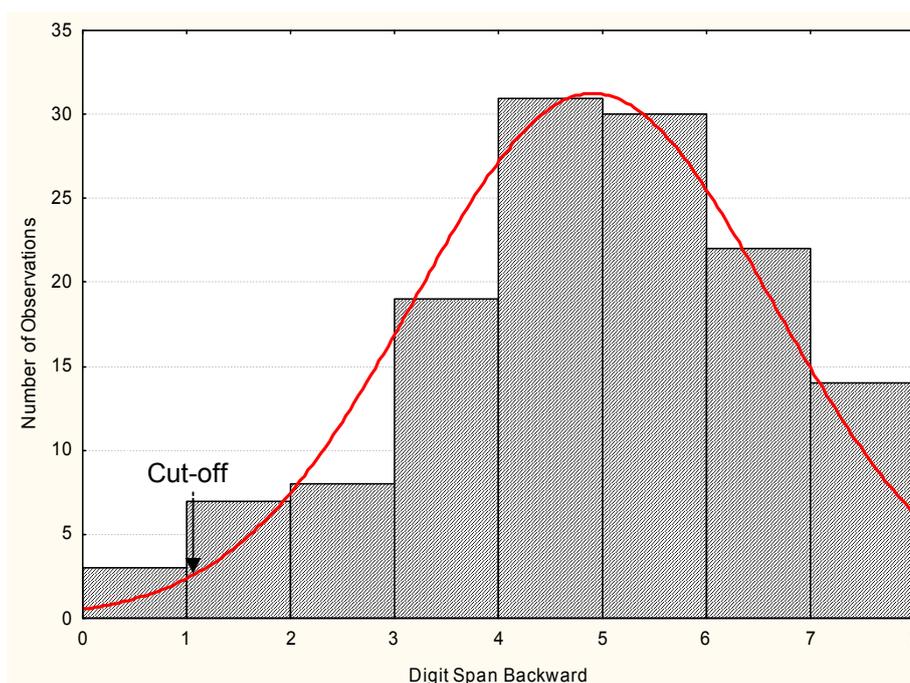


Figure 5.8 Frequency distribution of digit span backward scores

A correction grid with pre-calculated values adjusted for the effects of ethnicity and education is shown below for the different education groups. See Table 5.7a. The median value of each education category is used to generate the correction grid. Equivalent scores are presented in Table 5.7b.

*Table 5.7a**Correction grids for digit span forward scores with adjustments based on education*

	Years of Education		
	3-10 years	11-16 years	>17 years
Caribbean	2.04	0.48	-2.12
British	1.88	0.32	-2.28

*Table 5.7b**Equivalent scores for digit span backwards*

Test	Equivalent Scores				
	0	1	2	3	4
Digit Span Backwards	<1.13	1.14-2.07	2.08-3.02	3.03-3.96	3.97-4.91

5.1.7.5 DISCUSSION

These findings indicate that digit span scores are greatly affected by education. Individual scores should be adjusted before interpretation of an individual's performance is made and the provision of the correction formula enables this to be done on an individual basis. The median scores obtained after correction for both the forward and backward tasks fall well within reported ranges (Wechsler, 1944; Kaplan et al, 1991; Lezak, 2004). The forward span cut-off scores coincides with that suggested by Lezak (2004) with scores less than 3 indicating defect, however the cut-off score for the backwards task determined in this study of 1.3 is less than the cut-off of 2 recommended by Lezak (2004). This may be attributed to the higher levels of education in this sample and since the backward task is influenced to a greater degree by education than the forward task, this may explain the disparity in the cut-off scores. This finding also highlights the need for different and changing levels of education in target populations to be accounted for.

5.2 DIGIT CANCELLATION

Cancellation tests are used to assess sustained attention, accuracy of visual scanning and activation and inhibition of responses in the evaluation of attentional and visuospatial disorders as well as in response to traumatic brain injury, stroke and Alzheimer's disease (Geldmacher et al., 1995; Hills & Geldmacher, 1998; Baddeley et al., 2001; Lezak, 2004). The task involves the examinee searching for specific targets which are randomly interspersed among different foils. The targets may be numbers, letters, lines, symbols or pictures and the stimuli may be presented in rows or scattered randomly (Lezak, 2004). The task may be timed or untimed and scores are based on errors and omissions. The complexity of the task may be increased by decreasing the space between targets or by having multiple targets (Diller et al, 1974).

There is an abundance of cancellation tasks available. Examples of commonly used cancellation tasks include the Test of Visual Neglect (Albert, 1973), Line Crossing (Wilson, Cockburn and Halligan, 1987), Bells Test (Gauthier et al, 1989), Balloons Test (Edgeworth, Robertson and Macmillan, 1998), Star Cancellation (Halligan, Cockburn and Wilson, 1991; Wilson, Cockburn and Halligan, 1987); Two and Seven Test, (Ruff, Evans and Light, 1986; Ruff, Niemann, Allen et al, 1992).

5.2.1 FACTORS INFLUENCING PERFORMANCE ON CANCELLATION TESTS

Increasing age is associated with worse performance and longer completion times (Della Sala et al., 1992). Education also has a significant impact with more years of education associated with better performance. Heaton et al (1991) found education explained 16% of the variance in performance on cancellation. Fewer

studies have investigated the effects of ethnicity on cancellation tests. Byrd et al (2004) examined shape and letter cancellation performance in a sample of white, African-American and Hispanic healthy persons aged 65 years and older. They found ethnic minority elders made more errors than whites. While the samples were matched for years of education, when they were matched on literacy levels, the differences between performance for African Americans and whites were no longer significant. As mentioned in Chapter 1, Della Sala et al (1992) examined the performance of AD patients on timed digit cancellation tasks and found they exhibited passive or slow scanning in which they were 'looking but not seeing' and were also slow to make a decision.

5.2.2 STUDY 3

EXPLORING THE EFFECT OF AGE, GENDER, EDUCATION AND ETHNICITY ON CANCELLATION PERFORMANCE

5.2.2.1 AIM

The objectives of this study are to:

1. Assess the difference in performance on the cancellation task based on age, gender, education and ethnicity,
2. Identify the contribution of each predictor (age, gender, education and ethnicity) to performance on each measure
3. Assess the difference in completion time of the cancellation task in Caribbeans and British

5.2.2.2 METHOD

5.2.2.2.1 Participants

In this study, 118 participants (female= 67, male=51) from Trinidad and Tobago (n=57) and England (n=61) were assessed. The sample ranged in age from 18 to 87 years (m=47.37, sd=19.19) and years of education ranged from 3 to 30 years (m=14.49, sd=5.55). All participants were functionally independent, and those with any neurological or psychiatric impairment were excluded.

5.2.2.2.2 Materials

The cancellation test used numbers and consisted of three trials of increasing difficulty (Spinnler and Tognoni, 1987). Each trial consisted of 13 rows (the first two were practice rows) with 10 digits per row. The first trial contained one target (5), the second, two numbers (2, 6) and the third, three numbers (1, 4, 9). The number of targets in each trial was 10, 20 and 30 respectively amounting to a maximum score of 60.

5.2.2.2.3 Procedure

A stopwatch was used to time the task. Participants were given the instructions: 'I would like you to search these rows and cross out all the 5s like this (Examiner demonstrates). Let's practice first. Please cross out all the 5s in the first two rows. (The examiners correct any errors or omissions). Now I'd like you to do the rest of the rows. Work as quickly and correctly as you can. Start now.'

The stopwatch was started and stopped when the examinee completed the task. The number of correct responses made within a 45 second time span was recorded. If the examinee exceeded the 45 second limit, a note was made of the last target completed within the time frame. No credit was given for targets cancelled

after the time limit had expired. The total score recorded was the sum of correct responses in the three trials.

5.2.2.3 DESIGN AND STATISTICAL ANALYSIS

A univariate ANOVA was performed on the number of correct items, comparing the effects of age, gender, ethnicity and education.

Age was categorized as previously described. A Bonferroni correction was employed in the post hoc analyses of the effects of education and age.

Regression analyses were also performed to determine the contribution of age, gender, education and ethnicity to cancellation scores.

5.2.2.4 RESULTS

5.2.2.4.1 Cancellation total

ANOVA Analysis

Mean overall score on the cancellation task was 54.18 (sd=7.10) and scores ranged from 18 to 60. Results from the ANOVA analysis showed a significant effect of age ($F(5, 74)=3.29, p=.01$), ethnicity ($F(1,74)=7.97, p=.006$) and education ($F(2, 74)=11.62, p<0.001$). There was no main effect of gender. There were also two significant interaction effects between age and ethnicity ($F(5, 74)=3.59, p=.006$) and between education and ethnicity ($F(2, 74)=3.25, p=.044$). The interaction between age and ethnicity showed worse performance in the eldest age groups but more so in the Caribbean group (see Figure 5.9). The interaction of ethnicity and education also showed worse performance in the low education group and more so for the Caribbean versus the British group (see Figure 5.10).

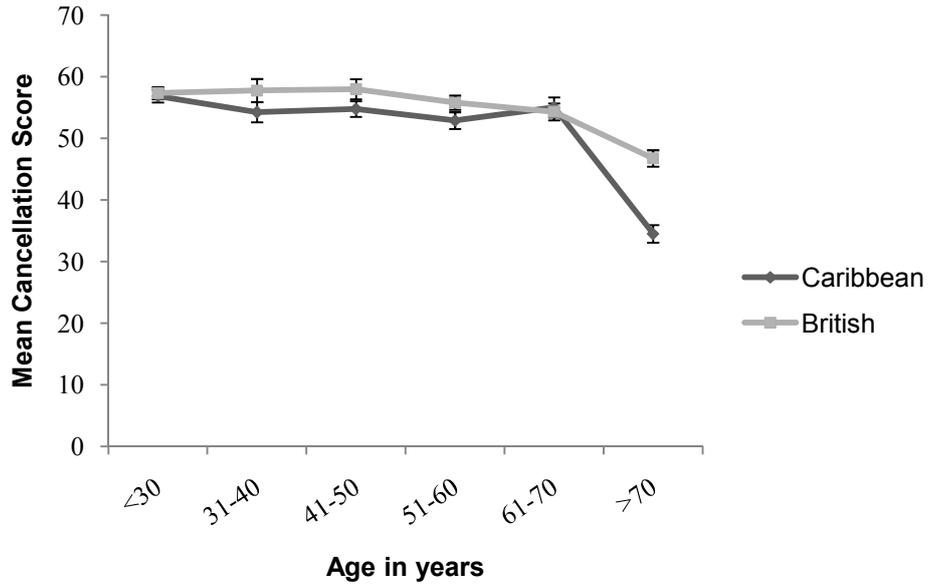


Figure 5.9 Graph showing interaction effect for age and ethnicity for cancellation scores.

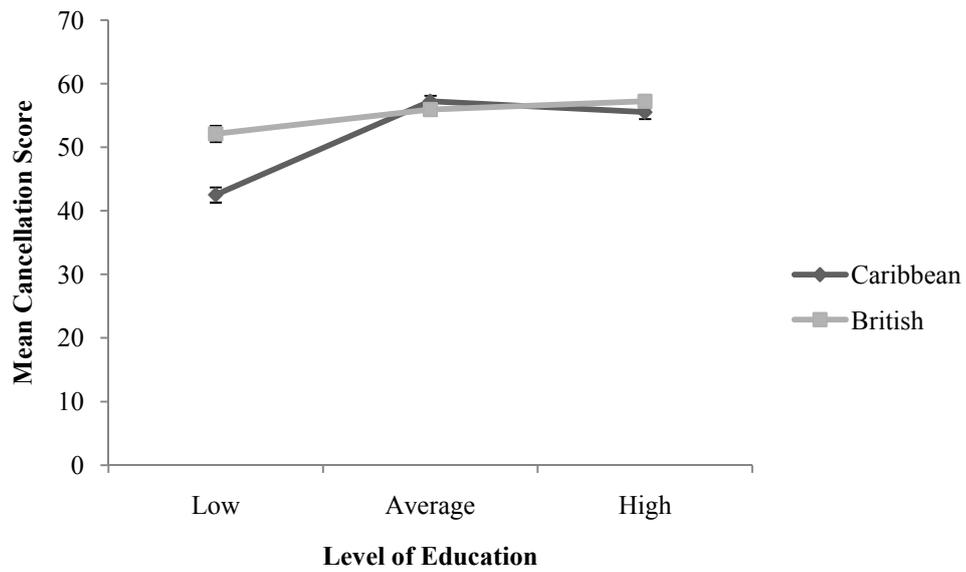


Figure 5.10 Graph showing interaction effect for education and ethnicity for cancellation scores.

Regression Analysis

The correlation between cancellation scores and predictors are shown in Table 5.8. Mean cancellation score was significantly correlated with age and

education which increasing age and fewer years of education were associated with lower scores.

Table 5.8

Correlation coefficients between cancellation scores and predictors

	Age	Gender	Education	Ethnicity
Cancellation	-.55*	.04	.53*	.15

*p<0.001

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 117)=21.17, p<0.001$). Of the four predictors, age, ethnicity and education made significant contributions to the overall model. A stepwise regression analysis was then performed with age, ethnicity and education as the only predictors and a significant model emerged ($F(3, 117)=21.24, p<0.001$) which accounted for 42% ($R^2=.42$), of the variance in performance. Age significantly predicted cancellation scores, $\beta=-.38, t(117) = -4.70, p<0.001$ and accounted for 31%, ($R^2 = .31$) of the variance in scores. Education accounted for a further 8% of the variance, ($R^2 = .08, \beta=.34, t(117) = 4.07, p<0.001$ and ethnicity contributed to 3% of the variance in scores, $R^2 = .03, \beta=.16, t(117) = 2.19, p=0.030$. The regression model is shown in Table 5.9 below.

Table 5.9

Multiple Regression Analysis- unstandardised and standardized coefficients for Cancellation

Item		B	SE B	β	R^2	
Cancellation	Model(Enter)	(Constant)	52.17	2.82		
		Age	-.14	.03	-.39	
		Gender	1.51	1.03	.11	
		Ethnicity	2.15	1.01	.15	
		Years of Education	.47	.11	.36	.42*
Cancellation	Model (Stepwise)	(Constant)	53.42	2.70		
		Age	-.15	.03	-.39	.31*
		Years of Education	.44	.11	.34	.08*
		Ethnicity	2.22	1.01	.16	.03*

*p<0.05

5.2.2.4.2 *Cancellation time*

One-way ANOVA

The total time taken for the three trials on the cancellation task was slightly longer for Caribbeans ($m=98.65\text{sec}$, $se=5.55$) than the British ($m=97.40\text{sec}$, $se=3.14$), however, this difference was not statistically significant.

5.2.2.5 DISCUSSION

Age, education and ethnicity all appear to influence performance on digit cancellation tests. Performance in the eldest age group showed Caribbean persons over 70 years of age performing much worse than their British counterparts. In younger age groups, the difference due to ethnicity was not significant. This finding concurs with that of Byrd et al (2004) who report worse performance in elderly ethnic minorities. The performance of Caribbean persons in the low education group was also considerably worse when compared to performance by low educated British. Education accounted for only 8% of the variance in scores and ethnicity even less at 3%. Thus the difference in performance may be attributable to a factor not included in the study. Byrd et al (2004) found ethnic differences disappeared when ethnic groups were matched on literacy levels rather than years of education. As mentioned previously, years of education may not be a suitable indicator of the quality or experience of education in ethnic groups and as such there may be other factors contributing to performance on cancellation.

Another explanation may lie in the timed nature of the cancellation task. Cultural differences in cognitive styles may result in different emphases being placed on accuracy and speed. Different authors have noted a less stringent approach to time in ethnic groups such as Hispanics and African-Americans (Helms, 1992; Jones, 1998; Levine, 1997; Llabre, 1991). The instructions of the cancellation task ask

participants to work quickly and correctly but it does not specify which is more important and as such, it may be left up to the respondent to choose. Byrd et al (2004) note that a strategy or cognitive style which favours accuracy over speed will ultimately penalise performance in a timed test like digit cancellation and make interpretation difficult as the examiner cannot be certain whether performance is a function of ability or style.

However, the difference in time taken by both groups was not statistically significant suggesting both groups perform the task at the same speed. Nevertheless, the instructions in the task explicitly asked the respondent to work as quickly as they can, thus this may have suppressed the use of a cultural style that deemphasises speed and as a result the Caribbean participants' lower performance could have been the result of a speed/accuracy trade-off. The Raven's matrices are another timed test in which completion times are recorded but the participant is not instructed to work at any particular pace. An examination of performance on that task and its implications for cognitive styles to timed tests will be discussed in Chapter 6.

5.2.3 STUDY 4

ACCOUNTING FOR AGE, EDUCATION, GENDER AND ETHNICITY EFFECTS ON PERFORMANCE ON CANCELLATION: A STANDARDIZATION STUDY

5.2.3.1 AIM

The objectives of this study are to:

1. Establish standardised scores for cancellation based on age, gender, years of education and ethnicity.

5.2.3.2 METHOD

5.2.3.2.1 *Participants*

The participants are the same as described in Section 5.2.3.2.1

5.2.3.2.2 *Materials*

The cancellation task was administered to all participants.

5.2.3.2.3 *Procedure*

The procedure is the same as that described in Study 1, Section 5.2.3.3

5.2.3.3 STATISTICAL ANALYSIS

The analysis is the same as that described in Section 4.1.11.3

5.2.3.4 RESULTS

The overall adjusted mean score for cancellation was 53.91 (sd=6.76) with scores ranging from 25.44 to 60. The variables selected for entry into the regression model were age, gender, education and ethnicity. Significant predictors were identified as age, education and ethnicity. Gender failed to significantly influence performance. A formula for correction was obtained as follows:

$$\begin{aligned} \text{Corrected cancellation score} = & \text{Raw score} + [(0.293) (\text{Age}^* - 46.86)] \\ & + [-(0.378) (\text{Education}^* - 14.21)] \\ & + [-(0.168) (\text{Ethnicity}^{***} - 1.54)] \end{aligned}$$

* Age in years **Years of education ***Caribbean ethnicity coded as 1, British coded as 2

The formula above allows for calculation of individual scores. The frequency distribution of scores on cancellation shows a negatively skewed distribution with a

median score of 55.33 (interquartile range: 49.36 – 60) (see Figure 5.11). Tolerance limits defined a cut-off score of 39.09.

A correction grid with pre-calculated values for the combined effect of the variables is shown below for a range of ages based on the education groups derived from the sample for each ethnicity (See table 5.10a and 5.10b). The median value of each education category is used to generate the correction grid. Equivalent scores are provided in Table 5.10c.

Table 5.10a

Correction grids for cancellation scores with adjustments based on education and age for Caribbean persons

Education	Age											
	20	25	30	35	40	45	50	55	60	65	70	75
3-10 years	-5.81	1.25	0.05	1.97	2.71	3.89	4.91	5.99	7.05	8.11	9.18	10.2
11-16 years	-7.32	-5.86	-4.39	-2.93	-1.46	0.00	1.47	2.93	4.40	5.86	7.33	8.79
17-30 years	-9.78	-8.31	-6.85	-5.38	-3.92	-2.45	-0.99	0.48	1.94	3.41	4.87	6.34

Table 5.10b

Correction grids for cancellation scores with adjustments based on education and age for British persons

Education	Age											
	20	25	30	35	40	45	50	55	60	65	70	75
3-10 years	-5.98	1.15	-0.08	1.85	2.59	3.77	4.79	5.87	6.93	7.99	9.05	10.12
11-16 years	-7.49	-6.02	-4.56	-3.09	-1.63	-0.16	1.30	2.77	4.23	5.70	7.16	8.63
17-30 years	-9.95	-8.48	-7.02	-5.55	-4.09	-2.62	-1.16	0.31	1.77	3.24	4.70	6.17

Table 5.10c

Equivalent scores for digit cancellation

Test	Equivalent Scores				
	0	1	2	3	4
Digit Cancellation	<39.09	30.10-43.15	43-16-47.21	47.22-51.27	51.28-55.33

The frequency distribution of the adjusted scores is presented in Figure 5.11.

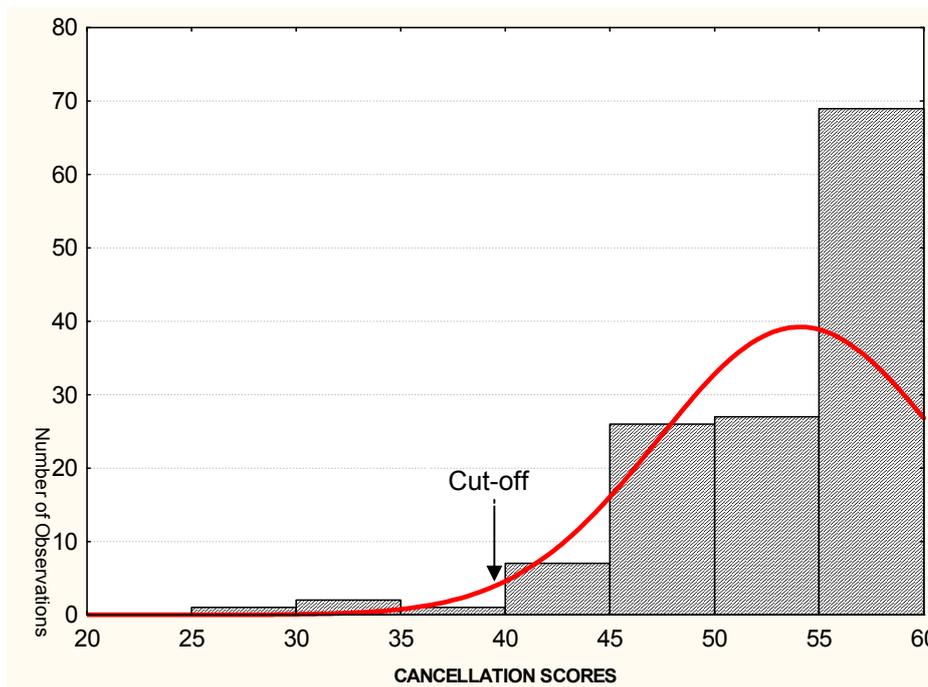


Figure 5.11 Frequency distribution of cancellation scores

5.2.5 DISCUSSION

These findings indicate that cancellation scores are affected by age, education and ethnicity. The derived formula provides a means whereby the effects of these variables can be accounted for. Individual scores should be adjusted to account for the relative effects of these variables before interpretation of an individual's performance is made. While there is a vast array of cancellation tasks available, there are few normative data available for the variant of the digit cancellation task used in this study. As such the cut-off score of 39.09 ((interquartile range: 49.36 – 60) obtained may provide a useful guideline for practitioners using this version of the task in these populations.

5.3 LOGICAL MEMORY

5.3.1 DESCRIPTION OF LOGICAL MEMORY

Logical memory is one of the subtests of the Wechsler Memory Scale (Wechsler, 1945, 1987, 1997). It is a form of story recall which is a measure of memory for information that exceeds the immediate memory span (Lezak, 2004). The test involves the auditory presentation of a story, immediately after which the respondent is required to recall the story exactly as they heard it. After a delay (usually 10 or 30 minutes), the respondent is again asked to recall the story. Scores are based on the number of correctly recalled story units. Two scores are obtained: an immediate and delayed score corresponding to the two retellings of the story. Analysis of the discrepancies between the two scores can yield information about the patient's short term and long term memory functioning (Groth-Marnat, 2009).

5.3.2 FACTORS INFLUENCING PERFORMANCE ON LOGICAL MEMORY

Performance on the Logical Memory test have been found to be affected by age however the effects may not be apparent until after age 60 or even later (Bak and Greene, 1981; Abikoff et al, 1987). Education also impacts performance with lesser educated individuals yielding lower scores (Bak and Greene, 1981). This effect is also seen in a comparison across studies in which studies using more educated persons have reported higher mean scores for both the immediate and delayed recall than studies using lower educated persons (Lichtenberg and Christensen, 1992). Gender effects are not usually found although women may have higher immediate recall scores (Ragland et al, 2000) and may perform better on the Anna Thompson story (Iverson, 1986). There are also no reports of ethnic differences on performance

on this task although this may be due to administrative and scoring differences due to the use of different stories or versions across cultures as well as variations in time span for the delayed recall (for example, different stories and different versions of stories are used in Italian settings as in De Renzi, (1977) and Bisiach, Cappa et al, (1983)). Comparison of immediate and delayed recall shows greater forgetting among AD patients than in healthy young and old controls (Butters et al, 1988).

5.3.3 STUDY 5

EXPLORING THE EFFECT OF AGE, GENDER, EDUCATION AND ETHNICITY ON LOGICAL MEMORY PERFORMANCE

5.3.3.1 AIM

The objectives of this study are to:

1. Assess the difference in performance on the logical memory task (immediate and recall) based on age, gender, education and ethnicity,
2. Identify the contribution of each predictor (age, gender, education) to performance on each measure

5.3.3.2 METHOD

5.3.3.2.1 Participants

The participants comprised 62 participants (33 female and 29 male) from Trinidad. Mean age was 47.73 years (sd=6.60) and ranged from 19 to 89 years. The average years of education was 47.73 (sd=18.43) and ranged from 3 to 30 years.

5.3.3.2.2 Materials

The Anna Thomson story of the Logical Memory test of the Wechsler Memory Scale (Wechsler, 1997) was used.

5.3.3.2.3 Procedure

The story was read aloud to the participant. Immediately after, they were required to retell the story. The story was then read again and the participant was asked to remember the story. Delayed recall was assessed after a 10 minute interval.

One variation was made to the story in which the denomination of sum of money was referred to in pounds for the British sample, whereas dollars was used for the Caribbean sample.

5.3.3.3 DESIGN AND STATISTICAL ANALYSIS

A univariate ANOVA was performed on the number of items recalled in both the immediate and delayed trials, comparing the effects of age, gender and education.

Age was categorized as previously described. A Bonferroni correction was employed in the post hoc analyses of the effects of education and age.

Regression analyses were also performed to determine the contribution of age, gender and education to logical memory scores.

5.3.3.4 RESULTS

5.3.3.4.1 Logical Memory Immediate

ANOVA Analysis

Mean score on the logical memory immediate recall task was 11.65 (sd=4.90) and scores ranged from 0 to 20. Results from the ANOVA analysis showed no significant main effects for any of the predictors: age, gender or education. There were no significant interaction effects.

Regression Analysis

The correlation between logical memory scores and predictors are shown in Table 5.12. Mean immediate recall score was significantly correlated with age and education with increasing age and fewer years of education associated with lower scores. Immediate recall was also positively correlated with delayed recall scores.

Table 5.12

Correlation coefficients between logical memory scores and predictors

	Gender	Education	LM Immediate Recall	LM Delayed Recall
Age	-.00	-.60*	-.49*	-.50*
Gender		-.07	-.08	-.04
Education			.64*	.66*
LM Immediate Recall				.83*

*p<0.001

A forced entry regression analysis with predictors age, gender and education produced a significant model ($F(3, 58)=14.59, p<0.001$). Of the four predictors, only education made a significant contribution. The regression equation was repeated with education as the only predictor and a significant model emerged ($F(1, 60)=42.33, p<0.001$) which accounted for 41% ($R^2=.41$), of the variance in performance. The regression model is shown in Table 5.13 below

5.3.3.4.2 Logical Memory Delayed Recall

ANOVA Analysis

Mean score on the logical memory delayed recall task was 15.15 (sd=5.37) and scores ranged from 0 to 24. Results from the ANOVA analysis showed a significant main effect of education. There were no other significant main effects or interaction effects. Post hoc analyses revealed significantly lower scores in the low education group (m=8.78, se=1.30) as compared to both the average (16.46, se=.93) and high education (m=18.23, se=1.15) groups. The difference between the average and high education group was not significant.

Regression Analysis

The correlation between logical memory scores and predictors are shown in Table 5.12. Mean delayed recall score was significantly correlated with age and education with increasing age and fewer years of education associated with lower scores. Delayed recall was also positively correlated with immediate recall scores.

Table 5.13

Multiple Regression Analysis- unstandardised and standardized coefficients for Logical Memory

Item			B	SE B	β	R ²
LM Immediate	Model(Enter)	(Constant)	8.002	2.750		
		Age	-.042	.033	-.157	
		Gender	-.346	.970	-.036	
		Years of Education	.405	.093	.545	.43*
	Model (Stepwise)	(Constant)	4.776	1.160		
		Years of Education	.477	.073	.643	.41*
LM Delayed	Model(Enter)	(Constant)	10.657	2.965		
		Age	-.044	.036	-.153	
		Gender	-.003	1.045	.000	
		Years of Education	.460	.100	.565	.45*
	Model (Stepwise)	(Constant)	7.453	1.250		
		Years of Education	.535	.079	.658	.43*

*p<0.01

A forced entry regression analysis with predictors age, gender and education produced a significant model ($F(3, 58)=15.66, p<0.001$). Of the four predictors, only education made a significant contribution. The regression equation was repeated with education as the only predictor and a significant model emerged ($F(1, 60)=45.75, p<0.001$) which accounted for 43% ($R^2=.43$), of the variance in performance. The regression model is shown in Table 5.13.

5.3.3.5 DISCUSSION

While age was significantly correlated with performance on both tasks, it failed to significantly predict performance. This may be due to the average age of the sample which at 47 is younger than the range at which age effects have been reported (Bak and Greene, 1981; Abikoff et al, 1987). There were no observed effects of ethnicity therefore this test appears to be resistant to the effects of culture. The consistent finding of the effect of education was also replicated in this study. Given the relatively high level of education in this sample and the contribution of education to scores on both the immediate and delayed recall of the task, this has implications for the interpretation of performance in groups with variable levels of education.

5.3.4 STUDY 6

ACCOUNTING FOR AGE, EDUCATION, GENDER AND ETHNICITY EFFECTS ON PERFORMANCE ON LOGICAL MEMORY: A STANDARDIZATION STUDY

5.3.4.1 AIM

The objectives of this study are to:

1. Establish standardised scores for logical memory immediate and delayed recall based on age, gender, years of education and ethnicity.

5.3.4.2 METHOD

5.3.4.2.1 Participants

The participants are the same as described in Section 5.3.3.2.1

5.3.4.2.2 Materials

The material was the same as described in Section 5.3.3.2.2

5.3.4.2.3 Procedure

The procedure is the same as that described in Section 5.3.3.2.3

5.3.4.3 STATISTICAL ANALYSIS

The procedure is the same as that described in Section 4.1.11.3

5.3.4.3 RESULTS

5.3.4.3.1 Logical memory immediate recall

The overall adjusted mean score for logical memory immediate recall was 11.65 (sd=3.78) with scores ranging from 3.30 to 21.03. The variables selected for entry into the regression model were age, gender, and education. Only education emerged as a significant predictor. A formula for correction was obtained as follows:

Corrected LM Immediate Recall score = Raw score

$$+ [-(0.545) (\text{Education}^* - 14.38)]$$

*Years of education

The formula above allows for calculation of individual scores. Tolerance limits defined a cut-off score of 2.86. The frequency distribution of scores on logical memory immediate recall shows a normal distribution with a median score of 12.12 (interquartile range: 9.26 – 14.12) (see Figure 5.12).

A correction grid with pre-calculated values is shown below for the different education groups. See Table 5.14a. The median value of each education category is used to generate the correction grid. Equivalent scores are provided in Table 5.14b.

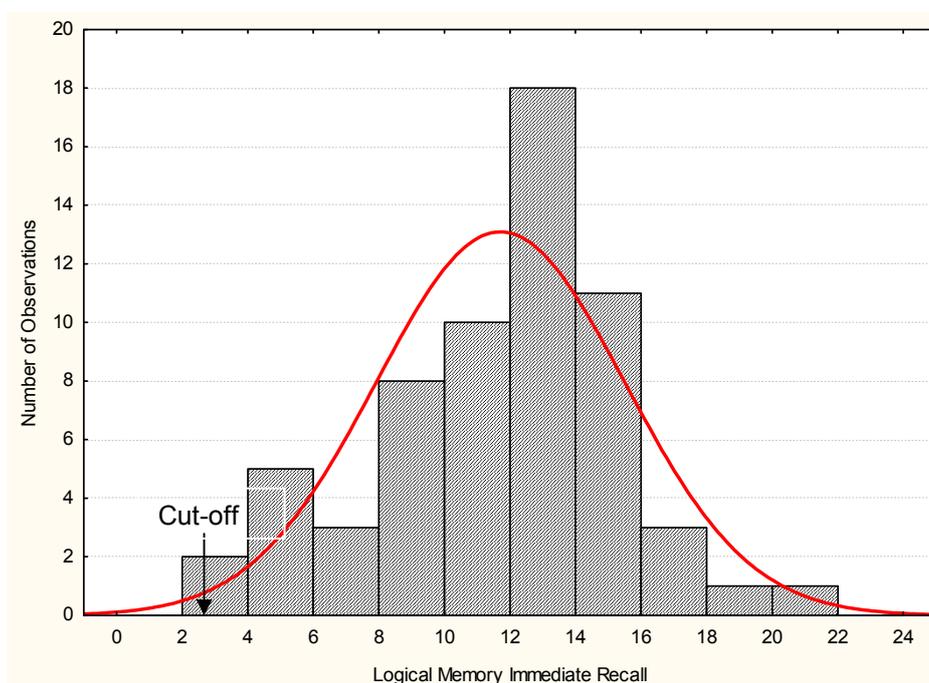


Figure 5.12 Frequency distribution of logical memory immediate recall scores

Table 5.14a

Correction grids for logical memory immediate recall scores with adjustments based on education

Years of Education		
3-10 years	11-16 years	>17 years
2.93	0.75	-2.79

Table 5.14b

Equivalent scores for Logical Memory Immediate

Test	Equivalent Scores				
	0	1	2	3	4
Logical Memory Immediate	<2.86	2.87-5.17	5.18-7.49	7.50-9.80	9.81-12.12

5.3.4.3.2 Logical memory delayed recall

The overall adjusted mean score for logical memory delayed recall was 15.10 (sd=4.06) with scores ranging from 6.44 to 22.78. The variables selected for entry into the regression model were age, gender and education. Education was the only significant predictor. A formula for correction was obtained as follows:

Corrected LM Delayed Recall score = Raw score

$$+ [-(0.565) (\text{Education}^* - 14.38)]$$

*Years of education

The formula above allows for calculation of individual scores. The frequency distribution of scores on logical memory delayed recall shows a negatively skewed distribution with a median score of 15.52 (interquartile range: 12.18-18.35) (see Figure 5.13). Tolerance limits defined a cut-off score of 5.74.

A correction grid with pre-calculated values for the effect of education is presented below. The median value of each education category is used to generate the correction grid. Equivalent scores are provided in Table 5.15b.

Table 5.15a

Correction grids for logical memory delayed recall scores with adjustments based on education

Years of Education		
3-10 years	11-16 years	>17 years
3.04	0.78	-2.89

Table 5.15b

Equivalent scores for Logical Memory Delayed

Test	Equivalent Scores				
	0	1	2	3	4
Logical Memory Delayed	<5.74	5.75-8.18	8.19-10.63	10.64-13.07	13.08-15.52

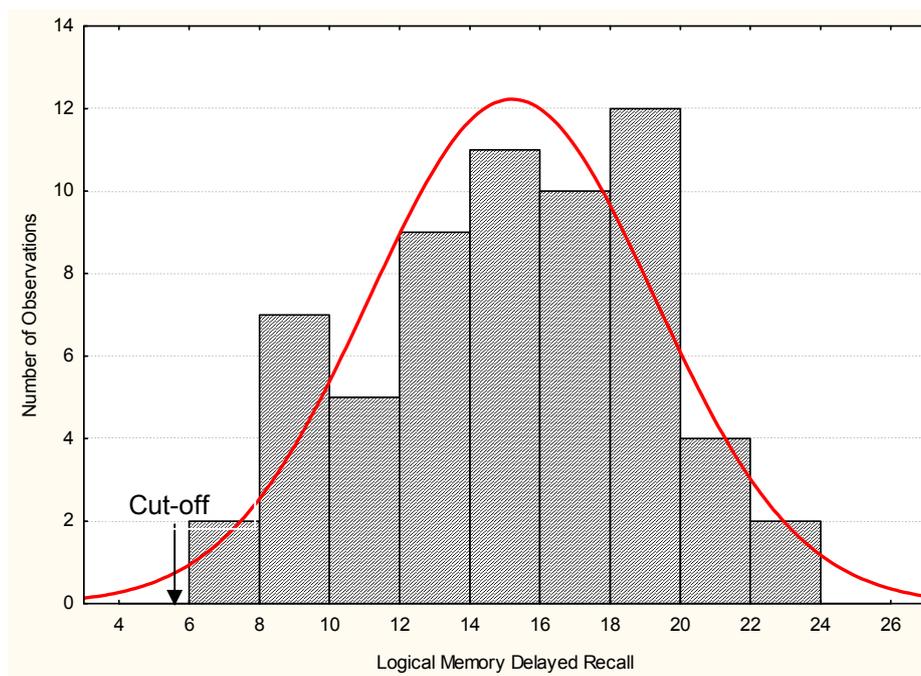


Figure 5.13 Frequency distribution of logical memory delayed recall scores

5.3.4.4 DISCUSSION

These findings indicate that logical memory scores are affected by education and the derived formula provides a means whereby the effects of these variables can be accounted for. Given the effects of education on scores on both immediate and delayed recall in logical memory, it reiterates the needs for scores to be adjusted appropriately and it also highlights the needs for updated norms to allow accurate interpretation of performance on such tasks.

5.4 CONCLUSION

This chapter highlighted the great impact of education on attention and memory tasks. For all tasks: digit span forward and backward, cancellation and logical memory immediate and delayed recall, education significantly influenced performance. On this basis, correction formulas were derived that would adjust for this effect. Patterns of impairment in AD are evident in decreased performance on digit span backwards (relative to digit span forward) and decreased performance in logical memory delayed recall (relative to immediate recall) and both these tasks were found to be heavily influenced by education. In individuals who have very low or very high levels of education, it may be difficult to ascertain whether their performance lies within normal limits, therefore the suggested adjustments can assist in more accurate interpretation of scores for these persons.

There was also a variable effect of ethnicity with effects found on the attentional and working memory tasks (cancellation and digit span backwards) rather than the short term memory task as in logical memory. This difference may be attributed to different abilities in the Caribbean and British groups but could also be attributed to the use of different cognitive styles and strategies which are culturally determined.

These findings have implications with respect to the administration and scoring of these tests. Firstly, digit span forward and backwards tasks should be considered separately and final completion times in cancellation tests should be considered. Secondly, given the varying impact of age, education and ethnicity on scores on these tests, corrections should be made to account for these effects before interpretation is carried out.

CHAPTER 6

EXECUTIVE FUNCTIONING AND ABSTRACT REASONING

6.0 INTRODUCTION

Difficulties in executive functioning and abstract reasoning are also features of dementia and performance on tests that measure both can be indicative of different dementia subtypes. For example, category fluency shows greater deterioration than letter fluency in AD whereas in Huntington's disease both types of fluency are equally impaired (Hart, Smith and Swash, 1988; Hodges and Patterson, 1995; Martin and Fedio, 1983; Monsch, Bondi, Butters et al, 1992). Scores on the Raven's Coloured Progressive Matrices can also differentiate AD patients from healthy controls (Baudic et al, 2006; Giovagnoli et al, 2008). Patients with VaD tend to show marked impairment in executive functioning while some authors suggest impairment may only occur in moderate to late stages in AD (Looi & Sachdev, 1999; Walker, Ayre, Cummings et al, 1991). In addition while problems in executive functioning occur in both AD and FTD, they are more prominent and prevalent in FTD (Askin,-Edgar et al, 2002; Mathuranath et al, 2000; Pachana,et al, 1996; Thompson, Stopford, Snowden et al, 2005). This chapter will address two commonly used measures: verbal fluency and the Raven's Coloured Progressive Matrices.

6.1 VERBAL FLUENCY

Verbal fluency tasks are popularly used in neuropsychological assessments ((Lezak, 2004; Spreen & Strauss, 1998). The first fluency task can be traced back to Thurstone's word fluency task (Thurstone, 1948) which comprised the larger

Primary Mental Abilities Test. This first verbal fluency test was a written task spanning over five minutes in which the individual was required to write down the names of words beginning with the letter S and C. A verbal version was later developed by Benton and colleagues using the letters FAS in which individuals responded over a one minute period as in the (as in the Controlled Oral Word Association Test (COWAT) (Benton and Hamsher, 1976).

The first set of norms for verbal fluency was reported by Borkowski, Benton and Spreen (1967) who established that different letters produced different norms. The letters of the alphabet with the exceptions of X and Z were normed and separated into different difficulty levels: hard (Q, J, V, Y, K, U), moderate (I, O, N, E, G, L, R) and easy (H, D, M, W, A, B, F, P, T, C, S). Subsequently, various sets of letters have come to be used to assess verbal fluency. Common letters used include FAS, CFL and PRW (Ruff et al, 1996).

Fluency assessed using letters as described above is referred to as phonemic fluency. Verbal fluency may also be assessed using categories in what is referred to as semantic fluency. Frequently used categories include animals, fruits, vegetables, cities and furniture. The Western Aphasia Battery (Kertesz, 1982) and the Boston Diagnostic Aphasia Examination (Goodglass and Kaplan, 1972) uses animals as its category, the Mattis Dementia Rating Scale (Mattis, 1988) uses items found in the supermarket and the Set Test (Issacs and Kenie, 1973) uses colour, animals, towns and fruits. The category most frequently used is animals (Tombaugh et al, 1999; Ardila et al, 2006). This may be so because its meaning is clear across most languages and cultures unlike some other categories. Ardila et al (2006) highlight the difficulties with using certain semantic categories such as vegetables which is only partially equivalent to the Spanish category of 'vegetales' in which trees or grass

would also be considered exemplars. They suggest that the animal category is far less ambiguous and the level of difficulty is low across countries, ages and educational levels (Ardila et al, 2006).

Verbal fluency is regarded as a measure of semantic knowledge, retrieval, abstract reasoning and executive functioning. Phonemic fluency is deemed more of an executive functioning test than semantic fluency which incorporates more lexical knowledge and semantic memory organization (Ardila et al, 2006). This view of semantic fluency was also espoused by Estes, (1974) who suggests that the more pertinent factor affecting performance 'is largely determined by the organization of an individual's long-term memory system and the way in which he makes use of this organization to guide performance in the testing situation' (Estes, 1974, p747).

It is thought that both tasks may involve different processes. Evidence for this assertion comes from PET studies which show greater activation of the temporal lobe in semantic fluency as compared to frontal lobe activation in phonemic fluency (Warburton, et al., 1996). Psychometric evidence also distinguishes the tasks; correlation between scores of phonemic and semantic fluency only show moderate to middle correlation (.30 to .60) (Ardila, Roselli & Bateman, 1994; Ardila, Galeano & Roselli, 1998; Ostrosky et al, 1999).

Organization may also differ for the two types of verbal fluency. Lezak, (2004) notes strategies for the letter fluency task may differ from those used on the category fluency task. For instance, letter fluency strategies may include generating words with the same initial consonant (e.g. print, pride, proof), variations on a word (free, freedom, freeness) or variations on a theme (pen, pencil, portrait). Category fluency offers more structure and good performance could entail the use of subcategories to search for words (e.g. a subcategory of animals may be farm

animals such as cow, pig, horse). Laine, (1988) refers to these as phonemic and semantic clusters respectively. In both tasks, when one strategy is exhausted, another is sought (e.g. move from farm to domestic animals, move from similar consonants to word variation) in a process known as clustering and switching (Troyer, Moscovitch, & Winocur, 1997).

Assessment of category and letter fluency tasks requires the individual to name as many words as they can that belong to the category or start with the letter in a given period of time (usually one minute). Scores are indicated by the number of unique, correct words generated within the time limit.

Performance on category fluency usually exceeds than in letter fluency. (Mitrushina, Boone, & D'Elia, 1999) report average figures for elderly controls of 12 to 16 in individual letter fluency whereas animal fluency figures ranged from 20.95 for controls aged 50 to 59 and 18.76 for controls aged 70 to 79. (Troyer, 2000) used a large community sample of adults ranging in age from 18 to 91 years and observed a total mean of 42.5 (sd=11) for letter fluency (FAS) and 19.5 (sd=5.3) for animals.

The norms for alternate versions of the task may vary based on varying word frequencies for each letter and as such researchers advise against using norms for different letters (Ruff et al, 1996; Spreen and Straus, 1998). This also applies for semantic categories in which researchers report differences in the number of exemplars produced for different categories (Hart, Smith and Swash; 1988, Hodges et al, 1992; Monsch et al, 1992) and as such raw scores for different categories are not comparable. In a study of 3000 Spanish speakers, Lopera (n.d) investigated the average number of words produced for 16 different semantic categories. Body parts, things to eat and animals were the easiest categories producing the most number of words (18, 17 and 16 respectively) while categories such as Flowers, furniture and

tools proved more difficult, generating the fewest exemplars (8, 10 and 10 respectively).

6.1.1 VERBAL FLUENCY AND AGE

The findings for the effects of age on fluency appears to be mixed with some authors finding no age effects (Hughes & Bryan, 2002) and others reporting a mixed finding with age predicting number of words generated for semantic and animal category fluency but not for letter fluency (Troyer, 2000). Another study found a significant effect for age with performance decreasing on both letter and category fluency but at a faster rate for category fluency (Brickman, et al., 2005). A meta-analysis of letter fluency studies involving use of the COWAT, and letters FAS found evidence of age-related decline (Loonstra, Tarlow, & Sellers, 2001), however not all studies reported this finding (Perlmutter, Tun, Sizer, McGlinchey, & Nathan, 1987).

6.1.2 VERBAL FLUENCY AND EDUCATION

Education is generally reported to have a positive effect on fluency- with higher education associated with better performance on both semantic and letter fluency (Benton et al, 1976; Tombaugh, Kozak and Rees, 1999; Troyer, 2000). The effect however, may vary by fluency task. Ardila et al (2000) reported 38.5% of variance in phonemic fluency for letter F and 23.6% of variance in semantic fluency for animals being accounted for by education in a sample of Mexican adults. Ratcliff et al (1998) studied Hindi speakers and found length of education to be significant for both types of fluency but more so for letter fluency.

Brickman et al (2005) however point out that while there is evidence to suggest that education has an impact on fluency performance, it is unclear as to

whether fluency varies as a function of education throughout life, with education providing some measure of cognitive reserve in old age.

The role and interaction of age and education in fluency may vary by task. Some studies highlight age and education as significant predictors of fluency (Tombaugh et al, 1999) while others fail to find any significant interaction effects for age and education (Kempler, Teng, Dick, Taussig, & Daviss, 1998). In a large normative study of Canadian adults, Tombaugh, Kozak and Rees (1999) found education accounted for more variance (19%) than age (11%) in the letter fluency task, however this pattern was reversed in the animal fluency task with age explaining a greater proportion of variance (23%) than education (14%). This finding is also supported by other research (Loonstra et al, 2001; Tun and Lachman, 2006) which report an effect of age for semantic fluency whereas an effect of education is found for phonemic fluency. Significant interaction effects for age and education are not generally found (Kempler et al, 1998) although Tombaugh, Kozak and Rees (1999) report a small but significant interaction between age and education for phonemic fluency but not for semantic fluency.

6.1.3 VERBAL FLUENCY AND GENDER

Many studies report no effect of gender on fluency performance (Brickman, et al, 2005; Gladsjo et al, 1999; Yeudall et al, 1986; Tombaugh, Kozak & Rees, 1999) while others have reported findings which show women performing better on letter fluency (Bolla, Lindgran, Bonaccorsy & Blleecker, 1990; Crossley, Darcy & Rawson, 1997; Loonstra et al, 2001; Tombaugh et al, 1999)). In semantic fluency, gender differences appear to depend on the category being assessed. Capitani et al (1999) examined word fluency in different semantic categories (animals, fruits, tools and vehicles) and found varying effects of gender. Whereas no gender effect was

found for animals, women outperformed men on fluency for fruits and men outperformed women on fluency for tools.

6.1.4 VERBAL FLUENCY AND ETHNICITY

Few studies examine the effects of ethnicity on verbal fluency. In one study of American adults aged 18 to 95, ethnic differences were observed in which Gladstjo et al (1999) found main effects for both letter fluency (FAS) and animal fluency tasks, in which Caucasian ethnicity was associated with higher scores when compared to African American scores. The factor of ethnicity accounted for approximately 4.8% of the variance in scores for letter fluency and approximately 10.2% of the variances in scores for animal fluency. In another study of male veterans aged 31-46 years, Johnson-Selfridge et al, (1998) found an effect of ethnicity for both letter (FAS) and animal fluency tasks in which Caucasians performed better than both African-Americans and Hispanics.

A more recent examination of category fluency suggests a role of culture in shaping semantic knowledge. Winkler-Rhoades, Medin, Waxman et al (2010) examined category fluency in children and adults in three American communities (urban, rural and rural Native American) and found the existence of cultural differences in the typicality or salience of animal names. Medin, Ross, Atran et al (2006) also suggest that since cultural knowledge shapes categorization skills, cultural differences can result in differences in organisation and accessibility of knowledge.

6.1.5 FLUENCY AND DEMENTIA

Different impairments result in different patterns of performance on fluency. Deficits in semantic fluency performance have been observed in frontal lobe

damage, Parkinson's disease, schizophrenia, head injury, depression, vascular dementia and Alzheimer's disease (Herrmann et al, 2003; Donovan et al, 1999; Troyer et al, 1997; Chen et al, 2000; Okada et al, 2003). In Huntington's disease, performance on both letter and category fluency have been found to be equally impaired. However, meta analyses of AD and Parkinson's disease show phonemic fluency to be more resistant to deterioration than semantic fluency and this finding has proven to a sensitive measure of AD (Hart, Smith and Swash, 1988; Hodges and Patterson, 1995; Martin and Fedio, 1983; Monsch, Bondi, Butters et al, 1992; Henry and Crawford, 2004; Henry, Crawford and Phillips, 2004; Monsch et al, 1994). AD patients tend to produce fewer and shorter items, more typical, frequent items and earlier acquired items (Forbes-McKay, Ellis, Shanks et al; 2005). This pattern has been so consistent in research findings that the discrepancy between letter and category fluency is thought to be useful indicator in the assessment of Alzheimer's disease (Crossley, D'Arcy & Rawson, 1997; Kozora and Cullum, 1995). Zec (1993) further highlights that semantic fluency is considerably more useful than phonemic fluency in the differential diagnosis of Alzheimer's disease at all stages of the disease.

6.1.6 STUDY 1

EXPLORING THE EFFECT OF AGE, GENDER, EDUCATION AND ETHNICITY ON VERBAL FLUENCY

6.1.6.1 AIM

The objectives of this study are to:

1. assess the difference in performance on letter fluency for the letters F, P and L, based on age, gender, education and ethnicity,

2. Assess the difference in performance on semantic fluency for the categories animals, fruits and cities,
3. Identify the contribution of each predictor to performance on each measure
4. Compare within group performance for phonemic and semantic performance.

6.1.6.2 METHOD

6.1.6.2.1 Participants

In this study, 123 participants (female= 69, male=54) from Trinidad and Tobago (n=61) and England (n=62) were assessed. The sample ranged in age from 18 to 89 years (m=47.37, sd=19.20) and years of education ranged from 3 to 30 years (m=14.49, sd=5.55). All participants were functionally independent, and those with any neurological or psychiatric impairment were excluded.

6.1.6.2.2 Materials

The letters used in the fluency task were F,P and L. The categories used in the semantic fluency task were animals, fruits and cities.

6.1.6.3 PROCEDURE

The semantic fluency task was administered first with the order of categories being determined by a Latin Square design. Participants were given the following instructions: "I'd like you to list as many items as you can that belong to a certain category. You cannot say any proper nouns. For example if I say colours, you can say red, green, blue etcetera. You have one minute. Please keep going until I tell you to stop. Start now." In the letter fluency task, the instructions were "Now I'd like you to list as many words as you can starting with a certain letter. For example if I say M,

you can say move, man, mango etcetera. You have one minute. Please keep going until I tell you to stop. Start now.”

A stopwatch was used to time the task. If participants ceased to give any further responses during the one minute interval, they were given one prompt “Please keep going, you still have some time left.” Participants’ responses were recorded by hand and also by audiotape.

The score recorded was the total number of correct words produced within the time limit. Repeated words were scored once. In the semantic task, if a supraordinate category was produced (e.g. bird), it was not scored if representatives of that category (e.g. chicken) were also produced. In the phonemic task, extensions of words were not counted (e.g. run, running, runner).

6.1.6.4 DESIGN AND STATISTICAL ANALYSIS

Univariate ANOVAs were performed on each of the six dependent variables (P, F, L, Letter Total (F+P+L), Animal, Fruits, Cities, Semantic Total (Animal+Fruits+Cities) comparing the effects of age, gender, ethnicity and education.

Age was categorized as previously described. A Bonferroni correction was employed in the post hoc analyses of the effects of education and age. A stepwise regression analysis was also performed to determine the contribution of age, gender, education and ethnicity to phonemic and semantic fluency scores. A mixed design ANOVA using fluency as the within subjects variable and ethnicity as the between subjects variable was used to compare performance within the two fluency tasks.

6.1.6.5 RESULTS

6.1.6.5.1 Phonemic Fluency

The mean performance for fluency on all three letter measures and the correlation between performance and predictors are shown in Tables 6.1 and 6.2

Table 6.1

Mean performance on measures of letter fluency

	Mean	Min	Max	Std. Dev.	N
Letter P	14.87	4	30	5.72	123
Letter L	14.28	2	26	5.44	123
Letter F	14.12	1	32	5.65	123
Phonemic Fluency Total	43.20	9	83	15.65	123

Table 6.2

Table showing correlation between letters and predictors

	Letter P	Letter L	Letter F	Letter Total	Age	Gender	Education	Ethnicity
Letter P		.78*	.77*	.91*	-.25*	-.04	.54*	.04
Letter L			.77*	.92*	-.29*	-.09	.57*	.06
Letter F				.91*	-.28*	.01	.54*	.03
Letter Total					-.30*	-.05	.60*	.03
Age						-.01	-.52*	.01
Gender							-.15	-.07
Education								-.02

6.1.6.5.1.1 Letter P

ANOVA Analysis

As seen in table 6.1, mean performance on letter P fluency was 14.87 (s.d. =5.72). The number of words produced ranged from a minimum of 4 to a maximum of 30.

Results from the ANOVA analysis showed no significant effects of age, gender or ethnicity on letter P fluency scores. However, a significant main effect for education was found, $F(2,123)=8.20, p=0.001$) and post hoc analysis using a Bonferroni correction showed significant differences between groups with word production increasing with years of education. The low education group had a significantly lower mean number of words produced ($m= 10.07, se= .95$) than both the average ($m=15.18, se=.60$) and high ($m=18.52, se=.91$) education groups. The difference between the average and high education groups was also significant. No significant interaction effects were observed.

Regression Analysis

Fluency scores for letter P correlated significantly with scores for letter L, Letter F, Letter Total, age and education but not ethnicity or gender (See Table 6.2). Increasing age and fewer years of education was associated with lower fluency scores for letter P. Neither gender nor ethnicity was significantly associated with fluency scores for letter P.

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 117)=12.17, p<0.001$). Of the four predictors, only education made a significant contribution to the overall model ($\beta=.56, t(117) = 6.14, p<0.001$). The regression analysis was repeated with education as the only predictor and a significant model was produced ($F(1, 120)=48.65, p<0.001$). Education significantly predicted letter P fluency scores, $\beta=.54, t(120) = 6.98, p<0.001$ and accounted for 28.8% of the variance.

6.1.6.5.1.2 Letter L

ANOVA Analysis

As seen in table 6.1, mean performance on letter L fluency was 14.28 (s.d. =5.44). The number of words produced ranged from a minimum of 2 to a maximum of 26. There was no significant effect of age, gender or ethnicity on Letter L fluency scores but there was a significant main effect for education, ($F(2,123)=9.22$, $p<0.001$). Post hoc analysis showed significant differences between all three groups with word production increasing with years of education. The low education group had a significantly lower mean number of words produced ($m= 9.07$, $se= .88$) than both the average ($m=14.82$, $se=.59$) and high ($m=17.76$, $se=.75$) groups. The difference between the average and high education groups was also significant. No significant interaction effects were observed.

Regression Analysis

Fluency scores for letter L correlated significantly with scores for letter P, Letter F, Letter Total, age and education but not ethnicity or gender (See Table 6.2). Increasing age and fewer years of education was associated with lower fluency scores for letter L. Neither gender nor ethnicity was significantly associated with fluency scores for letter L.

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 117)=14.12$, $p<0.001$). Of the four predictors, only education made a significant contribution to the overall model ($\beta=.56$, $t(117) = 6.29$, $p<0.001$). The regression analysis was repeated with education as the only predictor and a significant model was produced ($F(1, 120)=56.72$,

$p < 0.001$). Education significantly predicted fluency for letter L, $\beta = .57$, $t(120) = 7.53$, $p < 0.001$ and accounted for 32.1% of the variance in scores.

6.1.6.5.1.3 Letter F

ANOVA Analysis

As seen in table 6.1, mean performance on letter F fluency was 14.12 (s.d. = 5.65). The number of words produced ranged from a minimum of 1 to a maximum of 32. No significant effects of age, gender or ethnicity were observed for performance on Letter F fluency. However there was a significant main effect for education, $(F(2,123) = 8.20, p = 0.001)$. Post hoc analysis showed significant differences between the groups: the low education group had a significantly lower mean number of words produced ($m = 9.04, se = 1.02$) than both the average ($m = 14.82, se = 0.59$) and high ($m = 17.24, se = 0.83$) groups. The difference between the average and high education groups however, was not significant. No significant interaction effects were observed.

Regression Analysis

Fluency scores for letter F correlated significantly with scores for letter P, Letter L, Letter Total, age and education but not ethnicity or gender (See Table 6.2). Increasing age and fewer years of education was associated with lower fluency scores for letter F. Neither gender nor ethnicity was significantly associated with fluency scores for letter F.

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 117) = 12.85, p < 0.001$). Of the four predictors, only education made a significant contribution to the overall model

($\beta=.56$, $t(117) = 6.16$, $p<0.001$). The regression analysis was repeated with education as the only predictor and a significant model was produced ($F(1, 120)=50.33$, $p<0.001$). Education significantly predicted letter F scores, $\beta=.54$, $t(120) = 7.09$, $p<0.001$ and accounted for 29.5% of the variance.

6.1.6.5.1.4 Letter Total

ANOVA Analysis

As seen in table 6.1, mean performance on letter total fluency was 43.20 (s.d. =15.65). The number of words produced ranged from a minimum of 9 to a maximum of 83.

For the total letter fluency there was no significant main effect of age, gender or ethnicity but there was a significant main effect for education, ($F(2,123)=8.20$, $p=0.001$). Post hoc analysis showed significant differences between all three groups with word production increasing with years of education. The low education group had a significantly lower mean number of words produced ($m= 28.18$, $se= 2.69$) than both the average ($m=44.67$, $se=1.63$) and high ($m=53.52$, $se=2.08$) groups. The difference between the average and high education groups was also significant. No significant interaction effects were observed.

Performance in letter fluency across all letters and education groups is illustrated below in Figure 6.1.

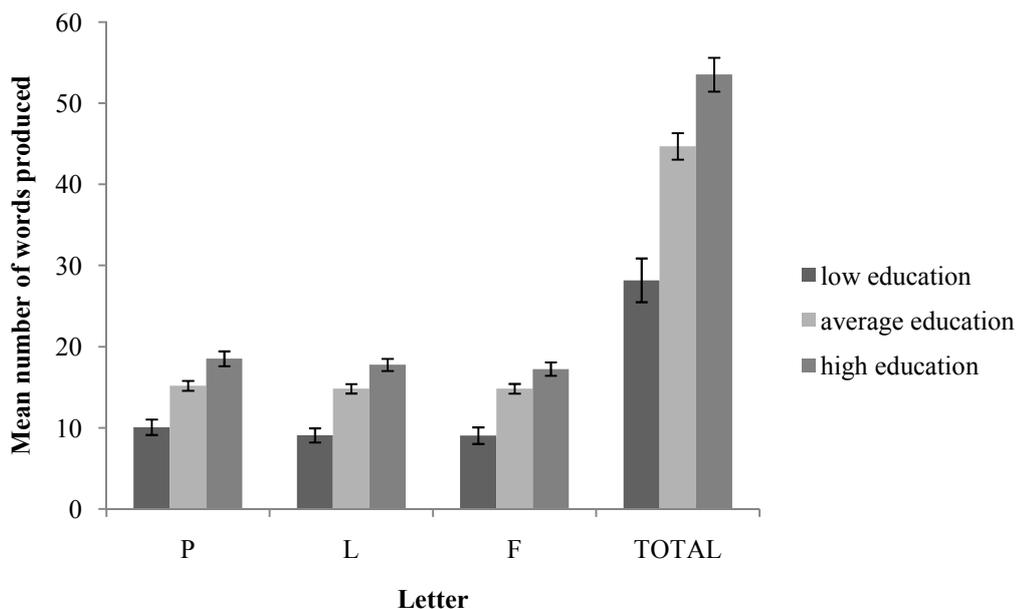


Figure 6.1 Mean number of words produced by education and letter

Regression Analysis

Fluency scores for total letter fluency correlated significantly with age and education but not ethnicity or gender (See Table 6.2). Increasing age and fewer years of education was associated with lower fluency scores for letter fluency. Neither gender nor ethnicity was significantly associated with fluency scores for letter fluency.

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 117)=16.21, p<0.001$). Of the four predictors, only education made a significant contribution to the overall model ($\beta=.60, t(117) = 6.86, p<0.001$). The regression analysis was repeated with education as the only predictor and a significant model was produced ($F(1, 120)=65.75, p<0.001$). Education significantly predicted total letter fluency scores, $\beta=.60, t(120) = 8.11, p<0.001$ and accounted for 35.4% of the variance. The results of the

multiple regression analysis for fluency performance for each letter is shown below in Table 6.3

Table 6.3

Multiple Regression Analysis- unstandardised and standardized coefficients for letter fluency

			B	SE B	β	R ²
Letter P	Model (Enter)	(Constant)	5.40	2.50		
		Age in years	.01	.03	.04	
		Gender	.55	.91	.05	
		Ethnicity	.51	.89	.05	
		Years of Education	.59	.10	.56	.29*
	Model (Stepwise)	(Constant)	6.84	1.24		
		Years of Education	.56	.08	.54	.29*
Letter L	Model (Enter)	(Constant)	6.00	2.32		
		Age in years	-.00	.02	-.01	
		Gender	-.07	.84	-.01	
		Ethnicity	.74	.83	.07	
		Years of Education	.56	.09	.56	.31*
	Model (Stepwise)	(Constant)	6.18	1.15		
		Years of Education	.56	.08	.57	.32*
Letter F	Model (Enter)	(Constant)	5.00	2.45		
		Age in years	.00	.02	.01	
		Gender	1.05	.89	.09	
		Ethnicity	.37	.87	.03	
		Years of Education	.58	.09	.56	.31*
	Model (Stepwise)	(Constant)	6.08	1.22		
		Years of Education	.56	.08	.54	.30*
Letter Total	Model (Enter)	(Constant)	17.45	6.53		
		Age in years	.00	.07		
		Gender	1.06	2.37	.03	
		Ethnicity	1.14	2.32	.04	
		Years of Education	1.71	.25	.60	.36*
	Model (Stepwise)	(Constant)	18.81	3.23		
		Years of Education	1.70	.21	.60	.35*

Note. $p < .001$

6.1.6.5.2 Semantic Fluency

Table 6.4 presents the mean performance on all three category measures and

Table 6.5 shows the correlation between measures and predictors.

Table 6.4

Mean performance on measures of semantic fluency

	Mean	Min	Max	Std. Dev.	N
Cities	18.07	2	46	7.17	123
Animals	19.23	7	42	6.46	123
Fruits	14.99	4	28	4.44	123
Semantic Total	51.88	18	100	14.41	123

Table 6.5

Table showing correlations between semantic categories and predictors

	Cities	Animals	Fruits	Semantic Total	Age	Gender	Education	Ethnicity
Cities		.42*	.38*	.79*	-.09	-.16	.43*	.25*
Animals			.55*	.76*	-.37*	-.08	.48*	.18*
Fruits				.75*	-.26*	.24*	.40*	.23*
Semantic Total					-.30	-.02	.56*	.26*
Age						.01	-.52*	.01
Gender							-.13	.07
Education								-.02

6.1.6.5.2.1 Category Cities

ANOVA Analysis

As seen in table 6.4, mean performance on fluency for cities was 18.07 (s.d.=7.17). The number of words produced ranged from a minimum of 2 to a maximum of 46.

Results from the ANOVA analysis showed no significant effects of gender. Effects for age approached significance, $F(5, 121)=2.23$, $p=0.060$. There was a significant main effect of education, $F(2,121)=3.34$, $p=0.041$) on city fluency. Post hoc analysis using a Bonferroni correction showed significant differences between groups with word production increasing with years of education. The low education group had a significantly lower mean number of words produced ($m= 14.11$, $se= .86$) than both the average ($m=17.70$, $se=.84$) and high ($m=22.18$, $se=1.41$) education

groups. The difference between the average and high education groups was also significant. No significant interaction effects were observed.

A significant main effect of ethnicity $F(1,121)=6.78, p=0.011$ was also found. The Caribbean group produced a significantly lower mean number of cities ($m=16.28, se=.85$) than the British ($m=19.82, se=.93$).

Regression Analysis

Fluency scores for cities correlated significantly with scores for animals, fruits and category total and also showed significant correlation with education and ethnicity but not age or gender (See Table 6.5). Fewer years of education and Caribbean ethnicity were associated with lower fluency scores for cities.

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 117)=11.42, p<0.001$). Of the four predictors, education and ethnicity made significant contributions to the overall model ($\beta=.50, t(117) = 5.38, p<0.001$) and ($\beta=.26, t(117) = 3.31, p=0.001$) respectively.

A stepwise regression analysis was then carried out with education and ethnicity as predictors and a significant model emerged ($F(2, 119)=19.48, p=0.002$). Education significantly predicted city fluency scores, ($\beta=.43, t(119) = 5.37, p<0.001$) as did ethnicity ($\beta=.26, t(119) = 3.19, p=0.002$). The model accounted for 24.7% of the variance in scores, $R^2 = .25, 2, 119)=19.48, p=0.002$ with education accounting for 18.2% of the variance and ethnicity accounting for a further 6.4% of the variance in performance on city fluency.

6.1.6.5.2.2 Category Animals

ANOVA Analysis

As seen in table 6.4, mean performance on animal fluency was 19.23 (s.d. =6.46). The number of words produced ranged from a minimum of 7 to a maximum of 42.

Results from the ANOVA analysis showed no significant effects of gender or age. There was a significant main effects of education, $F(2,121)=4.77$, $p=0.011$) on fluency for animals. Post hoc analysis using a Bonferroni correction showed significant differences between groups with word production increasing with years of education. The low education group had a significantly lower mean number of words produced ($m= 14.14$, $se= .97$) than both the average ($m=19.66$, $se=..77$) and high ($m=22.88$, $se=.98$) education groups. The difference between the average and high education groups was also significant. No significant interaction effects were observed.

A significant main effect of ethnicity $F(1,121)=4.50$, $p=0.037$) was also found. The Caribbean group produced a significantly lower mean number of animals ($m= 18.07$, $se= .93$) than the British ($m=20.37$, $se=.69$).

Regression Analysis

Fluency scores for animals correlated significantly with scores for all other fluency categories and also showed significant correlation with education, ethnicity and age but not gender (See Table 6.5). Fewer years of education, Caribbean ethnicity and increasing age were associated with lower fluency scores for animals.

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 117)=11.74, p<0.001$). Of the four predictors, only education and ethnicity made significant contributions to the overall model ($\beta=.39, t(117) = 4.22, p<0.001$) and ($\beta=.19, t(117) = 2.41, p=0.017$) respectively.

A stepwise regression analysis was then carried out with education and ethnicity as predictors and a significant model emerged ($F(2, 119)=21.44, p<0.001$). Education significantly predicted animal fluency scores, ($\beta=.48, t(119) = 6.11, p<0.001$) as did ethnicity ($\beta=.19, t(119) = 2.37, p=0.019$). The model accounted for 25.2% of the variance in scores, $R^2 = .25, (F(2,119)=21.44, p<0.001)$ with education accounting for 23% of the variance and ethnicity accounting for a further 3.5% of the variance in performance on animal fluency.

6.1.6.5.2.3 Category Fruits

ANOVA Analysis

As seen in table 6.4, mean performance on fluency for fruits was 14.99 (s.d. =4.44). The number of words produced ranged from a minimum of 4 to a maximum of 28.

No significant effects of age, or education were observed for fluency for fruits. However there was a significant main effect for gender, ($F(1,121)=4.21, p=0.044$). Men produced significantly fewer fruits ($m= 13.80, se= .59$) than women ($m=15.93, se=.52$).

A significant main effect of ethnicity $F(1,121)=8.56, p=0.005$) was also found. The Caribbean group produced a significantly lower mean number of fruits ($m=13.95, se=.56$) than the British ($m=16.02, se=.54$).

No significant interaction effects were observed.

Regression Analysis

Fluency scores for fruits correlated significantly with scores for all other fluency categories and also showed significant correlation with education, ethnicity, age and gender (See Table 6.5). Fewer years of education, Caribbean ethnicity, increasing age and male gender were associated with lower fluency scores for fruits.

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 117)=12.25, p<0.001$). Of the four predictors, education, ($\beta=.42, t(117) = 4.54, p<0.001$), gender, ($\beta=.28, t(117) = 3.60, p<0.001$) and ethnicity, ($\beta=.21, t(117) = 2.74, p<0.001$) made significant contributions to the overall model.

A stepwise regression analysis was then carried out with education, gender and ethnicity as predictors and a significant model emerged ($F(3, 118)=16.33, p<0.001$). Education significantly predicted fruit fluency scores, ($\beta=.44, t(118) = 5.64, p<0.001$) as did gender ($\beta=.29, t(118) = 3.65, p<0.001$) and ethnicity ($\beta=.21, t(118) = 2.74, p=0.007$). The model accounted for 29.3% of the variance in scores, $R^2 = .29, (F(3,118)=16.33, p<0.001)$ with education accounting for 16% of the variance, gender for 8.8% and ethnicity accounting for a further 4.5% of the variance in performance on fruit fluency.

6.1.6.5.2.4 Semantic Total

ANOVA Analysis

As seen in table 6.4, mean performance on letter total fluency was 51.88 (s.d. =14.41). The number of words produced ranged from a minimum of 18 to a maximum of 100.

For the total semantic fluency there was no significant main effect of age or gender but there was a significant main effect of education, ($F(2,121)=4.56$, $p=0.014$). Post hoc analysis showed significant differences between all three groups with word production increasing with years of education. The low education group had a significantly lower mean number of words produced ($m= 39.61$, $se= 10.60$) than both the average ($m=52.16$, $se=12.03$) and high ($m=61.91$, $se=13.73$) groups. The difference between the average and high education groups was also significant.

A significant main effect of ethnicity ($F(1,121)=10.73$, $p=0.002$) was also found. The Caribbean group produced a significantly lower mean number of words ($m= 48.08$, $se= 1.75$) than the British ($m=55.61$, $se=1.80$).

Performance in semantic fluency across all categories and education groups is illustrated below in Figure 6.2. Performance across all categories by ethnicity is illustrated in Figure 6.3. No significant interaction effects were observed.

Regression Analysis

Total semantic scores correlated significantly with scores for all other fluency categories and also showed significant correlation with education, ethnicity and age but not gender (See Table 6.5). Fewer years of education, Caribbean ethnicity and increasing age were associated with lower overall fluency scores.

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 117)=18.81, p<0.001$). Of the four predictors, only education, ($\beta=.56, t(117) = 6.61, p<0.001$) and ethnicity, ($\beta=.26, t(117) = 3.66, p<0.001$) made significant contributions to the overall model.

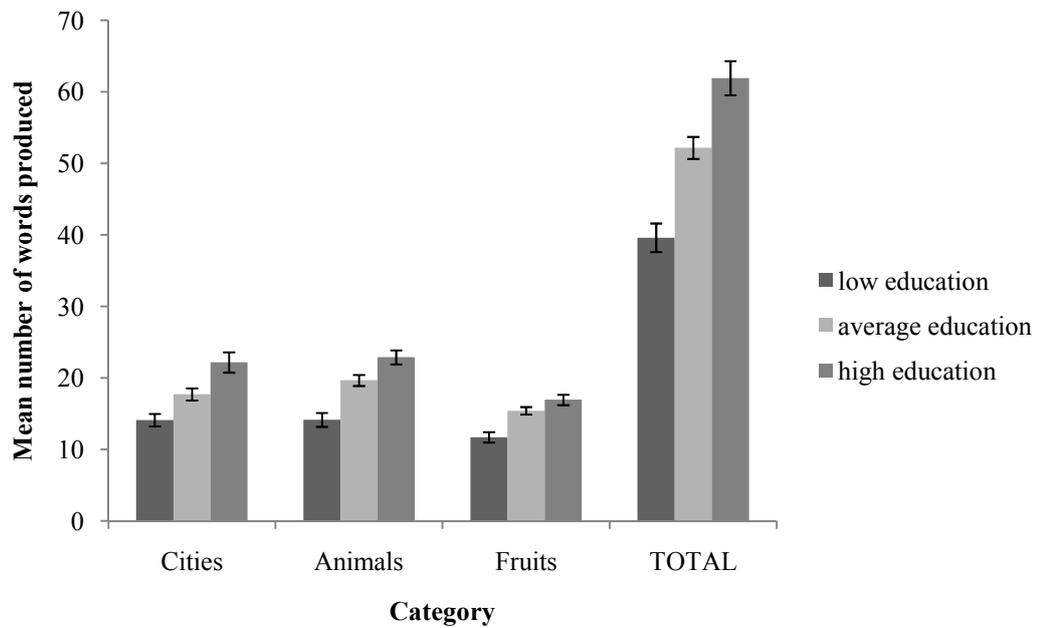


Figure 6.2 Mean number of words produced by education and category

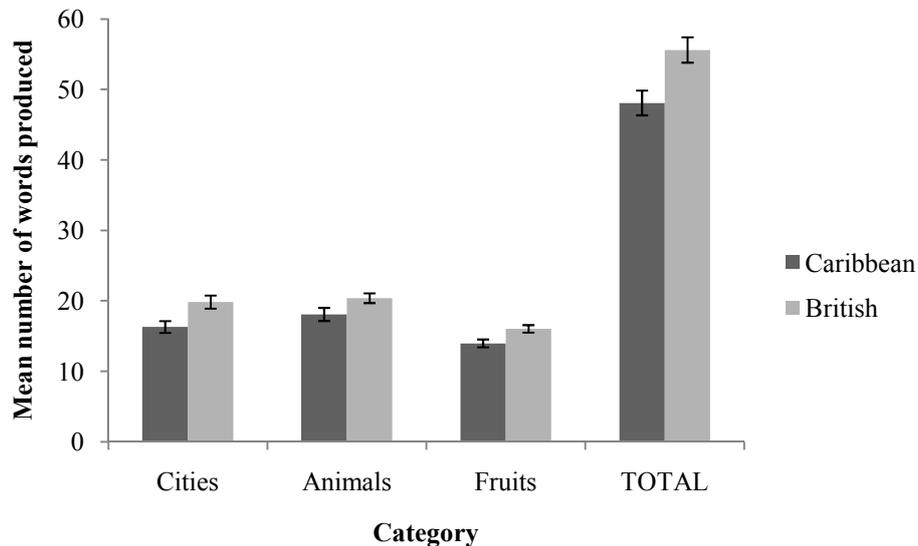


Figure 6.3 Mean number of words produced by ethnicity and category

Table 6.6

Multiple Regression Analysis- unstandardised and standardized coefficients for semantic fluency

			B	SE B	β	R ²	
Cities	Model(Enter)	(Constant)	4.75	3.17			
		Age in years	.06	.03	.17		
		Gender	-1.56	1.15	-.11		
		Ethnicity	3.73	1.13	.26		
		Years of Education	.65	.12	.50	.28*	
	Model(Stepwise)	(Constant)	8.21	1.70			
		Years of Education	.56	.10	.43	.18*	
		Ethnicity	3.63	1.14	.25	.06*	
	Animals	Model (Enter)	(Constant)	14.38	2.84		
			Age in years	-.06	.03	-.17	
Gender			-.43	1.03	-.03		
Ethnicity			2.44	1.01	.19		
Years of Education			.46	.11	.39	.29*	
Model (Stepwise)		(Constant)	9.91	1.51			
		Years of Education	.57	.09	.48	.23*	
		Ethnicity	2.40	1.01	.19	.04*	
Fruits		Model(Enter)	(Constant)	8.33	1.94		
			Age in years	-.01	.02	-.05	
	Gender		2.53	.70	.28		
	Ethnicity		1.89	.69	.21		
	Years of Education		.34	.07	.42	.30*	
	Model(Stepwise)	(Constant)	7.46	1.14			
		Years of Education	.36	.06	.44	.16*	
		Gender	2.55	.70	.29	.09*	
		Ethnicity	1.89	.69	.21	.05*	
SemanticTotal	Model(Enter)	(Constant)	26.70	5.86			
		Age in years	-.01	.06	-.02		
		Gender	1.28	2.12	.04		
		Ethnicity	7.61	2.08	.26		
		Years of Education	1.48	.22	.56	.39*	
	Model(Stepwise)	(Constant)	26.68	3.09			
		Years of Education	1.49	.19	.56	.32*	
		Ethnicity	7.70	2.06	.27	.07*	

*p<.001

A stepwise regression analysis was then carried out with education and ethnicity as predictors and a significant model emerged ($F(2, 119)=37.91, p<0.001$).

Education significantly predicted overall fluency scores, ($\beta=.56, t(119) = 7.87,$

$p<0.001$) as did ethnicity ($\beta=.26, t(119) = 3.73, p<0.001$). The model accounted for

38.9% of the variance in scores, $R^2 = .39$, ($F(2,119)=37.91$, $p<0.001$) with education accounting for 31.8% of the variance and ethnicity accounting for a further 7.1% of the variance in performance. The results of the multiple regression analysis for fluency performance for each category are shown in Table 6.6.

A linear regression analysis to determine the effect of education on semantic fluency for each ethnicity for each category was conducted. The percentage of variance explained by education was greater in the Caribbean group for all semantic categories except fruits in which the percentage of variance explained was equal to that of the British. See Tables 6.7 and Figure 6.4.

Table 6.7

Multiple Regression Analysis- unstandardised and standardized coefficients for semantic fluency for British and Caribbean groups

Category	Ethnicity		B	SE B	β	R^2
Cities						
Model (Enter)	Caribbean	(Constant)	9.29	1.84		
		Years of Education	.49	.12	.48	.23
	British	(Constant)	9.42	3.00		
		Years of Education	.73	.20	.43	.18
Animals						
Model (Enter)	Caribbean	(Constant)	10.15	1.99		
		Years of Education	.55	.13	.49	.24
	British	(Constant)	11.75	2.15		
		Years of Education	.61	.14	.48	.23
Fruits						
Model (Enter)	Caribbean	(Constant)	9.86	1.27		
		Years of Education	.28	.08	.42	.18
	British	(Constant)	10.00	1.77		
		Years of Education			.42	.18
Semantic Total						
Model (Enter)	Caribbean	(Constant)	28.61	3.33		
		Years of Education	1.35	.21	.64	.41
	British	(Constant)	30.04	5.44		
		Years of Education	1.79	.36	.54	.29

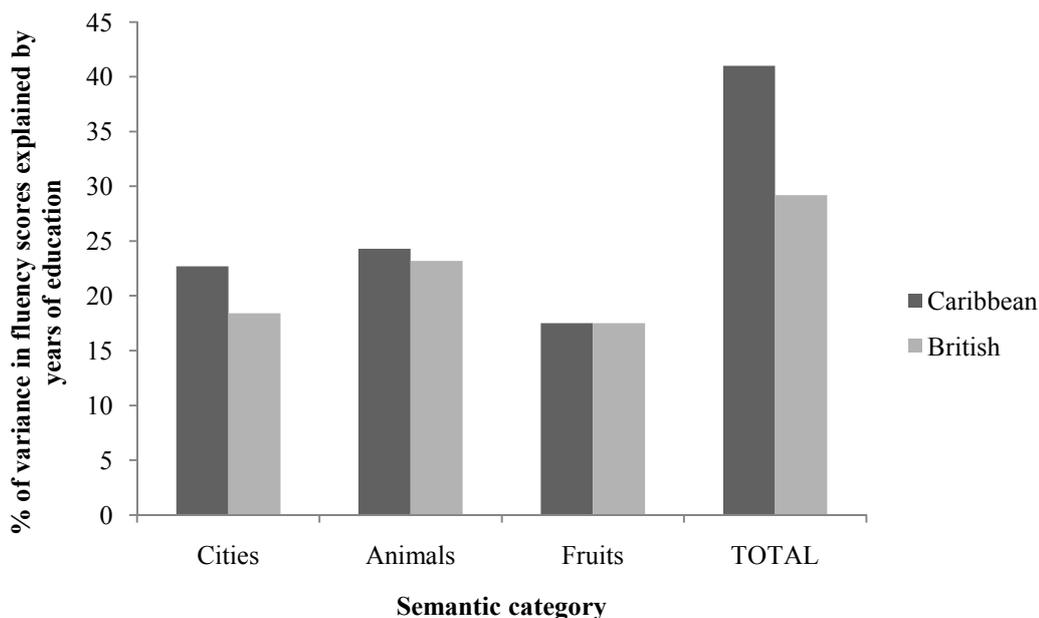


Figure 6.4 Percentage of variance in semantic fluency explained by education, category and ethnicity

6.1.6.5.3 Phonemic vs Semantic Fluency

Correlations between all semantic and phonemic measures were significant. Coefficients ranged from .31 to .63 for individual letters and categories and correlation between total phonemic fluency and total semantic fluency yielded a coefficient of .61. Figures are reported below in table 6.8.

Table 6.8

Correlations between semantic and phonemic measures

	P	F	L	Phonemic Total
Cities	.38	.31	.50	.40
Animals	.55	.55	.51	.54
Fruits	.41	.48	.40	.46
Semantic Total	.55	.63	.54	.61

p=0.01

ANOVA

There was a significant difference in the number of words produced in the semantic task as compared to the phonemic task ($F(1,122)=52.78, p<0.001$).

Participants produced significantly more words ($m=51.88$, $sd= 14.41$) in the semantic task than in the phonemic task ($m=43.20$, $sd=15.65$).

Mixed Design ANOVA

There were no significant differences in the mean number of words produced for the letters P, F or L. The averages were statistically similar and ranged from 14.12 to 14.87 words (See table 6.1). There was no main effect of ethnicity and there was no significant interaction effect with ethnicity and phonemic fluency.

Within the semantic fluency task, there were significant differences in the number of words produced by category ($F(2,121) = 26.85$, $p<0.001$). Fluency for animals produced the greatest number of words ($m=19.22$, $se=.63$), followed by cities ($m=18.05$, $se=.58$). There was no significant statistical difference between these two categories. However, the means for both animals and cities were significantly greater than the mean number of words produced for fruits ($m=14.98$, $se=.39$).

While there was a significant main effect of ethnicity for each semantic category, the interaction between ethnicity and semantic category was not significant. Both ethnic groups displayed a similar pattern of within category performance with fluency for animals and cities significantly exceeding that for fruits. The pattern of performance across phonemic and semantic fluency is illustrated below in Figure 6.5.

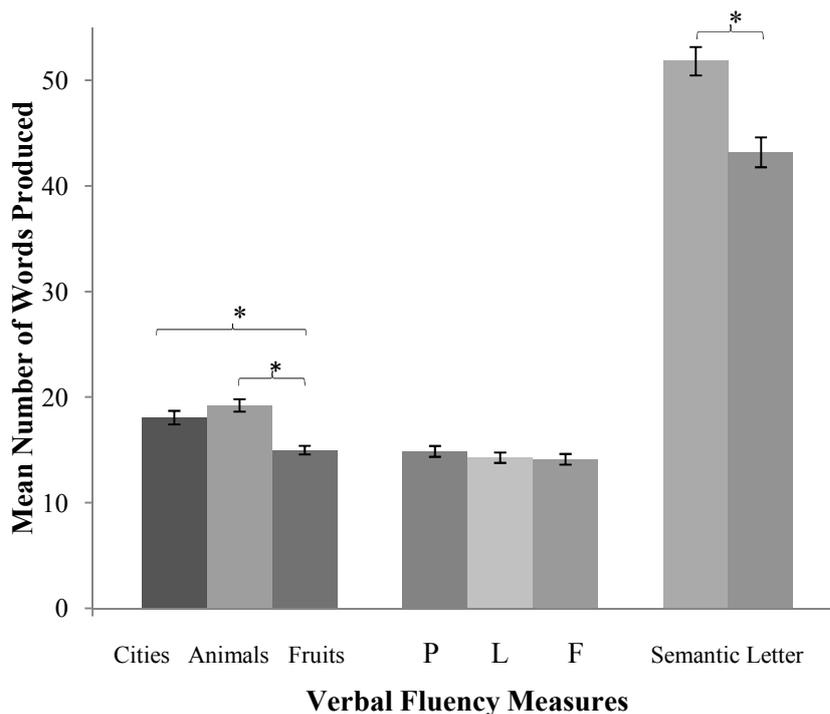


Figure 6.5 Mean number of words produced across phonemic and semantic fluency measures.

6.1.6.5 DISCUSSION

The average number of words produced for individual letters in phonemic fluency falls well within reported ranges of performance (Mitrushina et al, 1999; Troyer, 2000). Performance across individual letters was also similar; a finding which diverges from American norms reported by Borkowski, Benton and Spreen (1967) which suggest the letter L has a more moderate difficulty than letter P and F. Since within subject analyses reveal no significant differences in performance by letter for either ethnic group (British or Caribbean), it suggests the existence of differences in letter norms across different cultures of native English speakers and emphasizes the need for culturally relevant and updated population specific norms.

Fluency was highest for animals followed by cities and then fruits. Mean number of animal words produced are similar to figures reported in the literature

((Mitrushina et al, 1999; Troyer, 2000) and the finding in this study reiterates that of Lopera (n.d. cited from Ardila et al, 2006) which found animals to be one of the easiest semantic categories, producing higher numbers of words.

While age was significantly correlated with individual letter fluency and overall phonemic fluency, it failed to predict performance. This finding concurs with Troyer (2000) and Perlmutter et al (1987) who also report no evidence of age-related decline in phonemic fluency. Correlation between age and semantic category was mixed with significant correlations for animals and fruits but not for cities or overall semantic fluency. However, age failed to predict performance on any of the semantic fluency measures. This finding is consistent with Perlmutter et al (1987) but diverges from the findings of Troyer (2000) who report age-related decline in animal fluency.

While literature findings on gender effects on phonemic fluency are mixed, this study found no significant effects of gender in accordance with reports by Brickman, et al, 2005; Gladsjo et al, 1999; Yeudall, Fromm, Reddon & Stefanyk, 1986 and Tombaugh, Kozak & Rees, 1997. With regard to semantic fluency, gender was significantly correlated with and significantly predicted performance on fluency for fruits but failed to have an effect on any other category. This study's findings of no gender difference in fluency for animals and that women perform better on fluency for fruits was also reported by Capitani et al (1999) who state mixed effects for gender based on the type of category used. It may be suggested that gender effects may be a feature of semantic fluency but not phonemic fluency with a caveat that the effect on semantic fluency is contingent on the category being assessed.

Education was significantly correlated with all measures of phonemic fluency and proved to be a significant predictor accounting for 29%, 30% and 32% of

variance in individual letter performance for P, F and L respectively and 35% in overall letter fluency. This latter figure is somewhat lower than that reported by Ardila et al (2000) in which education explained 38.5% of the variance in phonemic fluency for the letter F in a Mexican sample and larger than the effect observed by Tombaugh et al (1997) in which education accounted for 19% of the variance in phonemic fluency scores (FAS) in a Canadian sample. The differences observed across countries may be explained in part by differences in sampling and demographic characteristics of the participants but it may also point to a difference in the role or influence of education across cultures.

Education was also a significant predictor of semantic fluency and was significantly correlated with all measures. It accounted for 16%, 18% and 23% of variance in individual categories for cities, animals and fruits respectively and 32% of variance in overall semantic fluency. The observed figure for animal fluency lies within the range reported in other studies: 23.6% reported by Ardila et al, (2000) and 14% by Tombaugh et al, (1999), but the variation also suggests that the effect of education may differ across cultures. The lesser effect of education on semantic fluency performance as compared to phonemic fluency is also consistent with reported literature (Ardila et al, 2000; Tombaugh et al. 1999; Ratcliff et al, 1998).

Differences in the effects and contributions of various predictors were observed between phonemic and semantic fluency. Specifically, there was the sole effect of education on phonemic fluency as compared to the significant effect of education and ethnicity and a mixed effect for gender on semantic fluency. These divergent findings can be regarded as psychometric evidence for the tasks measuring or involving different cognitive processes.

Ethnicity failed to predict performance on phonemic fluency with black Caribbean and British participants performing similarly on individual letters and overall phonemic fluency. This finding is at variance with the few studies reported in the literature (Gladjso et al, 1999; Johnson-Selfridge et al, 1998) in which Caucasian Americans performed better than African Americans and Hispanics on letter fluency tasks. The disparity in findings highlights a number of issues. Firstly, differences due to ethnicity are quite variable and need to be interpreted within a cultural context. As such, findings on minorities of African ethnicity in one country cannot be generalized to other populations of African minorities as in the Caribbean.

Ethnicity was significantly correlated with and significantly predicted performance on all measures of semantic fluency. Specifically British persons performed better in all semantic categories. This finding is similar to reports by Gladjso et al, (1999) and Johnson-Selfridge et al, (1998) who report significant effects of ethnicity in which Caucasian ethnic groups performed better than minority ethnic groups. Ethnicity accounted for 6.4% of variance in cities, 3.5% in animals, 4.5% in fruits and 7.1% of overall semantic fluency in this study whereas Gladjso et al attributed 10.2% of variance in animal fluency to ethnicity, a larger figure than that obtained in this study. In addition, in Gladjso et al's study, ethnicity accounted for 4.8% of the variance in phonemic fluency scores but ethnicity was not a significant predictor in this study.

This disparity in findings on the magnitude of the contribution of ethnicity may be also be explained by the differences in the sample used by Gladjso et al in which the African American group had a significantly lower level of education than the white American sample whereas in this study participants were matched on

educational level. Thus the effect of ethnicity may have been masking effects also due to education.

However, the finding of a difference in performance between the two ethnicities on semantic fluency and not phonemic fluency may also be suggestive of cultural differences impacting on categorical thinking. As discussed in Chapter 2 and mentioned earlier in this chapter, culture can shape the organization and accessibility of semantic knowledge (Winkler-Rhoades et al, 2010; Medin et al; 2006).

A further interesting finding from this study arose from the examination of the contribution of education to semantic fluency scores for each ethnic group which revealed a greater contribution of education to performance in Caribbean than British participants in two out of three categories (cities and animals) and similar contribution in the third category (fruits). Luria (1976) proposed that education was the means by which persons acquire the language skills necessary for the categorical and taxonomic thinking that would be needed for a task like semantic fluency and that when people acquire education, they make greater use of categorization. Given that the Caribbean is a developing society which still maintain many elements of traditional and less modernised standards of living, it is not surprising therefore that education would explain a greater proportion of performance in semantic fluency.

6.1.7 STUDY 2

ACCOUNTING FOR AGE, EDUCATION, GENDER AND ETHNICITY EFFECTS ON PERFORMANCE ON FLUENCY: A STANDARDIZATION STUDY

6.1.7.1 AIM

The objectives of this study are to:

1. Establish standardised scores for semantic and phonemic fluency tasks based on age, gender, years of education and ethnicity.

6.1.7.2 METHOD

6.1.7.2.1 Participants

The participants are the same as described in Section 6.1.6.2.1

6.1.7.2.2 Materials

The fluency task was administered to all participants.

6.1.7.2.3 Procedure

The procedure is the same as that described in Study 1, Section 6.1.6.2.3

6.1.7.3 STATISTICAL ANALYSIS

The procedure is the same as that described in Section 4.1.11.3

6.1.7.4 RESULTS

6.1.7.4.1 Semantic Fluency

6.1.7.4.1.1 Animal Fluency

The overall adjusted mean score for animal fluency was 17.87 (sd=6.52) with scores ranging from 2.69 to 41.92. The variables selected for entry into the

regression model were logarithm of age, gender, education and ethnicity. Significant predictors were identified as logarithm of age, education and ethnicity. Gender failed to significantly influence performance.

A formula for correction was obtained as follows:

$$\begin{aligned} \text{Corrected animal fluency} = & \text{Raw score} + [(-0.240) (\text{AgeLog}_{10}^* - 1.63)] \\ & + [(-0.503) (\text{Education}^{**} - 14.07)] \\ & + [(-0.261) (\text{Ethnicity}^{***} - 1.54)] \end{aligned}$$

* Logarithm of Age **Years of education ***Caribbean ethnicity coded as 1, British coded as 2

The formula above allows for calculation of individual scores. Tolerance limits defined a cut-off score of 6.78. The frequency distribution of scores for animal fluency shows a normal distribution with a median score of 17.51 (interquartile range: 13.96-28.82). See Figure 6.6.

Correction grid with pre-calculated values for the combined effect of the variables are provided for a range of ages based on the education groups derived from the sample for each ethnicity (See Tables 6.9a and 6.9b). The median value of each education category is used to generate the correction grid. Equivalent scores are provided in Table 6.10.

Table 6.9a

Correction grids for animal fluency scores with adjustments based on education and age for Caribbean persons

Education	Age											
	20	25	30	35	40	45	50	55	60	65	70	75
3-10 years	2.77	2.70	2.71	2.73	2.74	2.76	2.77	2.78	2.79	2.79	2.80	2.81
11-16 years	0.76	1.03	1.05	1.07	1.08	1.09	1.10	1.11	1.12	1.13	1.14	1.15
17-30 years	-2.51	-1.67	-1.65	-1.64	-1.62	-1.61	-1.60	-1.59	-1.58	-1.57	-1.57	-1.56

Table 6.9b

Correction grids for animal fluency scores with adjustments based on education and age for British persons

Education	Age											
	20	25	30	35	40	45	50	55	60	65	70	75
3-10 years	2.51	2.70	2.71	2.73	2.74	2.76	2.77	2.78	2.79	2.79	2.80	2.81
11-16 years	0.50	1.03	1.05	1.07	1.08	1.09	1.10	1.11	1.12	1.13	1.14	1.15
17-30 years	-2.77	-1.67	-1.65	-1.64	-1.62	-1.61	-1.60	-1.59	-1.58	-1.57	-1.57	-1.56

Table 6.10

Equivalent scores for animal fluency

Test	Equivalent Scores				
	0	1	2	3	4
Animal Fluency	<6.78	6.79-9.46	9.47-12.14	12.15-14.83	14.84-17.51

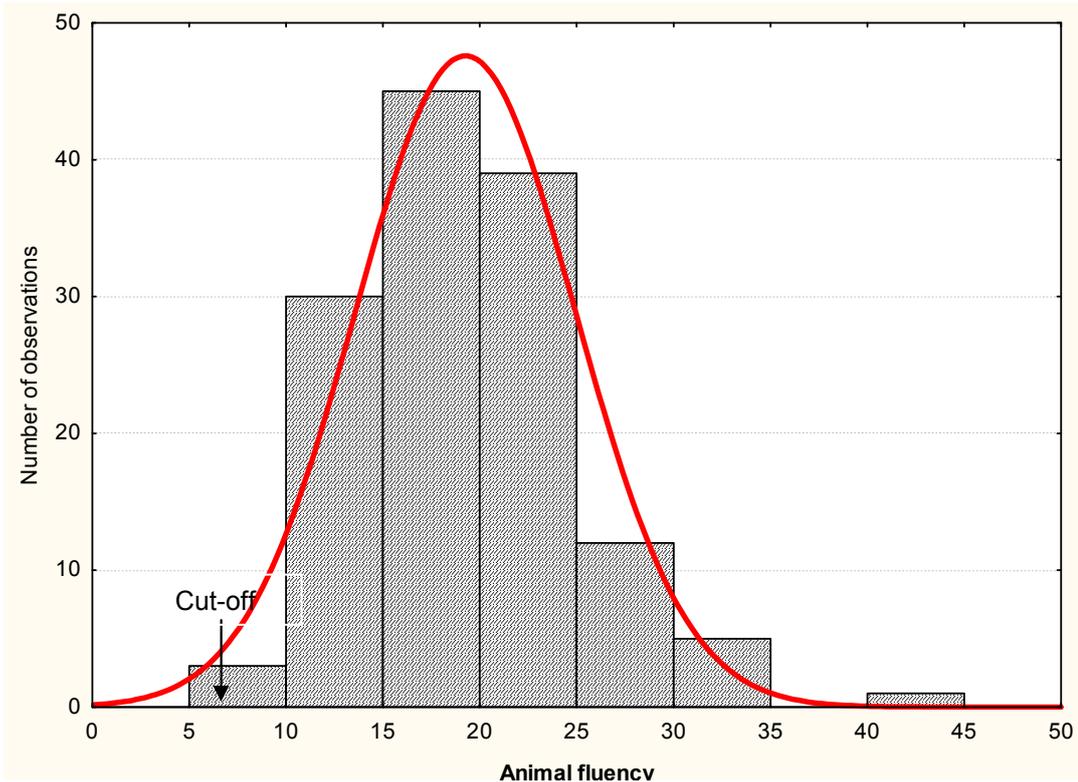


Figure 6.6 Frequency distribution for animal fluency scores

6.1.7.4.1.2 City Fluency

The overall adjusted mean score for city fluency was 19.16 (sd=5.66) with scores ranging from 8.13 to 42.97. The variables selected for entry into the regression model were logarithm of age, gender, education and ethnicity. Significant predictors were identified as logarithm of age, education and ethnicity. Gender failed to significantly influence performance. A formula for correction was obtained as follows:

$$\begin{aligned} \text{Corrected city fluency score} = & \text{Raw score} + [-(0.420) (\text{Education}^* - 14.07)] \\ & + [-(0.183) (\text{Ethnicity}^{**} - 1.54)] \end{aligned}$$

*Years of education **Caribbean ethnicity coded as 1, British coded as 2

The formula above allows for calculation of individual scores. Tolerance limits defined a cut-off score of 3.59. The frequency distribution of scores for city fluency shows a normal distribution with a median score of 19.05 (interquartile range: 15.04-22.14). See Figure 6.7.

A correction grid with pre-calculated values for the combined effect of the variables is shown for a range of ages based on the education groups derived from the sample for each ethnicity, see table 6.11a. The median value of each education category is used to generate the correction grid. Equivalent scores are provided in Table 6.11b.

Table 6.11a

Correction for city fluency based on education and ethnicity

	Years of Education		
	<10 years	11-16 years	>17 years
Caribbean	2.23	0.55	-2.18
British	2.04	0.36	-2.37

Table 6.11b

Equivalent scores for city fluency

Test	Equivalent Scores				
	0	1	2	3	4
City Fluency	<3.59	3.60-7.45	7.46-11.32	11.33-15.18	15.19-19.05

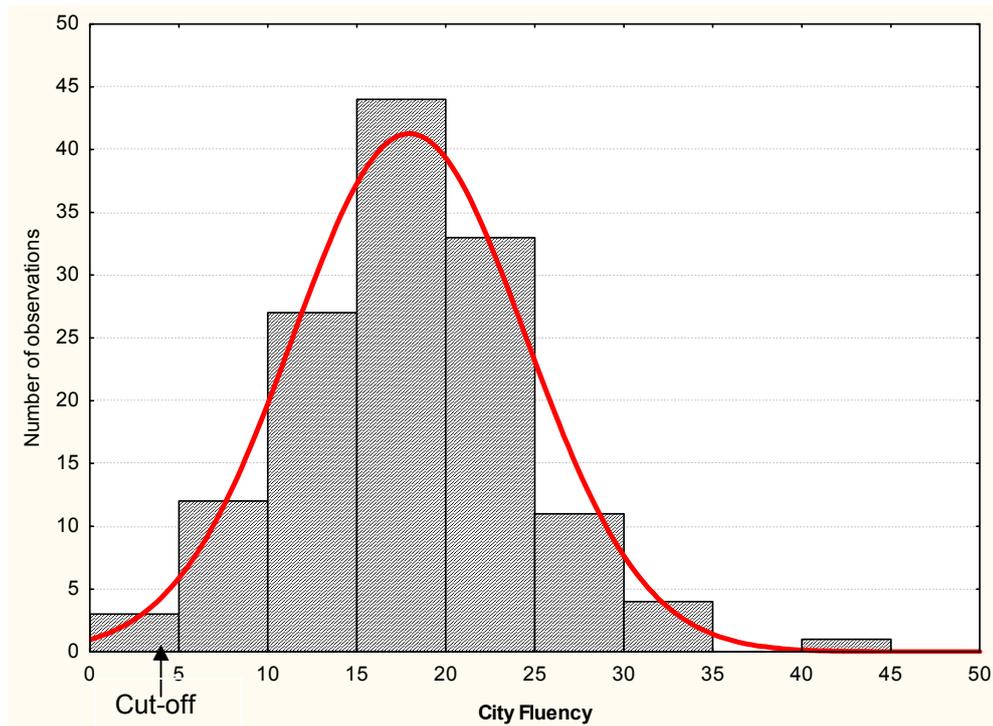


Figure 6.7 Frequency distribution for city fluency scores

6.1.7.4.1.3 Fruit Fluency

The overall adjusted mean score for fruit fluency was 14.95 (sd=4.10) with scores ranging from 3.03 to 26.11. The variables selected for entry into the regression model were logarithm of age, logarithm of gender, education and ethnicity. Significant predictors were identified as logarithm of gender and ethnicity.

A formula for correction was obtained as follows:

$$\begin{aligned} \text{Corrected fruit fluency score} = & \text{Raw score} + [(-0.211) (\text{Ethnicity}^* - 1.54)] \\ & + [(0.286) (\text{Gender Log}_{10}^{**} - 1.27)] \end{aligned}$$

*Caribbean ethnicity coded as 1, British coded as 2 **Male coded as 1, female coded as 2

The formula above allows for calculation of individual scores. Tolerance limits defined a cut-off score of 5.97. The frequency distribution of scores on fruit fluency shows a normal distribution with a median score of 15.30 (interquartile range: 12.17-17.45). See Figure 6.8. A correction grid with pre-calculated values for the combined effect of the variables is shown below in Table 6.12a. Equivalent scores are provided in Table 6.12b.

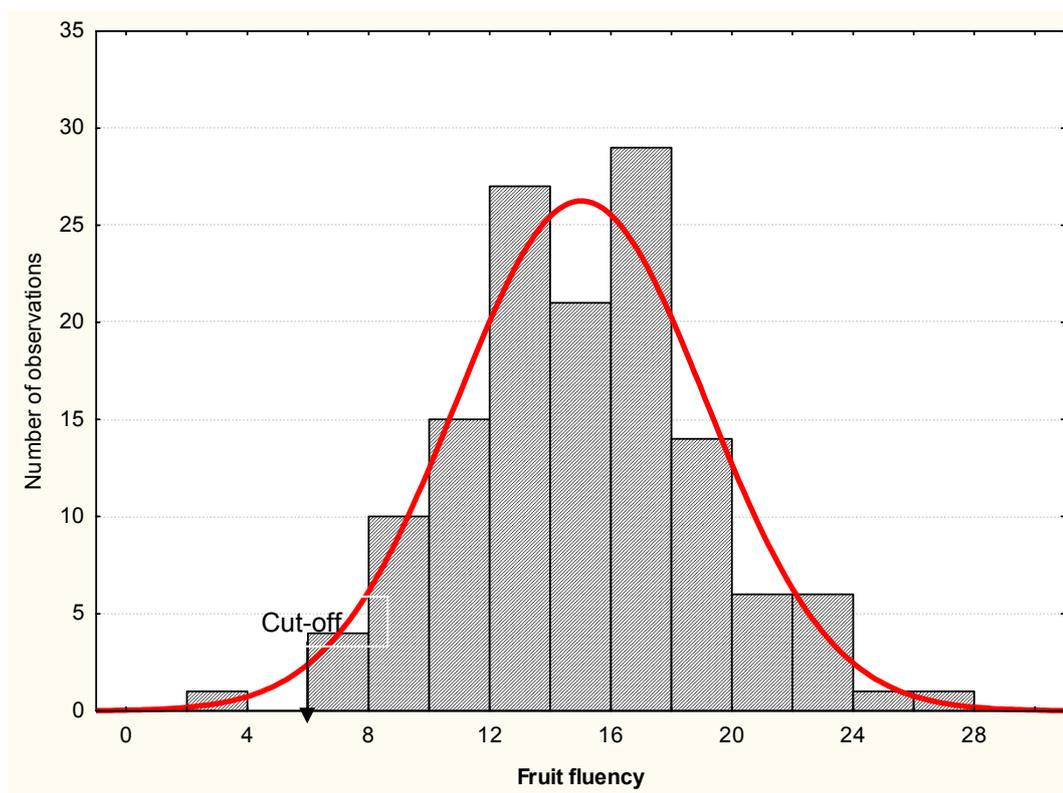


Figure 6.8 Frequency distribution for fruit fluency scores

Table 6.12a

Correction for fruit fluency based on gender and ethnicity

	Male	Female
Caribbean	-0.25	-0.17
British	-0.46	-0.38

Table 6.12b

Equivalent scores for fruit fluency

Test	Equivalent Scores				
	0	1	2	3	4
Fruit Fluency	<5.97	5.98-8.30	8.31-10.63	10.64-12.97	12.98-15.30

6.1.7.4.1.4 Semantic Fluency

The overall adjusted mean score for semantic fluency (the sum of all three categories) was 51.66 (sd=12.94) with scores ranging from 23.42 to 95.26. The variables selected for entry into the regression model were logarithm of age, gender, education and ethnicity. Significant predictors were identified as education and ethnicity. A formula for correction was obtained as follows:

$$\begin{aligned} \text{Corrected category fluency score} = & \text{Raw score} + [(-0.582) (\text{Education}^* - 14.07)] \\ & + [-(0.266) (\text{Ethnicity}^{**} - 1.54)] \end{aligned}$$

**Years of education **Caribbean ethnicity coded as 1, British coded as 2

The formula above allows for calculation of individual scores. Tolerance limits defined a cut-off score of 23.33. The frequency distribution of scores shows a normal distribution with a median score of 50.26 (interquartile range: 43.55 – 59.16). See Figure 6.9. A correction grid with pre-calculated values for the combined effect of the variables is shown in Table 6.13a. The median value of each education category is used to generate the correction grid. Equivalent scores are provided in Table 6.13b.

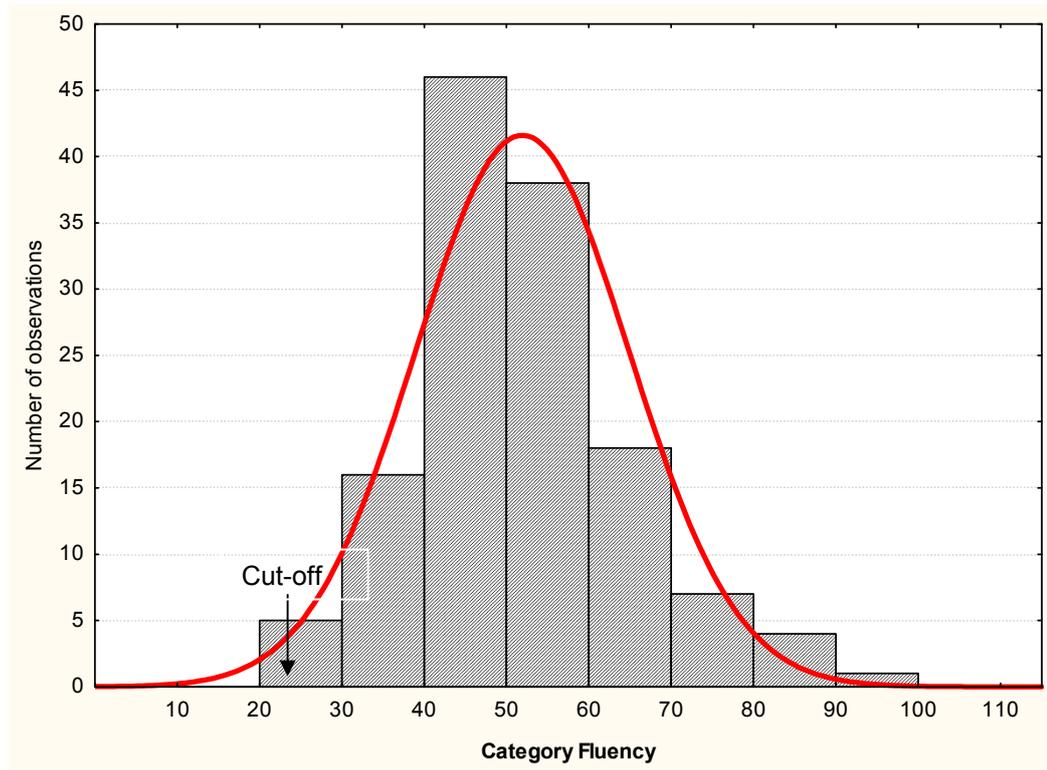


Figure 6.9 Frequency distribution for category fluency scores.

Table 6.13a

Corrections for semantic fluency based on education and ethnicity

	Years of Education		
	<10 years	11-16 years	>17 years
Caribbean	3.09	0.76	-3.02
British	2.83	0.50	-3.29

Table 6.13b

Equivalent scores for semantic fluency

Test	Equivalent Scores				
	0	1	2	3	4
Semantic Fluency	<23.33	23.34-30.06	30.07-36.79	36.80-43.53	43.54-50.26

6.1.7.4.2 Phonemic Fluency

6.1.7.4.2.1 Letter P Fluency

The overall adjusted mean score for letter P fluency was 14.69 (sd=4.98) with scores ranging from 4.06 to 27.17. The variables selected for entry into the regression model were logarithm of age, gender, education and ethnicity. Education was the only significant predictor.

A formula for correction was obtained as follows:

$$\text{Corrected letter P fluency score} = \text{Raw score} + [-(0.574) (\text{Education}^* - 14.07)]$$

* Years of education

The formula above allows for calculation of individual scores. Tolerance limits identified a cut-off score of 3.80. The frequency distribution of scores shows a normal distribution with a median score of 14.19 (interquartile range: 10.91 – 17.61). See Figure 6.10. A correction grid with pre-calculated values is shown below for education, see table 6.14a. The median value of each education category is used to generate the correction grid. Equivalent scores are provided in Table 6.14b.

Table 6.14a

Correction for Letter P fluency based on education

Years of Education		
<10 years	11-16 years	>17 years
2.91	0.61	-3.12

Table 6.14b

Equivalent scores for Letter P fluency

	Equivalent Scores				
Test	0	1	2	3	4
P Fluency	<3.8	3.9-6.40	6.41-8.99	9.00-11.59	11.60-14.19

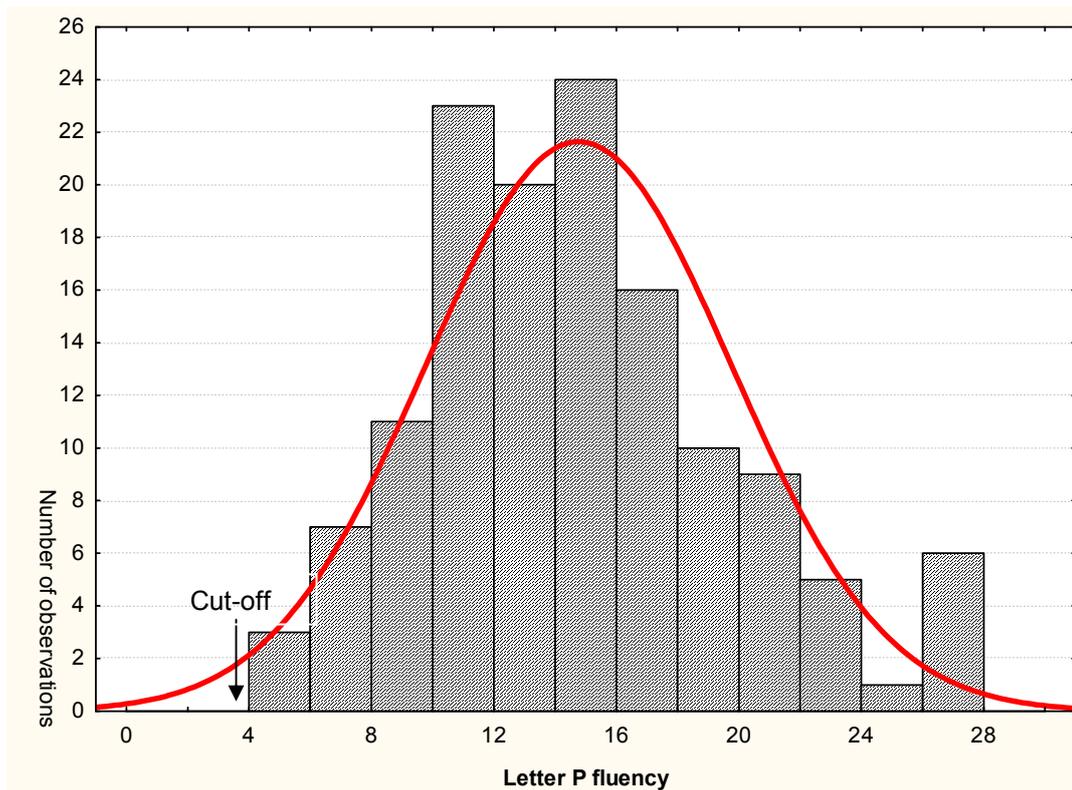


Figure 6.10 Frequency distribution for Letter P fluency

61.7.4.2.2 Letter L Fluency

The overall adjusted mean score for letter L fluency was 13.83 (sd=4.54) with scores ranging from 3.11 to 26.52. The variables selected for entry into the regression model were logarithm of age, gender, education and ethnicity. Education was the only significant predictor.

A formula for correction was obtained as follows:

$$\text{Corrected letter L fluency score} = \text{Raw score} + [-(0.620) (\text{Education}^* - 14.07)]$$

* Years of education

The formula above allows for calculation of individual scores. Tolerance limits identified a cut-off score of 3.88. The frequency distribution of scores shows a normal distribution with a median score of 13.29 (interquartile range: 10.80 – 17.06).

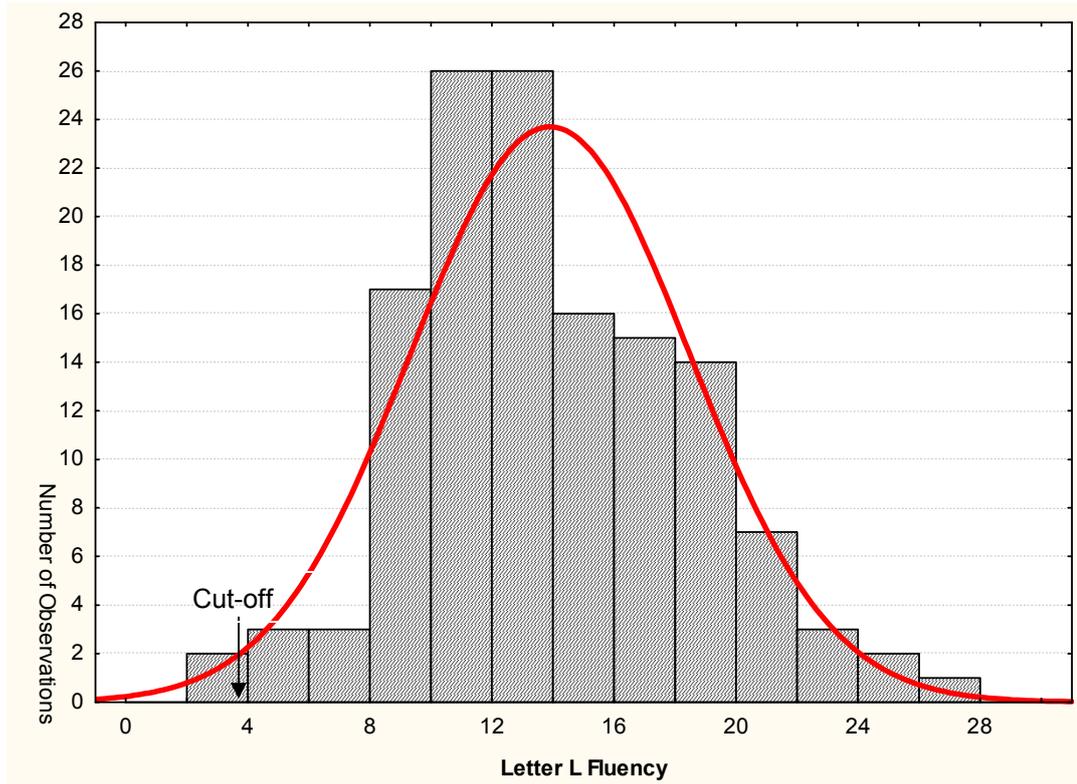


Figure 6.11 Frequency distribution for Letter L fluency

See Figure 6.11. A correction grid with pre-calculated values is shown below for education, see table 6.15a. The median value of each education category is used to generate the correction grid. Equivalent scores are provided in Table 6.15b.

Table 6.15a

Correction for Letter L fluency based on education

Years of Education		
<10 years	11-16 years	>17 years
3.14	0.66	-3.37

Table 5.15b

Equivalent scores for Letter L fluency

Equivalent Scores					
Test	0	1	2	3	4
L Fluency	<3.88	3.89-6.23	6.24-8.58	8.59-10.94	10.95-13.29

6.1.7.4.2.3 Letter F Fluency

The overall adjusted mean score for letter F fluency was 13.89 (sd=4.88) with scores ranging from 4.16 to 29.40. The variables selected for entry into the regression model were logarithm of age, gender, education and ethnicity. Education was the only significant predictor.

A formula for correction was obtained as follows:

$$\text{Corrected letter F fluency score} = \text{Raw score} + [-(0.589) (\text{Education}^* - 14.07)]$$

* Years of education

The formula above allows for calculation of individual scores. Tolerance limits identified a cut-off score of 3.22. The frequency distribution of scores shows a normal distribution with a median score of 13.22 (interquartile range: 10.22 – 17.25). See Figure 6.12. A correction grid with pre-calculated values is shown below for education, see table 6.16a. The median value of each education category is used to generate the correction grid. Equivalent scores are provided in Table 6.16b.

Table 6.16a

Correction for Letter F fluency based on education

Years of Education		
<10 years	11-16 years	>17 years
2.99	0.63	-3.20

Table 6.16b

Equivalent scores for Letter F fluency

Equivalent Scores					
Test	0	1	2	3	4
F Fluency	<3.22	3.23-5.72	5.73-8.22	8.23-10.72	10.73-13.22

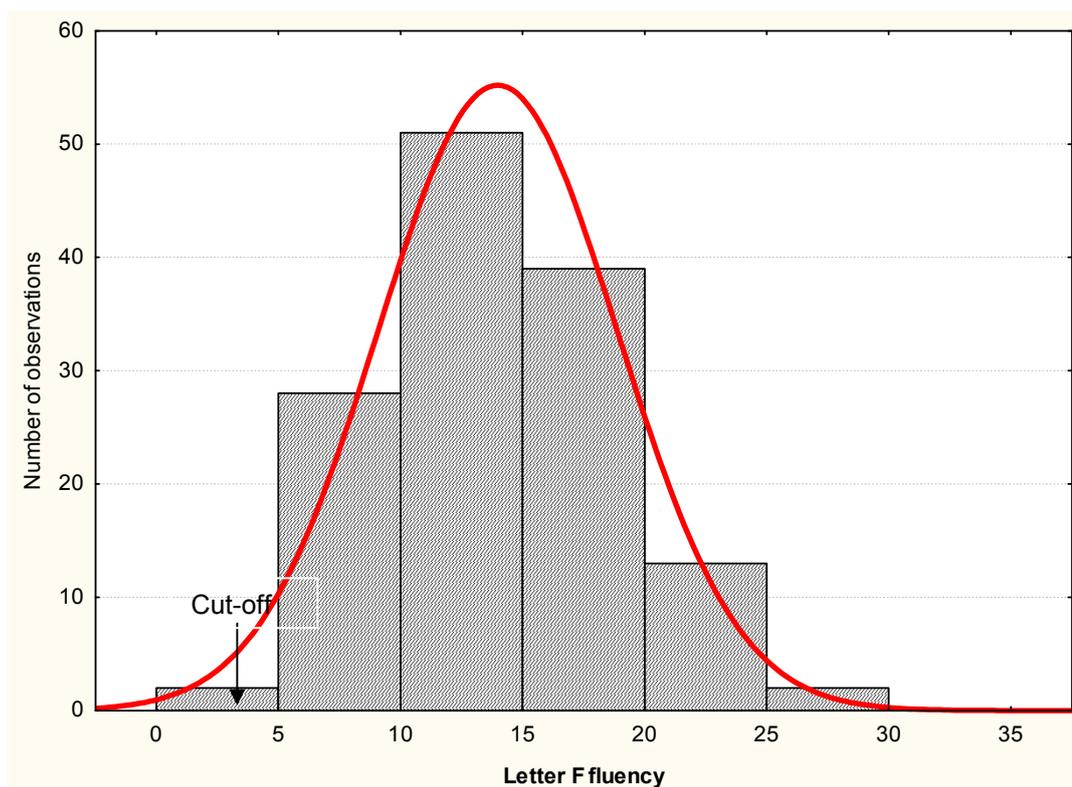


Figure 6.12 Frequency distribution for Letter F fluency

6.1.7.4.2.4 Phonemic Fluency

The overall adjusted mean score for phonemic fluency (the sum of all the letters) was 42.35 (sd=14.36) with scores ranging from 4.48 to 79.88. The variables selected for entry into the regression model were logarithm of age, gender, education and ethnicity. Education was the only significant predictor.

A formula for correction was obtained as follows:

$$\text{Corrected phonemic fluency score} = \text{Raw score} + [-(0.633) (\text{Education}^* - 14.07)]$$

* Years of education

The formula above allows for calculation of individual scores. Tolerance limits identified a cut-off score of 10.93. The frequency distribution of scores shows

a normal distribution with a median score of 31.98 (interquartile range: 28.52 – 34.30). See Figure 6.13. A correction grid with pre-calculated values is shown below for education, see table 6.17a. The median value of each education category is used to generate the correction grid. Equivalent scores are provided in Table 6.17b.

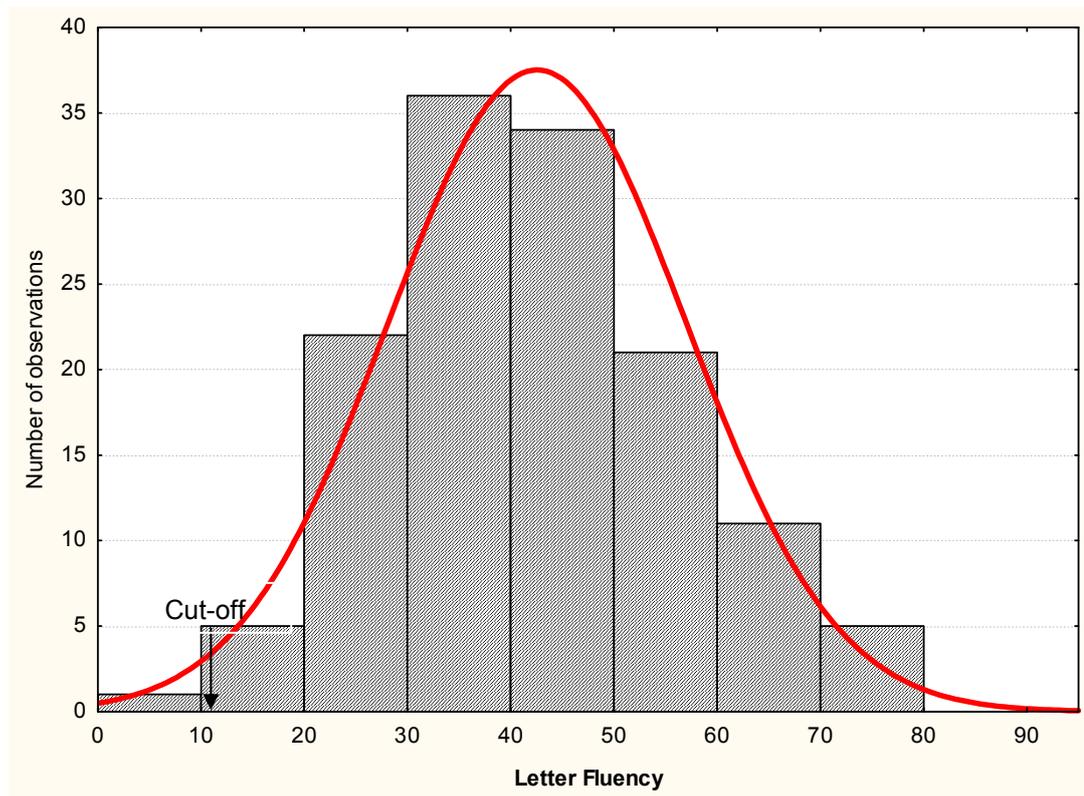


Figure 6.13 Frequency distribution for Letter fluency

Table 6.17a

Correction for phonemic fluency based on education

Years of Education		
<10 years	11-16 years	>17 years
3.21	0.68	-3.44

Table 6.17b

Equivalent scores for phonemic fluency

Test	Equivalent Scores				
	0	1	2	3	4
Phonemic Fluency	<10.93	10.94-16.19	16.20-21.45	21.46-26.72	26.73-31.98

6.1.7.5 DISCUSSION

A comparison of the mean scores obtained in this study and the reported findings is quite interesting. The medians obtained for individual letters P (14.19), L (13.29) and F(13.22) all fall within the range for individual letters (12 -16) reported by Mitrushina et al, (1999). The median of the summed phonemic fluency for P, L and F (42.35) also coincides with the mean reported by Troyer et al (2000) for the letters F,A,S (42.5). This suggests some similarity across both sets of letters and cultures for phonemic fluency. With respect to semantic fluency, mean figures reported for animal fluency of 20.95 (50 to 59 year olds), 18.76 (70 to 79 year olds) by Mitrushina et al, (1999) and 19.5 (Troyer et al, 2000) are somewhat higher than the figure obtained in this study of 17.87 (median = 17.51). This however may be explained by arguments posited earlier about the role of ethnicity and culture on semantic fluency. Thus the inclusion of a Caribbean sample is reflected in the obtained mean scores for fluency.

These findings confirm that verbal fluency scores are all affected by education and semantic scores additionally influenced by ethnicity. The derived formula therefore provides a means whereby the effects of these variables can be accounted for and it is recommended that individual scores should be adjusted to account for the relative effects of these variables before interpretation of an individual's performance is made.

6.2 RAVEN'S COLOURED PROGRESSIVE MATRICES (CPM)

6.2.1 DESCRIPTION OF RAVEN'S COLOURED PROGRESSIVE MATRICES (CPM)

The Ravens Progressive Matrices are tests of nonverbal abstract reasoning or concept formation ability developed by John Raven in 1936 and first published in 1938. Each item consists of a graphically displayed pattern problem which takes the form of a 4x4 or 3x3 or 2x2 matrix with one part removed. Below the pattern a series of options of which one is the correct solution. The test asks examinees to identify the missing part from the options. The task involves visual matching as well as analogy problems which requires spatial, design and numerical conceptualization (Lezak, 2004). Items range in difficulty from easy and concrete to very hard and abstract. There are three different series of progressive matrices: Standard Progressive Matrices (SPM), Coloured Progressive Matrices (CPM) and the Advanced Progressive Matrices (APM) and these are described in Table 6.18.

Table 6.18

Description of forms of Ravens Progressive Matrices

Form	Description
Standard Progressive Matrices	Original form of matrices. Presented in five sets of 12 items of increasing difficulty. All patterns are black printed on white background
Coloured Progressive Matrices	Designed for use with younger children (ages 5-12), elderly and persons with learning difficulties. Consists of 3 sets of 12 items. 2 of the 3 sets are printed in colour.
Advanced Progressive Matrices	For use with adults and adolescents of above average intelligence. Consists of 2 sets of increasing difficulty. Set 1 contains 12 items, set 2 contains 36 items.

The SPM are extensively used in many countries and normative data for many countries have been published (Irvine and Berry, 1988; Lynn and Vanhanen,

2002). Although it was not originally intended, performance on the SPM is generally seen to be a function of *g* (general intelligence) and scores on the SPM and CPM are often converted to IQ scores by converting to percentile scores which are then transformed to IQ scores with a mean of 100 and a standard deviation of 15. This procedure has been used to generate IQ scores which have been compared across different populations (Lynn, 2006; Lynn and Vanhanen, 2002; Lynn and Vanhanen, 2006). The Coloured Progressive Matrices (CPM) (Raven, 1956, 1990) is used extensively with elderly populations. While the majority of research literature on the CPM focuses on children (e.g. Khaleefa & Lynn, 2008; Sperazzo and Wilkins, 1958), a few studies have focused on older populations (Measso et al, 1993; Basso et al, 1987). Raven (1995) reported norms for sets A and B of the CPM for an elderly Dutch sample with median scores of 30 for ages 55-64, 28 for ages 65 to 74 and 23 for ages 75 to 85. Yeudall et al (1986) obtained a median score of 34.9 (sd=1.25) in a younger sample of Canadians aged 15 to 40 years.

6.2.2 CPM AND AGE

Significant effects for age have been found on the CPM (Panek and Stoner, 1980). Yeudall et al (1986) found no age effects in adults aged 15 to 40 years and surmised that age effects usually occur after age 40.

6.2.3 CPM AND GENDER

While a meta-analysis of studies on children and the CPM show an advantage for boys who consistently show higher scores (Lynn and Irwing, 2004), gender differences are not usually reported in adults (Yeudall et al, 1986).

6.2.4 CPM AND EDUCATION

Increasing years of education is generally thought to be associated with better performance on Raven's matrices (Burke, 1985; Marcopulos et al, 1997; O'Leary et al, 1991). A cross-cultural meta-analysis of 45 countries found number of years of education to be the greatest predictor of performance across all of the Raven's matrices (Brouwers et al, 2009).

6.2.5 CPM AND ETHNICITY

The Raven's matrices are thought to be less influenced by culture due to its non verbal nature, and less susceptible to the effects of education and socioeconomic status than other tests (Templer and Arikawa, 2006; Raven, 2000; Rushton et al, 2004). Carlson and Jensen (1981) compared the reliability of CPM scores in white, black and Hispanic American children aged 5 ½ to 8 ½ years and found the CPM to be equally reliable for all three groups. However other studies counter this culture assertion. Valencia (1979) examined differences in performance on the CPM between boys of Mexican descent and white ethnicity in the United States and found significantly higher scores in the white group with ethnicity accounting for 4% of the variance in performance. Scores of African samples are also consistently found to be lower than that of British samples (Wicherts et al, 2010; Lynn and Vanhanen, 2002, 2006)

6.2.6 CPM AND DEMENTIA

Scores on the Raven's CPM can distinguish between patient groups and healthy controls. In an Italian study, Giovagnoli et al (2008) found significantly lower scores in both AD patient and frontal variant FTD patients than controls. Baudic et al (2006) also found significantly lower CPM scores in French mild AD

m=19.9, sd=5.3) and very mild AD ((m=22.9, sd=6.0) patients when compared to healthy controls (m=30.9, sd=3.0).

6.2.7 STUDY 3

EXPLORING THE EFFECT OF AGE, GENDER, EDUCATION AND ETHNICITY ON CPM PERFORMANCE

6.2.7.1 AIM

The objectives of this study are to:

1. Assess the difference in performance on the CPM based on age, gender, education and ethnicity,
2. Identify the contribution of each predictor (age, gender, education and ethnicity) to performance on the CPM
3. Assess the difference in completion times in Caribbean and British participants

6.2.7.2 METHOD

6.2.7.2.1 Participants

In this study, 121 participants (female= 69, male=52) from Trinidad and Tobago (n=59) and England (n=62) were assessed. The sample ranged in age from 18 to 87 years (m=46.94, sd=18.92) and years of education ranged from 3 to 30 years (m=14.56, sd=5.52). All participants were functionally independent, and those with any neurological or psychiatric impairment were excluded.

6.2.7.2.2 Materials

The Ravens Coloured Progressive Matrices consisting of sets A, Ab and B, each containing 12 items was administered to all participants.

6.2.7.2.3 Procedure

A stopwatch was used to time the task. Participants were given the instructions: 'I am going to show you a pattern with a piece missing and I'll like you to show me which piece is missing from the six options below.' A practice item was then administered. If an error was made, it was corrected and the correct answer identified and explained. The rest of the test was then introduced by saying 'I am going to show you some more patterns like these. They start off easy and then get harder. For each one, show me the missing part.' The stopwatch was started when the participant started the first item and stopped when all 36 items were completed.

The score recorded was the total number of correct items produced within a 10 minute time period. If participants exceeded the 10 minute time period, the score recorded was the number of correct items produced within the time limit.

6.2.7.3 DESIGN AND STATISTICAL ANALYSIS

Univariate ANOVAs were performed on the number of correct on CPM comparing the effects of age, gender, ethnicity and education.

Age was categorized into 6 levels corresponding to 18-30, 31-40, 41-50, 51-60, 61-70 and >70 years of age. Education was categorized into three levels- low, average and high education. The inclusion for each group was determined as follows: low education- 25th percentile (equivalent to a cut off of 10 years or fewer), above the 25th and below the 75th percentile comprised the average education category (equivalent to 11 to 16 years inclusive) and above the 75th comprised the

high education category (equivalent to 17 or more years of education). A Bonferroni correction was employed in the post hoc analyses of the effects of education and age.

Regression analyses were also performed to determine the contribution of age, gender, education and ethnicity to CPM scores.

A one-way ANOVA was used to compare differences in completion times between the two groups.

6.2.7.4 RESULTS

6.2.7.4.1 CPM total

ANOVA Analysis

Mean overall score on the CPM was 30.747 (sd=5.51) and scores ranged from 12 to 36. Results from the ANOVA analysis showed no significant effects of age or gender. However, significant main effects for ethnicity $F(1,75)=37.88$, $p<0.001$) and education $F(2,75)=3.74$, $p=0.03$) were found. The Caribbean group had a significantly lower mean performance ($m=28.42$, $se=.57$) than the British group ($m=32.96$, $se=0.54$). Post hoc analysis using a Bonferroni correction showed significant differences between education groups. The low education group had a significantly lower mean score ($m=24.97$, $se=.84$) than the average ($m=31.91$, $se=.56$) and high ($m=32.54$, $se=.71$) education groups. The difference between the average and high groups was not significant and there were no significant interaction effects. The mean scores for each education and ethnic group are shown below in Figure 6.14.

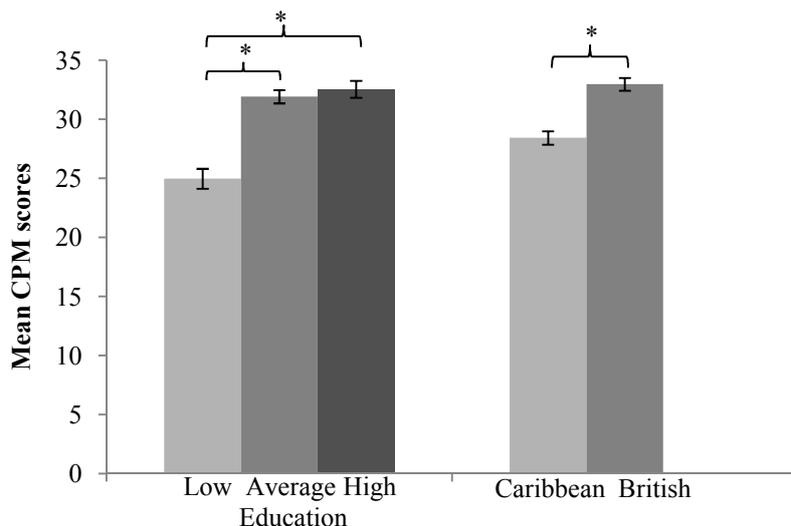


Figure 6.14 Mean scores on CPM by education and ethnicity

Regression Analysis

The correlation between CPM and predictors are shown in Table 6.19. Mean CPM score was significantly correlated with age, education and ethnicity in which increasing age, fewer years of education and Caribbean ethnicity were associated with lower scores. There was no significant correlation with gender.

Table 6.19

Correlation coefficients between CPM scores and predictors

	Age	Gender	Education	Ethnicity
CPM	-.44*	-.13	.49*	.39*

* $p < 0.001$

A forced entry regression analysis with predictors age, gender, education and ethnicity produced a significant model ($F(4, 115) = 25.39, p < 0.001$). Of the four predictors, age, ethnicity and education made significant contributions to the overall model. A stepwise regression analysis was then performed with age, ethnicity and education as the only predictors and a significant model emerged ($F(3, 116) = 33.32, p < 0.001$) which accounted for 46% ($R^2 = .46$), of the variance in performance.

Education significantly predicted CPM scores, $\beta=.37$, $t(116) = 4.68$, $p<0.001$ and accounted for 24%, $R^2 = .24$ of the variance in scores,. Ethnicity accounted for a further 17% of the variance, $R^2 = .17$, $\beta=.41$, $t(116) = 6.07$, $p<0.001$ and age contributed to 6% of the variance in scores, $R^2 = .06$, $\beta=-.27$, $t(116) = -3.49$, $p=0.001$. The regression model is shown in Table 6.20 below.

Table 6.20

Multiple Regression Analysis- unstandardised and standardized coefficients for CPM

Item			B	SE B	β	R ²
CPM	Model(Enter)	(Constant)	27.55	2.09		
		Age	-.08	.02	-.28	
		Gender	-.88	.77	-.08	
		Ethnicity	4.59	.75	.42	
		Years of Education	.35	.08	.35	.47*
Model (Stepwise)	(Constant)	26.82	1.99			
	Years of Education	.37	.08	.37	.24*	
	Ethnicity	4.55	.75	.41	.17*	
	Age	-.08	.02	-.27	.06*	

* $p<0.001$

6.2.7.4.2 CPM completion time

Results from the one-way ANOVA show a significant difference in completion times between Caribbeans and British ($F(1,120) = 11.072$, $p=0.001$). Caribbean persons took significantly longer ($m=362.05$, $se=16.27$) than British persons (285.73 , $se=16.16$) to complete the CPM.

6.2.7.5 DISCUSSION

Both education and ethnicity were found to have an impact on CPM scores. Consistent with the literature (Burke, 1985; Marcopulos et al, 1997; O'Leary et al, 1991, Brouwers et al, 2009), education had the biggest impact on performance and accounted for the greatest proportion of explained variance in the scores. Low education groups perform considerably worse than higher educated persons on this

task. While there was no difference in performance between separate age groups, age did account for a small percentage of the variance in performance. This may be due to the wide age range used in this sample as Yeudall et al (1986) suggest that age differences may only be apparent in older ages. No gender differences were found which also confirms other findings (Yeudall et al, 1986).

A significant effect for ethnicity was found in which Caribbean persons had lower scores than the British group. As previously discussed, one avenue for explanation could be nature of the task and the cultural differences between the groups. Luria (1976) hypothesises that abstraction may be a function of development and modernisation therefore these skills may prove more challenging to persons from less modernised countries. Indeed, scores among Africans have also been consistently found to be lower than that of the British (Wicherts et al, 2010; Lynn and Vanhanen, 2002, 2006). Thus, assertions of the Raven's matrices being culture free may hold only for societies that are comparable in terms of development.

In addition, scrutiny of the completion times may account for some of the difference in performance. Caribbean persons took significantly longer to complete the task. The number of correct items however is recorded as only those which were completed within a 10 minute time limit. Thus accuracy (as defined by items completed in the time limit) would have been adversely affected in slow respondents. This may be related to a cultural difference in cognitive styles used to approach timed tests in which accuracy is favoured over speed. As mentioned in Chapter 2, some ethnic groups appear to have a 'less rushed temporal perspective' than whites (Byrd et al, 2004, pg 402) which may influence their performance on timed tasks. As such, poorer performance in Caribbeans may be related to cognitive style and not lesser ability. As such, performance on measures like the CPM may be

more accurately measured by suspending time constraints or by using caution in interpreting the performance of 'slow' participants.

6.2.8 STUDY 4

ACCOUNTING FOR AGE, EDUCATION, GENDER AND ETHNICITY EFFECTS ON PERFORMANCE ON RAVEN'S COLOURED PROGRESSIVE MATRICES (CPM): A STANDARDIZATION STUDY

6.2.8.1 AIM

The objectives of this study are to:

1. Establish standardised scores for cancellation based on age, gender, years of education and ethnicity.

6.2.8.2 METHOD

6.2.8.2.1 Participants

The participants are the same as described in Section 5.4.2.1

6.2.8.2.2 Materials

The CPM task was administered to all participants.

6.2.8.2.3 Procedure

The procedure is the same as that described in Study 1, Section 5.4.2.3

6.2.8.3 STATISTICAL ANALYSIS

The procedure is the same as that described in Section 4.1.11.3

6.2.8.4 RESULTS

The overall adjusted mean score for the CPM was 30.79 (sd=4.87) with scores ranging from 16.42 to 36. The variables selected for entry into the regression model were logarithm of age, gender, education and ethnicity. Significant predictors were identified as logarithm of age, education and ethnicity. A formula for correction was obtained as follows:

$$\begin{aligned} \text{Corrected CPM score} = & \text{Raw score} + [(0.238) (\text{AgeLog}_{10}^* - 1.63)] \\ & + [-(0.416) (\text{Education}^{**} - 14.21)] \\ & + [-(0.418) (\text{Ethnicity}^{***} - 1.54)] \end{aligned}$$

*Logarithm of age **Years of education ***Caribbean ethnicity coded as 1, British coded as 2

The formula above allows for calculation of individual scores. Tolerance limits revealed a cut-off score of 20.12. The frequency distribution of scores on the CPM shows a negatively skewed distribution with a median score of 31.98 (interquartile range: 28.52 – 34.3). See Figure 6.15.

A correction grid with pre-calculated values for the combined effect of the variables is shown below for a range of ages based on the education groups derived from the sample for each ethnicity. See tables 6.21a and 6.21b. The median value of each education category is used to generate the correction grid. Equivalent scores are provided in Table 6.21c.

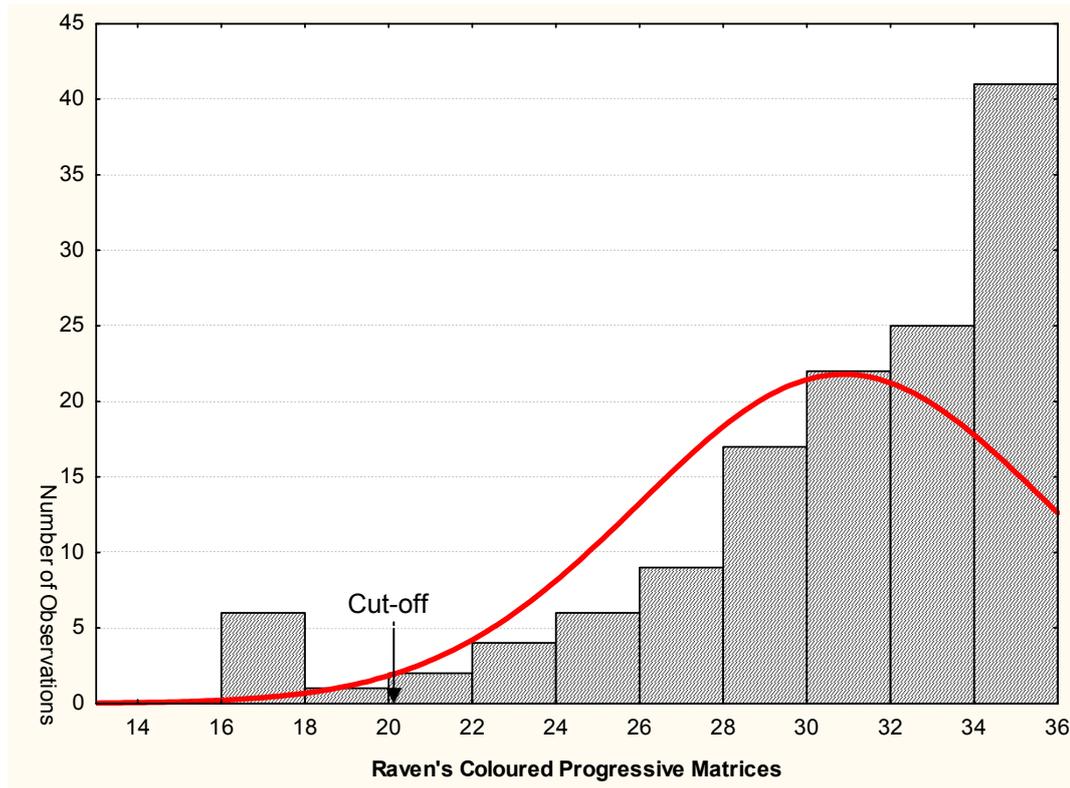


Figure 6.15 Frequency distribution of CPM scores

Table 6.21a

Correction grids for CPM scores with adjustments based on education and age for Caribbean persons

Education	Age											
	20	25	30	35	40	45	50	55	60	65	70	75
3-10 years	2.31	2.34	2.36	2.37	2.39	2.40	2.41	2.42	2.43	2.44	2.44	2.45
11-16 years	0.65	0.67	0.69	0.71	0.72	0.73	0.75	0.76	0.76	0.77	0.78	0.79
17-30 years	-2.05	-2.03	-2.01	-2.00	-1.98	-1.97	-1.96	-1.95	-1.94	-1.93	-1.92	-1.92

Table 6.21b

Correction grids for CPM scores with adjustments based on education and age for British persons

Education	Age											
	20	25	30	35	40	45	50	55	60	65	70	75
3-10 years	1.90	1.92	1.94	1.95	1.97	1.98	1.99	2.00	2.01	2.02	2.03	2.03
11-16 years	0.23	0.26	0.27	0.29	0.30	0.32	0.33	0.34	0.35	0.35	0.36	0.37
17-30 years	-2.47	-2.45	-2.43	-2.41	-2.40	-2.39	-2.38	-2.37	-2.36	-2.35	-2.34	-2.33

*Table 6.21c**Equivalent scores for Ravens' CPM*

Test	Equivalent Scores				
	0	1	2	3	4
Raven's CPM	<20.12	20.12-23.08	23.09-26.05	26.06-29.01	29.02-31.98

6.2.8.5 DISCUSSION

These findings clearly indicate that CPM scores are affected by demographic variables of age, education and ethnicity. The derived formula provides a means whereby the effects of these variables can be accounted for. The obtained median score of 31.98 in this study is higher than that obtained by Raven (1995) (medians scores ranged from 23 to 30), however that study comprised an elderly sample (55 to 85 years). It is also lower than the median of 34.19 obtained by Yeudall et al (1986) who tested a younger Canadian sample aged 15 to 40 years. It is consistent then that the median score obtained in this study falls between the scores obtained in other studies using older and younger samples.

6.3 CONCLUSION

The findings in this chapter implicate a great role for the effects of education and ethnicity in performance on verbal fluency and Raven's matrices. Education exerts an influence on all tasks and the suggested correction formulas address this effect. The ethnicity effect in both these tasks may be narrowed down to a consideration of categorical thinking or skills of abstraction which may be a function of the development of the society and which is facilitated by educational achievement. The finding of an ethnicity effect on both the semantic fluency and Raven's matrices tasks suggest that greater consideration needs to be given to these

factors both in terms of individual assessment and interpretation but also in terms of cross-cultural comparisons of test performance.

CHAPTER 7

GENERAL DISCUSSION

The unprecedented ageing in many societies and its implications for the increasing prevalence of dementia especially in developing society warrants an appropriate response from the scientific community. With an increase in ethnic diversity within countries, epidemiological studies and clinical trials globally, cross-cultural neuropsychology is gaining stride in its relevance to the diagnosis and assessment of dementia. As previously mentioned, the use of instruments in populations for whom they have not been normed renders the validity of such instruments questionable. This thesis sought to develop normative data for a short neuropsychological dementia assessment battery for use in Caribbean populations.

7.1. EFFECTS OF DEMOGRAPHIC VARIABLES OF AGE, GENDER, EDUCATION AND ETHNICITY ON PERFORMANCE

Two globally popular screening instruments: the MMSE and ADAS-cog, were investigated. A number of demographic factors were found to exert an influence on performance on the MMSE. Males and females performed similarly on the MMSE and this is a usual finding in most studies. Another consistent finding was the impact of age, in which increasing age is associated with poorer performance. Age also influenced performance on three of the items: spelling backwards, recall and repetition. The impact of age was less than reported in other studies (Crum et al, 1993) however this may be explained by the relatively high levels of education in this sample with over 75% having more than 10 years of education. Education may

provide a cognitive reserve which protect against decline in old age, thus the effects of age in a more educated sample would be less apparent. Furthermore it may be assumed that the elderly of today are more and better educated than the cohort used in Crum et al's study almost 20 years ago. Earlier norms may not be reliable or valid for a contemporary cohort. Differences in educational attainment across cultures and generations highlight the needs for norms to be periodically revised in order to be considered representative of current populations. This view is further endorsed by Caffarra et al (2003) who reiterate the importance of accurate cut-offs especially in elderly populations for whom diagnostic sensitivity is critical in detecting early impairment.

Education had the greatest impact of all predictors on performance on the MMSE. Analysis by group showed higher and average educated persons performed better than those with fewer years of education, thus the effect of education may be apparent largely in those with low education, which in this study corresponds to 10 or fewer years of education or those who have had some primary or incomplete secondary school education. Education also affected scores on orientation, spelling backwards, recall and repetition.

An effect of ethnicity was found on MMSE performance in which Caribbean persons performed worse than British persons but this effect of ethnicity interacted with that of education and further analysis revealed that the differences due to ethnicity are only apparent in the lowest education group. Caribbean and British persons with more than 10 years of education perform similarly on the MMSE. However, in the lower educated groups, Caribbean persons tend to perform worse than British persons with a similar level of education. The implications of this is that low educated Caribbean persons may display lower levels of cognitive functioning

usually associated with impairment when they are in fact healthy and functioning well.

An effect of ethnicity was also found on two of the MMSE items, firstly the recall item in which there was a similar interaction with education. Ethnic differences on recall also revealed that among higher educated persons, both ethnicities perform similarly but in the low educated group, Caribbeans show worse performance than their British counterparts. In the serial sevens item, Caribbeans performed worse than British persons, however, this effect was independent of education levels. Since this is an item based on arithmetic calculation, the difference could have been attributed to differences in arithmetic ability.

The second study addressed this issue and compared serial sevens performance among age, gender and education matched university students from Britain and Trinidad. The serial sevens difference persisted and could not be attributed to arithmetic ability since Caribbean students performed better on a written arithmetic test than British students. This finding is significant because worse performance by Caribbeans on the serial sevens were also found to have an impact on the overall MMSE score. Total scores calculated using serial sevens performance were significantly lower than total scores calculated using the spelling backwards item. As a result, the administration and scoring variant used becomes significant in Caribbean populations and the recommended strategy is the use of the higher of the two item scores in calculating the total MMSE score.

The ADAS-cog is the gold standard measure of cognitive functioning in clinical drug trials and while it is reputed to be unaffected by ethnicity and less affected by education, this assertion has not been tested in Caribbean populations.

The results of this study show no effects of gender and significant effects of age and education on the ADAS-cog which are consistent with other reported findings (e.g. Pena-Cassanova, 1997). Comparisons of the relative contribution of education to performance also confirm that the ADAS-cog is less affected by education than the MMSE.

No effects of ethnicity were found for ADAS-cog performance or for any of the individual items. This suggests that the components of cognitive functioning that are assessed by the ADAS-cog may be less susceptible to influence by cultural factors. This makes the ADAS-cog especially suitable for use within diverse populations and for comparison across countries.

The assessment battery also included a number of measures assessing memory and attention. In the digit span task, different demographic variables predicted performance on both tasks. While digit span forward was influenced by education alone digit span backward was influenced by both education and ethnicity. Specifically, low educated and Caribbean persons performed similarly to higher educated and British persons on digit span forward, but the performance of these groups was significantly lower in the digit span backwards task. The finding of an effect of education on digit span as well as a greater impact of education on digit span backwards is a consistent one and reiterates theoretical arguments that the tasks measure different cognitive functions. Ethnic differences in scores also support this argument. This has implications for administration and scoring procedures for the digit span task and as such, rather than summing scores to produce a global measure, scores on digit span forward and backward should be interpreted separately, especially for low educated and Caribbean persons.

The digit cancellation task is regarded as a measure of attention and performance was found to be affected by age, education and ethnicity. Interaction effects between age and ethnicity as well as between education and ethnicity showed that the eldest Caribbeans and the low educated Caribbeans had the worst performance. In logical memory, education was the only demographic variable to have a significant impact on both immediate and delayed recall. This effect was more pronounced in the groups in delayed recall with the low educated group having the worst performance. These findings suggest performance on attention and memory tasks are all affected by education with attentional tasks also affected by ethnicity. The serial sevens task of the MMSE is a task of attention and this was also found to be affected by ethnicity. Thus there seems to be a recurrent finding of a role of ethnicity in attentional tasks.

Two sets of tasks measuring executive functioning and abstract reasoning were assessed. The first was verbal fluency consisting of semantic and phonemic fluency. Semantic fluency exceeded phonemic fluency and this is a consistent finding. There was no difference in performance across each of the different letters (P, L, F) with each yielding a similar mean number of words produced. This suggests a similar level of difficulty for each letter which is at variance with the American norms reported by Borkowski et al (1967) who rated L as having moderate difficulty and P and F as being easy. Since the British and Caribbean samples are both native English speaking samples and there was no difference between groups, it suggests that letter norms may not be invariant and may differ across time and cultures, even among native English speakers.

Average number of words produced in semantic fluency for this study suggests animals are the easiest category followed by cities and then fruits. Animals

are widely regarded as an easier semantic category prompting a higher number of words and this study confirms this (Ardila et al, 2006). Age effects were not apparent in either semantic or phonemic fluency and the effects of gender were mixed. While there was no difference among letters, females outperformed males on one semantic category: fruits. As such the gender effect seems limited to semantic fluency but only for certain categories.

Education was the biggest predictor of all types of phonemic and semantic fluency. However while education alone impacted performance on phonemic fluency, ethnicity proved a significant predictor for all categories of semantic fluency. Caribbean persons produced a similar number of words as British for letters but they produced significantly fewer words for each semantic category.

An explanation for this may lie in the nature of the difference between the two tasks. Phonemic fluency is thought to involve executive functioning more so than semantic fluency which incorporates semantic memory organization or categorical thinking. As presented in Chapter 2 and discussed in Chapter 6, if acquisition of abstraction or categorical thinking skills is regarded a function of a society's development, then persons in developing countries may show lesser abilities in abstraction and categorical thinking which may affect their performance on a task like semantic fluency. Since categorical thinking is less of a requirement for phonemic fluency, this explains the lack of an effect of ethnicity on that task.

Similarly, on the Raven's Coloured Progressive Matrices, effects of education and ethnicity were observed in which persons with fewer years of education and Caribbean ethnicity show worse performance. Again, as with the semantic fluency task, the CPM requires abstraction or generalization in order to

detect the pattern and this ability may be less developed in persons from developing countries and among lesser educated persons.

7.2 OTHER EXPLANATIONS OF PERFORMANCE

A comparison of performance across tasks may also highlight some of the issues involved in explaining differences due to ethnicity. Main effects for ethnicity were observed in both the serial sevens task of the MMSE and the digit span backwards task. Both these items can also be conceived of as invoking working memory, specifically numerical working memory. There was no effect of ethnicity on the digit forwards task or the logical memory tasks, findings which rule out a deficit in short-term memory in Caribbean persons. As such, the differences observed in the serial sevens as well as the digit span backwards task may point to cultural and ethnic differences in working memory or alternatively it may point to the use of different cognitive strategies or cognitive styles as a result of different instructional styles in schooling or informal cultural standards (e.g. Imbo and Lefevre, 2009).

Another factor that may account for ethnic differences in performance may relate to different temporal perspectives and its impact on task completion. If Caribbeans are regarded as having a less rushed temporal perspective than British persons, then it follows that they may adopt a cognitive style that favours accuracy over speed. In the two timed tasks of digit cancellation and Raven Coloured Progressive Matrices, Caribbean persons performed worse. Comparisons of completion times showed no difference for cancellation but a significantly longer completion time for the Raven matrices task. However, the instructions of the tasks may prove insightful; in the cancellation task, participants are explicitly told to work

as fast as they can. In the Raven matrices they are not told of any time constraints. As such, the time prompt in the cancellation task may have sped up Caribbean responders. In both tasks, correct responses are counted as only those which were completed within the stipulated time frame. Correct answers outside of this time frame are not scored. If Caribbeans do endorse a less rushed approach to tasks then timed tasks may ultimately prove disadvantageous. One recommendation would be to consider both the scores in the timed and untimed conditions of the task.

7.3 STANDARDISATION OF NEUROPSYCHOLOGICAL INSTRUMENTS

The standardisation of all instruments was undertaken and correction formulas were provided for each task. Corrections for education were suggested for most all measures of the neuropsychological battery: MMSE, ADAS-cog, digit span (forwards and backwards), cancellation, Logical Memory immediate and delayed recall, semantic fluency for animals and cities, phonemic fluency for letters P, L and F, and Raven's Coloured Progressive Matrices. The exception was semantic fluency for fruits. Corrections for age were suggested for scores on ADAS-cog, digit cancellation, Raven's Coloured Progressive Matrices and semantic fluency for animals. Corrections for gender for scores were suggested for one task- semantic fluency for fruits. Corrections for ethnicity were suggested for scores on the MMSE, digit span backwards, digit cancellation, semantic fluency for animals, cities and fruits and the Raven's Progressive Matrices.

The suggested cut-off scores are also based on adjustments for the effects of age, gender, education and ethnicity and provide meaningful limits for practitioners and researchers for gauging abnormal behaviour. The derived cut-off score of 23 or

less for the MMSE also coincides exactly with the widely used and traditional cut-off suggested by Folstein et al (1975). The revised cut-off recommended for the ADAS-cog of 10 is lower than the traditionally used value of 18, however, it does correspond to scores suggested in other recent studies (Wouters et al, 2009). For all instruments, cut-off scores based on corrections for age, gender, education and ethnicity were consistent with those reported in the literature.

7.4 VALIDATION STUDIES

Validation of the MMSE based on corrected cut-off resulted in a decrease in sensitivity but a considerable 35% increase in specificity. The severity of disease in the validation sample was unknown and this may have affected the sensitivity rates. However, the MMSE is regarded as a crude measure of impairment and the sensitivity scores may be a reflection of this. The increase in specificity however suggests that the correction provided makes the MMSE especially efficient at ruling out impairment in healthy persons. Given the financial and time constraints faced by many health care services worldwide, this high specificity is a valued attribute of the MMSE and a testimony for its future use in screening for dementia.

The derived cut-off score for the ADAS-cog resulted in very high rates for both sensitivity (89%) and specificity (89%). Use of the corrected scores made a slight improvement to sensitivity of raw scores and maintained high specificity rates. The cut-off scores and resulting rates obtained in this study are also consistent with rates found in other countries (Monllau et al, 2007; Wouters et al, 2009).

The low false positive rates of 5% and 11% obtained for the MMSE and ADAS-cog respectively are a testimony to the sound validity of the use of the derived cut-off scores with Caribbean populations.

7.5 CONCLUSION

This dissertation set out to provide normative data for a brief battery of neuropsychological instruments for use in dementia assessment in Caribbean population. It also took into consideration major demographic variables that can impact performance and provided correction formulas to adjust scores for the effects of these variables. The specification of cut-off scores and median scores can assist in the interpretation of individual performance. The provision of equivalent scores for each test also enables the comparison of performance across tests.

This body of work highlighted and addressed the necessity for standardisation of neuropsychological instruments for cross-cultural evaluation but has also identified a vital need for the periodic updating of norms which accurately reflects the abilities and functioning of target groups. This practice can increase the accuracy and validity of assessment and diagnostic procedures. Furthermore, the increasing availability of anti-dementia drug treatment makes early diagnosis critically important. Accurate diagnosis in the early stages of cognitive decline is often challenging as it is difficult to ascertain whether observed scores on neuropsychological measures falls within the range of normal performance. This is an especially cogent challenge in both poorly educated and highly educated groups. As such, provision of culturally relevant and contemporary norms such as these, can be regarded as invaluable tools in the assessment and diagnosis of dementia.

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